IARC 50 YEARS

C A N C E R

OCCURRENCE / CAUSES / PREVENTION

Global Cancer

Occurrence, Causes, and Avenues to Prevention

A conference to discuss today's challenges and help design tomorrow's agenda

ABSTRACTS

7–10 JUNE 2016
Lyon, France

International Agency for Research on Cancer
World Health Organization

www.iarc-conference2016.com

Programme at a glance

TUESDAY 7 JUNE 2016

16:00 – 20:00	Registration
18:00 – 19:30	Opening Reception

LEGEND

- All plenary sessions and panel debates will be held in **Amphithéâtre 3000, on level 0**
- Parallel sessions on "Epidemiology" will be held in **Amphithéâtre 3000, on level 0**
- Parallel sessions on "Mechanisms" will be held in the **Tête d'Or rooms, on level 1**
- Parallel sessions on "Prevention & Mortality Reduction" will be held in the **Gratte-Ciel rooms, on level 2**
- The poster area is **on level –2**
- Lunch and coffee breaks will be served **on level –2, including in the poster area**
- The conference dinner will be served **on level –2**

To find all the conference abstracts, go to the detailed programme page on the conference website:

www.iarc-conference2016.com/programme

To find your way through the Congress Centre, see the venue map at the back of the programme, on page 42.

WEDNESDAY 8 JUNE 2016

7:00 – 8:30	**Registration**
8:30 – 9:10	Opening Ceremony
9:10 – 9:40	**Christopher P. Wild** IARC: 50 years of cancer research for cancer prevention
9:40 – 10:00	**HRH Princess Dina Mired** Caring about cancer
10:00 – 10:30	**Douglas Lowy** The potential of cost-effective precision medicine in the low- and middle-income countries
10:30 – 11:00	Coffee break
11:00 – 11:30	**Freddie Bray** The global burden of cancer
11:30 – 12:15	**Panel Debate 1** **Cancer research investment should shift from late-stage treatment to early-stage detection** Pro: **Rengaswamy Sankaranarayanan** Anti: **Soo Khee Chee**
12:15 – 14:00	Lunch break and Poster session
14:00 – 14:30	**Michael Stratton** Signatures of mutational processes in human cancer
14:40 – 15:40	**Parallel Sessions (details on page 13)** **E** **M** **P**
15:40 – 16:00	Coffee break
16:00 – 17:00	**Parallel Sessions (details on page 14)** **E** **M** **P**
17:10 – 17:40	**Recipient of 2016 IARC Medal of Honour** **Elizabeth Blackburn** ***The American Association for Cancer Research Lecture*** Telomeres, biology and cancer
17:40 – 18:10	**David Hunter** Cancer, NCDs and global health

Programme at a glance

THURSDAY 9 JUNE 2016

8:00 – 9:00	**"50 for 50" parallel sessions** For "50 for 50" fellows only
9:00 – 9:30	**Stephen Chanock** Germline mutations
9:30 – 10:00	**Valerie Beral** The impact of tobacco, alcohol and hormones on women's cancers
10:00 – 10:30	**Recipient of 2016 IARC Medal of Honour** **Lynette Denny** Screening and early detection of cervical cancer in Africa
10:30 – 11:00	Coffee break
11:00 – 12:00	**Parallel Sessions (details on page 21)** **E** **M** **P**
12:10 – 12:55	**Panel Debate 2** **E-cigarettes represent a barrier to effective tobacco control** Pro: **Armando Peruga** Anti: **Jean-François Etter**
12:55 – 14:30	Lunch break and Poster session
14:30 – 15:30	**Parallel Sessions (details on page 22)** **E** **M** **P**
15:30 – 16:00	Coffee break
16:00 – 17:00	**Parallel Sessions (details on page 23)** **E** **M** **P**
17:10 – 17:40	**Michael Marmot** Reducing inequalities in risk
17:40 – 18:10	**Graham Colditz** Implementing strategies to prevent cancer
18:30 – 19:00	**Jazz Concert** (in Amphithéâtre 3000)
19:30	**Conference Dinner**

FRIDAY 10 JUNE 2016

8:00 – 9:00	**"50 for 50" parallel sessions** For "50 for 50" fellows only
9:00 – 9:30	**Walter Willett** ***The American Institute for Cancer Research and World Cancer Research Fund International Lecture*** Diet, weight control and energy balance in cancer
9:30 – 10:00	**George Davey Smith** Causality and chance in the origins of cancer
10:00 – 10:30	**Flora van Leeuwen** Risk factors for second cancers
10:30 – 11:00	Coffee break
11:00 – 12:00	**Parallel Sessions (details on page 29)** **E** **M** **P**
12:10 – 12:55	**Panel Debate 3** **Screening for lung cancer should be implemented now** Pro: **John Field** Anti: **Harry J. de Koning**
12:55 – 14:00	Lunch break and Poster session
14:00 – 15:00	**PROFFERED PAPERS PLENARY SESSION** 1. **Ling Yang (China)** 2. **Ausrele Kesminiene (IARC)** 3. **Loic Le Marchand (USA)** 4. **Stephen Hecht (USA)** 5. **Rafaela Naves (Brazil)** 6. **Willie Yu (Singapore)**
15:00 – 15:30	**Elio Riboli** Consortia, big data and the future of population research
15:30 – 16:00	**Richard Peto** Successes in understanding the causes of cancer
16:00 – 16:30	**Closing of Conference**

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PLENARY SESSIONS

WEDNESDAY 8 JUNE

IARC: 50 YEARS OF CANCER RESEARCH FOR CANCER PREVENTION

Wednesday 8 June - 09:10-09:40

Christopher P. Wild
Director, International Agency for Research on Cancer, Lyon, France

Christopher Paul Wild obtained his PhD in 1984 from the University of Manchester, United Kingdom, while working on DNA damage and repair. He was awarded a postdoctoral fellowship from the International Agency for Research on Cancer (IARC) to work in Lyon, France, and subsequently a United Kingdom Royal Society European Exchange Fellowship to spend a year at the Netherlands Cancer Institute in Amsterdam. In 1987, Dr Wild re-joined IARC as a staff scientist and later became Chief of the Unit of Environmental Carcinogenesis. In 1996, he was appointed to the Chair of Molecular Epidemiology at the University of Leeds, was Head of the Centre for Epidemiology and Biostatistics and later became Director of the Leeds Institute of Genetics, Health and Therapeutics in December 2005. Dr Wild was elected Director of IARC from 1January 2009. His main research interest is to understand the interplay between environmental and genetic risk factors in the causation of human cancer. He has particularly sought to apply biomarkers in population-based studies to this end. His specific areas of research have been focused on liver and oesophageal cancers.

ABSTRACT:
IARC was established in 1965 as an autonomous research agency within the framework of the World Health Organization (WHO)[1]. Its primary purpose was “to promote international collaboration in cancer research”. Through the collaboration of many thousands of colleagues worldwide this vision has become a reality. From the outset, IARC scientists sought to understand the causes of cancer through the study of international variations in incidence. This interest resulted in a long-standing commitment to improve the quality and coverage of cancer registries in order to provide a vital foundation for cancer control planning. Geographic variations in cancer incidence implicitly pointed to opportunities for prevention, by avoiding or reducing exposure to identified carcinogens. IARC took a pioneering approach, bringing laboratory, epidemiology and biostatistics to bear on the questions addressed. In 2015, cancer remains a global health problem. As a result of population growth, increasing life expectancies and changes in underlying incidence, the annual number of cancer cases continues to rise, being expected to increase by around 60% worldwide in the next 20 years. However, by far the largest relative increases are set to occur in developing countries. Therefore, the conduct of “cancer research for cancer prevention”, by necessity, remains at the heart of IARC’s strategy. Fifty years is a long time in cancer research. In 1965 the genetic alterations underlying pathways to cancer were unknown; today our knowledge is transformed. In stark contrast, many of the global disparities in cancer incidence and outcomes, evident in the mid-1960s, are still all too easily recognisable today. As the number of cancer patients and the costs of care spiral, cancer prevention must be prioritized. International studies are increasingly needed to answer national questions. Consequently, looking forward, the Agency finds its mission ever more pertinent, conscious not only of the opportunities but also the responsibilities: much has been done, much remains to be done.

(1) Saracci R, Wild CP. The First Fifty Years, 1965-2015. Lyon: International Agency for Research on Cancer, 2015. http://www.iarc.fr/en/publications/books/iarc50/index.php.

CARING ABOUT CANCER

Wednesday 8 June - 09:40-10:00

HRH Princess Dina Mired

Director General, King Hussein Cancer Foundation and Honorary Chairperson of the Jordan Breast Cancer Program, Amman, Jordan

HRH Princess Dina Mired has led the King Hussein Cancer Foundation (KHCF) in Jordan as Director General since 2002. In that capacity, she founded, developed and institutionalized the fundraising and development function and programs at the Foundation, which is now the largest source of non-profit funds dedicated to fighting cancer in Jordan. Under her direct leadership, KHCF has succeeded in enlisting all segments of society in the fight against cancer with the sole purpose of supporting cancer patients in Jordan and the Arab world. HRH Princess Dina Mired is also the Honorary Chairperson of the Jordan Breast Cancer Program (JBCP). As a global advocate, HRH Princess Dina Mired delivered the keynote speech on behalf of all civil society (social, civic and voluntary organizations) at the September 2011 opening of the United Nations General Assembly High-Level Meeting on Non-Communicable Diseases (NCDs); HRH Princess Dina Mired is also an Honorary Co-President of the Harvard University Global Task Force for Expanded Access to Cancer Care and Control in the Developing World. She is also a member of the Presidential Advisory Panel of the Union for International Cancer Control (UICC).

THE POTENTIAL OF COST-EFFECTIVE PRECISION MEDICINE IN THE LOW- AND MIDDLE-INCOME COUNTRIES

Wednesday 8 June - 10:00-10:30

Douglas Lowy

Acting Director of the United States National Cancer Institute (NCI) and Chief of the intramural Laboratory of Cellular Oncology in the Center for Cancer Research at the NCI, Bethesda, USA

Douglas Lowy received his medical degree from the New York University School of Medicine, and trained in internal medicine at Stanford University and dermatology at Yale University. His research includes papillomaviruses and the regulation of normal and neoplastic growth. The papillomavirus research is carried out in close collaboration with John Schiller, with whom he has co-authored more than 100 papers over the past 25 years. In the 1980s, he studied the genetic organization of papillomaviruses and identified the oncogenes encoded by the virus. More recently, he has worked on papillomavirus vaccines and the papillomavirus life cycle. Their laboratory was involved in the initial development, characterization, and clinical testing of the preventive virus-like particle-based HPV vaccines that have been approved by the United States Food and Drug Administration and many other countries. It is for this body of work that Drs Lowy and Schiller received the 2007 Federal Employee of the Year Award from the Partnership for Public Service, the 2007 Dorothy P. Landon-American Association for Cancer Research Prize for Translational Cancer Research, the Sabin Gold Medal in 2011, and the National Medal of Technology and Innovation from President Obama in 2014. Dr Lowy also received the 2007 Medal of Honor for basic research from the American Cancer Society. He is listed by the Institute for Scientific Information as one of the most highly cited authors in microbiology, and is a member of the National Academy of Sciences (NAS) and the Institute of Medicine of the NAS.

ABSTRACT:

Although precision medicine in oncology (precision oncology) is often discussed as though it is primarily concerned with new targeted cancer treatment, which is usually expensive, precision oncology approaches are equally applicable to disease prevention and screening, and may be relevant in low- and middle-income countries (LMICs). Precision oncology includes interventions to prevent, diagnose, or treat cancer, based on a molecular or mechanistic understanding of the causes, pathogenesis, or pathology of the disease. Where the individual characteristics of the patient are sufficiently distinct, interventions can be concentrated on those who will benefit, sparing expense and side effects for those who will not.

Two examples of precision medicine relevant to LMICs are HPV-based testing for cervical cancer screening and HPV vaccination for cancer prevention. Both approaches are derived from identification of HPV as the

main etiologic agent for virtually all cases of cervical cancer. Compared with cytology, the greater sensitivity and negative predictability of HPV-based screening enables screening intervals to be longer than with cytology. Furthermore, less training is required for high quality HPV testing than for high quality cytological testing. In principle, HPV vaccination can prevent the vast majority of cervical cancers attributable to the HPV types targeted by the vaccine. The first generation HPV vaccines target HPV16/18, which together account for about 70% of cervical cancer. The second generation HPV vaccine targets more HPV types, which together account for close to 90% of cervical cancer. Tiered pricing by the commercial producers of the vaccines has made them more affordable in LMICs. The number of doses required for young adolescents has recently been reduced from three to two, and some post-hoc research raises the possibility that new clinical trials may develop evidence that even a single HPV vaccine dose could be sufficient for inducing long-term protection.

THE GLOBAL BURDEN OF CANCER

Wednesday 8 June - 11:00-11:30

Freddie Bray
Head, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France

Freddie Bray has a PhD in Epidemiology from the London School of Hygiene and Tropical Medicine, and degrees in Statistics from the University of Aberdeen and Medical Statistics from the University of Leicester, United Kingdom. He has worked previously at IARC from 1998 to 2005 and at the Cancer Registry of Norway and the University of Oslo from 2005 to 2010. His areas of research revolve around the descriptive epidemiology of cancer, including the estimation of the global cancer burden and the analysis of time trends, including global predictions of the future scale and profile of cancer linked to human development transitions. He has close to 200 book chapters and articles in journals including The Lancet, The Lancet Oncology, JNCI and Nature Reviews Cancer. In support of the overwhelming need for high-quality cancer surveillance systems given their current paucity and an ever-increasing cancer problem, Dr Bray leads the Global Initiative for Cancer Registry Development (http://gicr.iarc.fr), an international multi-partner programme designed to ensure a sustainable expansion of the coverage and quality of population-based cancer registries in low- and middle-income countries through tailored, localized support and advocacy to individual countries.

ABSTRACT:
The global cancer burden is increasing and disparities are widening. A potential doubling of the number of new cancer cases is predicted by 2035, with a proportionally greater burden falling on countries undergoing major social and economic change, often ill-equipped at present to respond adequately to the emerging cancer problem.
The presentation will highlight the increasing prominence of cancer in the context of communicable and non-communicable diseases worldwide, and how the changing scale and profile of cancer is linked to levels of human development. That cancer is now the leading cause of death in 50 countries can be seen as part of longstanding and continuing epidemiologic and mortality transitions.
In the wake of the rising cancer burden, the need for long-term investments in prevention and early detection will be stressed, as will IARC's efforts to globally coordinate a step-change in the coverage and quality of incidence data to enable the planning, monitoring and evaluation of cancer control interventions. The presentation will close by arguing that, in line with the cancer continuum, a broad set of data sources and cancer surveillance statistics are required nationally and regionally in order to measure the impact of actions across the cancer control spectrum.

PANEL DEBATE 1 - CANCER RESEARCH INVESTMENT SHOULD SHIFT FROM LATE-STAGE TREATMENT TO EARLY-STAGE DETECTION

Pro: Rengaswamy Sankaranarayanan, IARC, Lyon, France

Rengaswamy Sankaranarayanan
Special Advisor on Cancer Control and Head of the Screening Group, International Agency for Research on Cancer, Lyon, France

Rengaswamy Sankaranarayanan has an MD degree in radiation oncology, followed by postdoctoral training at the University of Pittsburgh and the University of Cambridge. After several years of experience in clinical oncology and cancer control in India, Dr Sankaranarayanan joined the International Agency for Research on Cancer in 1993. Through the IARC Screening Group, and through innovative partnerships with other international organizations, national institutions and investigators, Dr Sankaranarayanan is involved in conducting several studies worldwide with the aim of providing scientific evidence to support the development of appropriate public health policies of screening for common cancers in a range of health care settings, particularly in lowand middle-income countries. These studies provide valuable data on the accuracy, reproducibility, efficacy, benefits, harmful effects and cost-effectiveness of different screening interventions for cervical, oral, colorectal and breast cancers, leading to the rational utilization of health care resources in the design, implementation, monitoring and evaluation of screening programmes. Dr Sankaranarayanan has a strong commitment to research, training, programme development and technical assistance in the early detection and control of cancer, particularly breast, cervical, colorectal and oral cancers in low- and middle-income countries. He has taught as a faculty member in over 40 international courses on cervical cancer screening, colposcopy, diagnosis and treatment of cervical neoplasia, cancer registry epidemiology and cancer control. He is also an author on more than 240 papers in international peer-reviewed journals, and his manuals on early detection of cervical cancer have been translated into several languages.

Anti: Soo Khee Chee, National Cancer Centre Singapore

Soo Khee Chee
Director, National Cancer Centre Singapore, Senior Vice Dean (Clinical, Academic and Faculty Affairs), Duke-NUS Graduate Medical School and Deputy Group CEO (Research and Education), Singapore Health Services, Singapore

Dr Soo Khee Chee is a surgical oncologist. He is still in active practice. He is the founding Director of the National Cancer Centre Singapore. This centre treats about half of all cancer patients in the country. Additional administrative responsibilities include being the Senior Vice Dean of Clinical, Academic and Faculty Affairs of the Duke-NUS Graduate Medical School, and Deputy Group Chief Executive Officer of Research and Education for the largest health cluster in Singapore: the Singapore Health Services.

SIGNATURES OF MUTATIONAL PROCESSES IN HUMAN CANCER

Wednesday 8 June - 14:00-14:30

Michael Stratton
Director, Wellcome Trust Sanger Institute, Cambridge, United Kingdom

Michael Stratton's primary research interests have been in the genetics of cancer. His early research focused on inherited susceptibility. He mapped and identified the major high-risk breast cancer susceptibility gene BRCA2 and subsequently a series of moderate-risk breast cancer and other cancer susceptibility genes. In 2000 he initiated the Cancer Genome Project at the Wellcome Trust Sanger Institute, which conducts systematic genome-wide searches for somatic mutations in human cancer. Through these studies he discovered somatic mutations of the BRAF gene in malignant melanoma and several other mutated cancer genes in lung, renal, breast and other cancers. He has described the basic patterns of somatic mutation in cancer genomes, revealing underlying DNA mutational and repair processes. He is a Fellow of the Royal Society (FRS) and was knighted by the Queen in 2013.

ABSTRACT:
All cancers are caused by somatic mutations. However, the processes underlying the genesis of somatic mutations in human cancer are remarkably poorly understood. Recent large-scale cancer genome sequencing initiatives have provided us with new insights into these mutational processes through the mutational signatures they leave on the cancer genome. In this talk I will review the mutational signatures found across cancer and consider the underlying mutational processes that have been operative.

TELOMERES, BIOLOGY AND CANCER

Wednesday 8 June - 17:10-17:40

Elizabeth Blackburn, Recipient of 2016 IARC Medal of Honour
President of the Salk Institute for Biological Studies, La Jolla, USA

Elizabeth Blackburn became President of the Salk Institute for Biological Studies on 1 January 2016. Dr Blackburn is a pioneering molecular biologist. Since 2001 she had served as a Salk Non-Resident Fellow while she was a Professor in the Department of Biochemistry and Biophysics at the University of California, San Francisco. Dr Blackburn won the Nobel Prize in Physiology or Medicine in 2009 for discovering the molecular nature of telomeres, the ends of chromosomes that serve as protective caps essential for preserving genetic information, and for co-discovering telomerase, an enzyme that maintains telomere ends. Both telomeres and telomerase are thought to play central roles in ageing and diseases such as cancer, and her work helped launch entire new fields of research. In addition to the Nobel Prize, Dr Blackburn has received nearly every major award in science, including the Lasker, Gruber, and Gairdner prizes. In 2007, she was named one of Time magazine's 100 most influential people in the world. She is a member of numerous prestigious scientific societies, including the National Academy of Sciences, the National Academy of Medicine, and the Royal Society of London. She has served as president of both the American Association for Cancer Research and the American Society for Cell Biology, and has served on the editorial boards of several journals, including Cell and Science. Helping to guide public science policy, she was a member of the Stem Cell Research Advisory Panel for the California State Legislature and a member of the President's Council of Bioethics, an advisory committee to the President of the USA.

ABSTRACT: Perspectives on Telomeres and Telomerase in Human Aging and Cancers
Telomeres protect eukaryotic chromosome ends, and their compromise can lead to maladaptive cellular changes and block tissue replenishment. As humans age, average telomere length declines. Independently of age and other known mortality risk factors, observed telomere shortness predicts all-cause human mortality rates. Non-genetic factors associated with telomere shortness include social, environmental and lifestyle factors, such as smoking or exercise.
The cellular ribonucleoprotein enzyme telomerase, by adding telomeric DNA repeat sequences to the ends of chromosomes, can compensate for their attrition. Stem cells and a majority of malignant human cancer cells have high telomerase activity that prolongs cell division capacity. Insufficient telomerase leads to progressive telomere shortening during cell divisions and eventual cellular senescence. How telomere

maintenance perturbations – upward or downward – interact with cancer etiology and progression varies among different cancer types. Genetic deficiencies in telomerase (caused by monogenetic mutations) hasten telomere shortening and cause a spectrum of diseases, including certain cancers: hematological (leukemias and myelodysplastic syndrome), squamous-cell skin and gastrointestinal cancers. These inherited telomere syndromes also include loss of immune function through loss of bone marrow stem cell reserves. This potentially impacts on the immune surveillance mechanisms that can control cancers. However, for certain subsets of cancers, subtly over-active telomere maintenance is cancer-promoting. For instance, common germline allelic variants in known telomere maintenance genes, associated with longer leukocyte telomere length, raise risks of melanomas, non-smokers' lung cancer and many gliomas. This mode of increased telomere maintenance may prolong the survival of cancer-prone or pre-cancerous cells, increasing the probability that the multiple steps toward tumorigenesis can occur.
Telomere length maintenance is highly interactive and telomere shortness shows much greater predictive power when combined with other factors than when considered alone. How genetic and non-genetic determinants of telomere length maintenance interact - with each other and other cancer etiologies - requires future research.

CANCER, NCD'S AND GLOBAL HEALTH

Wednesday 8 June - 17:40-18:10

David Hunter
Acting Dean, Vincent L. Gregory Professor of Cancer Prevention, Harvard T.H. Chan School of Public Health, Boston, USA

David Hunter's principal research interests are the etiology of cancer, particularly breast, prostate, pancreas and skin cancers. He analyzes inherited susceptibility to cancer and other chronic diseases using molecular techniques and gene-environment interactions. This work is largely based in subcohorts of the Nurses' Health Study and the Health Professionals Follow-up Study. Dr Hunter supervised laboratories at the Harvard School of Public Health in which gene sequence information from these samples is obtained. Dr Hunter has also studied HIV transmission for over 20 years, initially in Kenya and then in Tanzania. He has collaborated with investigators in Dar es Salaam to understand the relationship of nutritional status to progression of HIV disease and perinatal transmission. Professor Hunter was the Director of the Harvard Center for Cancer Prevention from 1997 to 2003. In June 2009, he was appointed Dean for Academic Affairs at the School. He is also the Vincent L. Gregory Professor of Cancer Prevention. He is the founding Director of HSPH's Program in Molecular and Genetic Epidemiology and is Principal Investigator of a number of ongoing breast and prostate cancer studies. He co-chaired the Steering Committee of the National Cancer Institute (NCI) Breast and Prostate Cancer Cohort Consortium, was co-Director of the NCI Cancer Genetic Markers of Susceptibility (CGEMS) Special Initiative, and was a member of the Board of Scientific Counselors of the NCI. He is Contact Principal Investigator of the DRIVE (Discovery, Biology and Risk of Inherited Variants in Breast Cancer) Consortium.

ABSTRACT:
Cancer deaths in the world will increase by about 50% in the next 15 years, driven by ageing and expanding populations, as well as increases in the prevalence of some risk factors. The global shift towards death from other NCD's is fueled by many of the same factors. Primary prevention is critical to reducing cancer incidence, however, the global community has not effectively tackled key drivers such as tobacco consumption and obesity. Immunization against cancer-causing infections is incomplete, and absent entirely in some countries. We still have little understanding of the causes of some cancers e.g. prostate cancer and leukemias, and thus cannot propose interventions to reduce incidence, putting an upper bound on the proportion of cancer that can be prevented. While much of the focus of the cancer research establishment is on developing molecularly targeted therapies to extend life, most people with cancer in the world have little access to the cancer diagnostic capacity and the surgery, radiation therapy and proven medications that have partially contributed to declines in cancer mortality in developed countries. A renewed focus on primary prevention and greater access to diagnosis and treatment is needed to limit the global surge in cancer mortality. Reductions in risk factors such as smoking and weight gain will have benefits for other NCD's such as cardiovascular disease, stroke and diabetes suggesting common approaches to prevention of a substantial fraction of NCD's. Greater access to diagnosis and treatment of cancer however, require more specialized cancer-specific services. Primary prevention of cancers needs an even higher profile in planning for control of NCD's.

PLENARY SESSIONS

THURSDAY 9 JUNE

GERMLINE MUTATIONS

Thursday 9 June - 09:00-09:30

Stephen Chanock
Director of the Division of Cancer Epidemiology and Genetics, United States National Cancer Institute, Bethesda, USA

Dr Stephen Chanock is a leading expert in the discovery and characterization of cancer susceptibility regions in the human genome. He has received numerous awards for his scientific contributions to our understanding of common inherited genetic variants associated with cancer risk and outcomes. Dr Chanock received his MD from Harvard Medical School in 1983 and completed clinical training in pediatrics, pediatric infectious diseases, and pediatric hematology/oncology and research training in molecular genetics at Boston Children's Hospital and the Dana-Farber Cancer Institute, Boston. Since 1995, Dr Chanock has served as the Medical Director for Camp Fantastic, a week-long recreational camp for pediatric cancer patients, which is a joint venture of the NCI and Special Love, Inc. From 2001 to 2007, he was a tenured investigator in the Genomic Variation Section of the Pediatric Oncology Branch in the NCI Center for Cancer Research. He also served as Co-Chair of NCI's Genetics, Genomics and Proteomics Faculty for five years. In 2001, he was appointed as Chief of the Cancer Genomics Research Laboratory (formerly Core Genotyping Facility), and in 2007 as Chief of the Laboratory of Translational Genomics, both within the NCI Division of Cancer Epidemiology and Genetics (DCEG). Dr Chanock co-led the Cancer Genetic Markers of Susceptibility project. From 2012 to 2013, he also served as Acting Co-Director of the NCI Center for Cancer Genomics. Dr Chanock was appointed Director of DCEG in August 2013.

ABSTRACT: Genetic Susceptibility to Cancer
For decades, the study of genetic susceptibility to cancer was conducted in families with multiple affected individuals and to date there are more than 115 known 'cancer predisposition genes', all rare in frequency. The emerging catalog of common variants by genome-wide association studies (GWAS) represents a distinct component of the underlying genetic architecture of cancer susceptibility, identifying regions that are specific to known cancer types; so far more than 500 independent regions have been identified and roughly 10% of the regions display pleiotropy across cancer types. Each susceptibility region harbors one or more alleles that alters regulation of redundant genes and pathways; interestingly, few result in protein coding changes and none appear to be 'drivers' of somatic alterations. Many are investigating the molecular basis of cancer susceptibility, specifically exploring how germline variants predispose individuals to specific cancers. We are also poised to investigate gene-environment interactions and further understand how the germline informs the landscape of somatic alterations. Sets of common variants identified in GWAS can be examined as a polygenic risk score and used to stratify populations in an effort to deliver precision prevention; the latter is based on profiles of genetic risk scores, along with other established risk factors and can be applied to public health measures. The study of germline variants has also revealed that with age, germline DNA can undergo somatic alterations as manifest as detectable genetic mosaicism across the spectrum from large structural alterations to point mutations. The patterns of these events underscore the complex nature of maintaining the stability of genomes, and with age, it appears that the genome begins to be at increased risk for events, some of which could be related to risk for cancer and other complex diseases.

THE IMPACT OF TOBACCO, ALCOHOL AND HORMONES ON WOMEN'S CANCERS

Thursday 9 June - 09:30-10:00

Valerie BERAL
Director, Cancer Epidemiology Unit, University of Oxford, United Kingdom

Born in Australia, Dame Valerie studied medicine at Sydney University, graduating in 1969. As the top graduate that year she was awarded the University Gold Medal, the first woman ever to receive this award in medicine. She worked for one of the first clinical epidemiologists in the United Kingdom, Charles Fletcher, who propelled her towards the London School of Hygiene and Tropical Medicine, where she worked for almost 20 years. In 1988 she became Director of the University of Oxford Cancer Epidemiology Unit, previously directed by Sir Richard Doll. Her major research interests include the role of reproductive, hormonal and infectious agents in cancer and other conditions. She is Principal Investigator of the Million Women Study, investigating the effects of a range of women's lifestyle factors on health, with focus initially on the effects of hormone replacement therapy. Since 1991, she has led international collaborative studies of breast, ovarian and endometrial cancers. She has served on many international committees, including the World Health Organization, the United States National Academy of Sciences, and various Australian cancer councils. Until recently, she chaired the United Kingdom Department of Health's Advisory Committee on Breast Cancer Screening and is currently a member of the Board of the Medicines and Healthcare Products Regulatory Agency. In 2006 she was elected Fellow of the Royal Society (FRS) for scientific contributions to epidemiology. Other honours include being invested as Dame of the British Empire (DBE) and Companion of Australia.

SCREENING AND EARLY DETECTION OF CERVICAL CANCER IN AFRICA

Thursday 9 June - 10:00-10:30

Lynette Denny, Recipient of 2016 IARC Medal of Honour
Chair and Professor of Obstetrics & Gynaecology and registered sub-specialist in Gynaecological Oncology at Groote Schuur Hospital and University of Cape Town, South Africa

Lynette Denny is the Chair and Professor of Obstetrics & Gynaecology and registered sub-specialist in Gynaecological Oncology at Groote Schuur Hospital and the University of Cape Town. Her research interest for the past 15 years has been in preventing cervical cancer in low-resource settings, and she has published over 100 peer-reviewed papers on the subject. She has been a keynote speaker at numerous international conferences. She was awarded the Distinguished Scientist for Improving the Quality of Life of Women by the South African Department of Science and Technology in 2006 and is a B2 rated scientist by the National Research Foundation of South Africa. She was the first recipient of the Shoprite Checkers SABC 2 Women of the Year award for Science and Technology in 2004. She was awarded the South African Medical Association award for Extraordinary Service to Medicine (2012) and given a fellowship ad eundem to the Royal College of Obstetrics and Gynaecology, United Kingdom (2012). Professor Denny was presented with the BSCCP Founders' Medal at the 15th World Congress for Cervical Pathology and Colposcopy in London, United Kingdom in May 2014. This award is in recognition of the outstanding contribution she has made to women's health and the prevention of cervical cancer in Africa. In October 2015 Professor Denny was presented with the International Federation of Gynecology and Obstetrics (FIGO) Award in Vancouver, Canada. This award is in recognition of women obstetricians and gynaecologists.

ABSTRACT:
Sub-Saharan Africa (SSA) consists of 54 countries almost all of which have the lowest ranked Human Development Index (HDI) and highest Human Poverty Indices (HPI). With a total population estimated in 2008 of 812 million (404 million men and 408 million women), only 7.2% were covered by medically certified causes of death and 8.3% by population based registries. The African continent has 130 medical schools located in 41 countries, but facilities for training in cancer diagnosis and management are found mainly in North Africa and South Africa with limited facilities elsewhere. Adding to the complexity of the challenges facing SSA (ranging from environmental disasters, to competing health needs, endemic civil strife, war, lack of safe water and sanitation to name a few) has been the HIV/AIDS epidemic, where 70% of the world's cases of HIV are diagnosed. It is well known that HIV infection increases the risk of developing certain

cancers and Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer have been classified as AIDS defining diseases since 1993.
Women infected with HIV have an increased risk of being infected with HPV and are therefore considered at higher risk for cervical cancer. However, the expected increase in women diagnosed with cervical cancer in Africa during the HIV pandemic was not convincingly observed, most likely due to most at-risk women dying from other opportunistic infections prior to developing cervical cancer or its precursors. In the era of anti-retroviral medication, this scenario is expected to change.
One of the initial problems encountered in initiating screening programs in LMICs is the detection of a relatively large number of incident cancers. This poses an ethical and logistical dilemma as access to treatment in many developing countries is extremely limited. Most patients cannot afford to pay the costs of cancer therapy, even where it exists.

PANEL DEBATE 2: E-CIGARETTES REPRESENT A BARRIER TO EFFECTIVE TOBACCO CONTROL

Pro: Armando Peruga, World Health Organization, Geneva, Switzerland

Armando Peruga
Programme manager of Tobacco Free Initiative, World Health Organization, Geneva, Switzerland

Dr Peruga began to work with the Pan American Health Organization in 1990. He was the leader of the tobacco control team of this organization until the beginning of 2006, when he moved to Geneva as the Coordinator for the capacity building unit of the Tobacco Free Initiative of the World Health Organization. In Spain, he was the Director of the Research Institute on Health and Welfare in Madrid. He later became the Dean of the National School of Public Health. When he went to the USA in the early 1980s, he worked for the DC Commission of Public Health as a behavioral change epidemiologist. Dr Peruga graduated in Medicine in Spain. He later graduated from Master's and Doctoral programs of the Johns Hopkins Bloomberg School of Public Health.

A**nti: Jean-François Etter, University of Geneva, Switzerland**

Jean-François Etter
Professor, Faculty of Medicine, University of Geneva, Switzerland

Jean-François Etter has been conducting research on smoking etiology, prevention and cessation for over 20 years. He has published widely on smoking cessation trials and various psychological questions related to tobacco dependence and smoking cessation. He is an internationally known expert on e-cigarettes. He has published a comprehensive book on e-cigarettes and is credited with publishing some of the first scientific papers on the reasons and patterns of e-cigarette use. Professor Etter's basic training was in political science and public health. He is a Professor in the Faculty of Medicine of the University of Geneva, Switzerland.

REDUCING INEQUALITIES IN RISK

Thursday 9 June - 17:10-17:40

Michael Marmot
Director, University College London Institute of Health Equity (Marmot Institute), United Kingdom

Sir Michael Marmot has led research groups on health inequalities for more than 35 years. He chaired the Commission on Social Determinants of Health, set up by WHO in 2005, and produced the report Closing the Gap in a Generation in 2008. He conducted a Strategic Review of Health Inequalities in England Post-2010, which published the report Fair Society, Healthy Lives in 2010. He chaired the European Review of Social Determinants of Health and the Health Divide, for the WHO European Regional Office, and the Breast Screening Review for the NHS National Cancer Action Team, and was a member of The Lancet-University of Oslo Commission on Global Governance for Health. He is a Principal Investigator of the Whitehall II studies of health inequalities among British civil servants, and leads the English Longitudinal Study of Ageing. He is a former President of the British Medical Association and the current President of the British Lung Foundation. He was a member of the Royal Commission on Environmental Pollution for six years, and in 2000 was knighted by the Queen, for services to epidemiology and the understanding of health inequalities. He won the Balzan Prize for Epidemiology in 2004, gave the Harveian Oration in 2006, and won the William B. Graham Prize for Health Services Research in 2008. He was awarded a Harvard Lown Professorship for 2014–2017. He is President of the World Medical Association since 2015. He has been awarded honorary doctorates from 14 universities.

ABSTRACT: The health gap: the challenge of an unequal world
Taking action to reduce health inequalities is a matter of social justice. In developing strategies for tackling health inequalities we need to confront the social gradient in health not just the difference between the worst off and everybody else. There is clear evidence when we look across countries that national policies make a difference and that much can be done in cities, towns and local areas. But policies and interventions must not be confined to the health care system; they need to address the conditions in which people are born, grow, live, work and age. The evidence shows that economic circumstances are important but are not the only drivers of health inequalities. Tackling the health gap will take action, based on sound evidence, across the whole of society.

IMPLEMENTING STRATEGIES TO PREVENT CANCER

Thursday 9 June - 17:40-18:10

Graham Colditz
Deputy Director, Institute for Public Health; Chief, Division of Public Health Sciences; Niess-Gain Professor of Surgery, School of Medicine; and Associate Director, Prevention & Control, Siteman Cancer Center, Washington University in St. Louis, USA

Dr Colditz is an internationally recognized leader in cancer prevention. As an epidemiologist and public health expert, he has a longstanding interest in the preventable causes of chronic disease, particularly among women. He focuses his research on early life and adolescent lifestyle, growth, and breast cancer risk. He is also interested in strategies to speed translation of research findings into prevention strategies that work. Dr Colditz developed the award-winning Your Disease Risk website (www.yourdiseaserisk.wustl.edu), which communicates tailored prevention messages to the public. He has published over 975 peer-reviewed publications, six books and six reports for the Institute of Medicine, National Academy of Sciences. In October 2006, on the basis of professional achievement and commitment to public health, Dr Colditz was elected to membership of the Institute of Medicine, an independent body that advises the United States government on issues affecting public health. In 2011, he was awarded the American Cancer Society Medal of Honor for cancer control research. In 2012 he received the AACR-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention. He also received awards in 2014 for cancer prevention research from ASCO and from AACR.

ABSTRACT:
Over 12 Million new cases of cancer were diagnosed world wide in 2012. Refining strategies to implement and sustain cancer prevention interventions that are established as effective to reduce cancer incidence offers the best and fastest return on our past investment in cancer research 1. Accelerating the implementation of what we know can maximize our return on our past research investment and maximize global health benefits.

What we currently know:
- There are effective cancer prevention strategies, including[1]:
    - Colorectal cancer screening – 50% reduction colorectal cancer
    - HPV and HepB vaccines – 70 to 100% reduction (cervix and liver cancer)
    - SERMs – 40 to 50% reduction in breast cancer
    - Aspirin – 40% reduction in colon cancer
    - Smoking cessation – 75 % in lung cancer
- Across prevention targets, there are many persistent disparities among and within countries across race/ethnic and income groups [2,3]
- Health care system's general approach to cancer screening can be improved. In the USA, only about 43% of adults are current on all cancer screenings needed[4]. For colorectal cancer alone it is estimated that over 24 million adults need to be screened in the next 3 years to reach the target; 80% population coverage by 2018 [5].

A key opportunity is to determine how to increase uptake of known cancer prevention strategies across all populations and design new interventions with implementation and dissemination in mind.

Some key implementation science questions include:
1. How to speed the uptake of effective cancer prevention strategies in community settings so they can reach populations that will benefit the most?
2. Does implementation of known effective prevention and screening strategies as a cohesive integrated set of cancer prevention services increase their uptake, and what would the impact be on cancer outcomes?
3. What components or organizational features of the provider setting support integrated cancer prevention service delivery?
4. How do different population groups perceive cancer precision medicine (and screening?) approaches, and what are the barriers to their uptake?
5. How do we communicate complex prevention concepts to different groups?

Answering these questions through rigorous implementation science across community, provider, and organizational strategies offers opportunities for widespread impact. It should also reduce or eliminate cancer disparities.

Literature cited:
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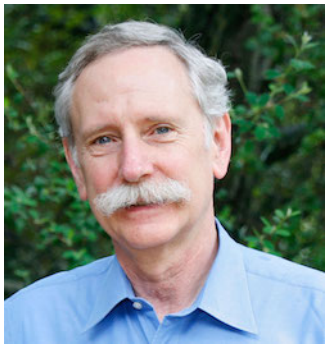
2. Steele CB, Rim SH, Joseph DA, et al. Colorectal cancer incidence and screening - United States, 2008 and 2010. MMWR Surveill Summ. 2013;62 Suppl 3:53-60.
3. Meyer PA, Yoon PW, Kaufmann RB, Centers for Disease C, Prevention. Introduction: CDC Health Disparities and Inequalities Report - United States, 2013. MMWR Surveill Summ. 2013;62 Suppl 3:3-5.
4. Emmons KM, Cleghorn D, Tellez T, et al. Prevalence and implications of multiple cancer screening needs among Hispanic community health center patients. Cancer Causes Control. 2011;22(9):1343-1349.
5. Fedewa SA, Ma J, Sauer AG, et al. How many individuals will need to be screened to increase colorectal cancer screening prevalence to 80% by 2018? Cancer. 2015;121(23):4258-4265.

PLENARY SESSIONS

FRIDAY 10 JUNE

DIET, WEIGHT CONTROL AND ENERGY BALANCE IN CANCER

Friday 10 June - 09:00-09:30



Walter Willett
Professor of Epidemiology and Nutrition and Chairman of the Department of Nutrition at the Harvard T.H. Chan School of Public Health and Professor of Medicine at Harvard Medical School, Boston, USA

Dr Walter Willett is Professor of Epidemiology and Nutrition and Chairman of the Department of Nutrition at the Harvard T.H. Chan School of Public Health and Professor of Medicine at Harvard Medical School. Dr Willett studied food science at Michigan State University, and graduated from the University of Michigan Medical School before obtaining a Doctorate in Public Health from the Harvard School of Public Health. Dr Willett has focused much of his work over the last 35 years on the development of methods, using both questionnaire and biochemical approaches, to study the effects of diet on the occurrence of major diseases. He has applied these methods starting in 1980 in the Nurses' Health Studies I and II and the Health Professionals Follow-up Study. Together, these cohorts that include nearly 300 000 men and women with repeated dietary assessments are providing the most detailed information on the long-term health consequences of food choices. Dr Willett has published over 1500 articles, primarily on lifestyle risk factors for heart disease and cancer. Dr Willett is the most cited nutritionist internationally, and is among the five most cited persons in all fields of clinical science. He is a member of the Institute of Medicine of the National Academy of Sciences and the recipient of many national and international awards for his research.

ABSTRACT: Diet, weight control and energy balance in cancer
The topic of diet and cancer has been the focus of much research since the early 1980's when Doll and Peto suggested that about 35% of cancer might be caused by, or prevented by, dietary factors. At that time total dietary fat was believed to be the most important factor underlying the high rates of many cancers in western countries. Since then, large prospective studies and several randomized trials have not supported dietary fat, at least during midlife and later, as an important cause of cancer. Also, initial enthusiasm for a major role of fruits and vegetables in prevention of cancer has been tempered by the results of prospective studies showing little or no relation with overall cancer incidence, although some benefit for specific subsets of cancer has been documented. In contrast with these studies, excess body fat and particularly weight gain during adult life has been shown to be a major cause of many types of cancer, ranking close to smoking as a potentially modifiable cause of cancer in some populations. Considerable evidence suggests that other specific dietary factors including soy foods, specific carotenoids, and dairy products also contribute to the cause and prevention of specific cancer. Importantly, the role of diet during childhood, adolescence, and early adult life in the etiology of cancers diagnosed decades later has been minimally studied, but recent findings suggest that reducing consumption of red meat and increasing intakes of fruits, vegetables, whole grains, and soy products could reduce risk of breast cancer.

CAUSALITY AND CHANCE IN THE ORIGINS OF CANCER

Friday 10 June - 09:30-10:00

George Davey Smith
Professor of Clinical Epidemiology, University of Bristol; Honorary Professor of Public Health, University of Glasgow; Visiting Professor, The London School of Hygiene and Tropical Medicine, United Kingdom

George Davey Smith is Professor of Clinical Epidemiology at the University of Bristol, Honorary Professor of Public Health at the University of Glasgow and Visiting Professor at the London School of Hygiene and Tropical Medicine. He is Scientific Director of the Avon Longitudinal Study of Parents and Children and Director of the Medical Research Council's Integrative Epidemiology Unit. His major research interests relate to the use of genetic epidemiology for informing understanding of the causal influence of environmentally modifiable risk factors and how social inequalities in health are generated by exposures acting over the entire lifecourse. Professor Smith has also worked on HIV/AIDS prevention in Nicaragua and India and on issues around the history of epidemiology, meta-analysis, lay epidemiology and epidemiological methodology. He is co-editor of the International Journal of Epidemiology.

RISK FACTORS FOR SECOND CANCERS

Friday 10 June - 10:00-10:30

Flora van Leeuwen
Head of the Division of Psychosocial Research and Epidemiology, Netherlands Cancer Institute, Amsterdam, Netherlands

Flora E. van Leeuwen graduated from the Wageningen Agricultural University (MSc in Human Nutrition) in 1981 (cum laude). In the same year she became Head of the Department of Tumor Documentation, Clinical Trials and Epidemiology of the Netherlands Cancer Institute in Amsterdam, with the specific task to start an Epidemiology Group in that institute. In 1982–1983, she was awarded a research training fellowship by the International Agency for Research on Cancer and obtained an MSc degree in Epidemiology from the Department of Epidemiology of the School of Public Health of the University of Alabama in Birmingham, USA. From 1986 to 2010, she was Head of the Epidemiology Group of the Netherlands Cancer Institute. From 2010 onwards, she has been heading the Division of Psychosocial Research and Epidemiology in the Netherlands Cancer Institute. Her research group currently focuses on two main research lines: (i) the assessment of the long-term risks of second malignancy, cardiovascular disease and other comorbidities following treatment for Hodgkin's lymphoma, breast cancer, testicular cancer and childhood malignancy; the development and evaluation of cancer survivorship care programs and (ii) the assessment of the roles of hormone-related and genetic risk factors in the etiology of breast and ovarian cancers; special interest is in late effects of ovarian stimulation for in vitro fertilization and cancer etiology in BRCA1/2 families. In 1998 Flora van Leeuwen obtained a Chair in Cancer Epidemiology at The Faculty of Medicine from the Vrije Universiteit in Amsterdam.

ABSTRACT:
Currently, 17-19% of all new primary malignancies occur in individuals who have already survived a primary malignancy. In the Netherlands, the proportion of second and subsequent malignancies (including second cancers in paired organs) increased from 10% in 1989 to 17% in 2013. Most of this increase can be attributed to improved cancer survival. The occurrence of two primary malignancies in the same individual may result from host susceptibility factors (genetic predisposition, immunodeficiency), lifestyle or environmental risk factors in common, treatment for the first malignancy, or interaction between these factors. Alternatively, two primary malignancies in a single individual may be unrelated and arise by chance alone. SMNs occurring at early ages are more likely to be caused by genetic factors or treatment of the first malignancy, while SMNs occurring at older ages are more likely to be related to lifestyle, or to arise through the play of chance.
Research conducted over the last three decades has clearly demonstrated that, paradoxically, several treatments used successfully to treat cancer have the potential to induce new primary malignancies: increased SMN risks have been observed after radiotherapy, certain chemotherapy regimens and hormonal treatments. Radiotherapy is associated with moderately increased risks of solid malignancies in the organs

or tissues irradiated. The relative risk of solid tumors increases steadily with increasing follow-up time from 5-15 years since radiotherapy and remains elevated for at least 40 years. The relative risk of solid SMNs increases strongly with younger age at first treatment; this effect is most notable for breast cancer. The risks of lung, breast and gastrointestinal cancers increase with higher radiation dose, while the risks of leukemia and thyroid cancer decrease at high doses. According to recent estimates, radiotherapy accounts for 8% of all subsequent malignancies. This proportion, however, is much larger (30-70%) for SMNs occurring after primary malignancies (which used to be) treated with intensive radiation and chemotherapy regimens, such as childhood cancer and Hodgkin lymphoma.
Recent studies show that alkylating agent chemotherapy does not only increase risk of acute myeloid leukemia, but can also increase the risk of solid malignancies, in particular cancers of the lung and gastrointestinal tract. Smoking appears to multiply the radiation- and chemotherapy-associated risks of lung cancer. Therefore, all cancer patients should be strongly advised to stop smoking.

PANEL DEBATE 3: SCREENING FOR LUNG CANCER SHOULD BE IMPLEMENTED NOW

Pro: John Field, University of Liverpool Cancer Research Centre, United Kingdom

John Field
Director of Research, Roy Castle Lung Cancer Research Programme, University of Liverpool Cancer Research Centre, United Kingdom

Professor John Field has a Personal Clinical Chair in Molecular Oncology at the University of Liverpool. He is a Visiting Professor at University College London and holds the post of Director of Research of the Roy Castle Lung Cancer Research Programme. He is the Chief Investigator for the UK Lung Cancer Screening Trial and Chair of the European Union-United States Spiral CT Collaborative Group (2011–). He was the previous Chair of the International Association for the Study of Lung Cancer (IASLC) Screening Prevention & Early Detection Committee and he formed the IASLC Strategic Screening Advisory Group, which he chairs. He was presented with the IASLC Joseph Cullen Award at the World Conference on Lung Cancer in 2011, in recognition of his lifetime scientific achievements in lung cancer prevention research. He is the Principal Investigator of the Liverpool Lung Project, a molecular-epidemiological study into the early detection of lung cancer, funded by the Roy Castle Lung Cancer Foundation. He is also PI on the large EU Early Lung Cancer study funded by the European Commission. Both of these trials form part of the National Cancer Research Institute Lung Cancer Clinical studies group's portfolio. A Partner in the FP7 CURELUNG and Lung Cancer Artificial Olfactory System projects, he is also heavily involved in the identification of molecular diagnostic markers in lung and head and neck cancers. His research funding has been provided mainly by the Rarer Cancers Foundation, North West Cancer Research Fund, the Medical Research Council, Cancer Research UK, the European Union, the National Institutes of Health and Health Technology Assessment.

Anti: Harry J. de Koning, Erasmus Medical Center, Rotterdam, Netherlands

Harry J. de Koning
Professor of Public Health & Screening Evaluation, Department of Public Health, Erasmus Medical Center, Rotterdam, Netherlands

Born in the Netherlands, Professor Henricus (Harry) J. de Koning worked as a Researcher and an Assistant Professor in the department of Public Health of the Erasmus University in Rotterdam from 1987 to 1999. He became an Associate Professor in 1999, and in 2008 he was appointed Professor of Public Health & Screening Evaluation in the same department in Rotterdam. He was also Senior Associate in the Department of Health Policy and Management at the Johns Hopkins Bloomberg School of Public Health from 2011 to 2012. Since 2011, he has been a Member of the Medical Advisory Board of the Royal Netherlands Academy of Arts and Sciences (KNAW). His major scientific contributions are in the areas of: designing, running and evaluating largescale multidisciplinary population-based randomized controlled screening trials to establish the efficacy of screening, evaluating active international screening programmes and tests to establish effectiveness, guiding public health policies using predictions of favourable and unfavourable effects and the cost of screening, based on micro-simulation modeling of the natural history of disease, and cost-effectiveness and cost-utility analyses.

PROFFERED PAPERS PLENARY SESSION

Parity, Age at First Birth, Breastfeeding and Breast Cancer Risk: a Nationwide Prospective Study of 300,000 Chinese Women

LING YANG, UNIVERSITY OF OXFORD, UNITED KINGDOM
LI L. [2,3] , CHEN Y. [1] , GUO Y. [2] , PETO R. [1] , CHEN Z. [1]

[1] *1 CTSU, Nuffield Department of Population Health, University of Oxford, UK; 2 Chinese Academy of Medical Sciences, Dong Cheng District, Beijing, China; 3 Department of Public Health, Beijing University, Beijing, China*

Background: Previous studies, mostly from West have reported inconsistent findings on the associations between childbearing related aspects and risk of breast cancer. Little is known in China where women's reproductive factors patterns differ importantly from the West and the incidence of breast cancer rapidly increased.
Methods: The China Kadoorie Biobank recruited 302,632 women aged 30-79 (mean (SD) 50.8 (10.6)) years in 2004-8 from 10 diverse regional sites across China, including 55.6% postmenopausal women. During 7 years follow-up, 1,353 incident breast cancer cases were reported among 284970 women who had no prior history of cancer at baseline. Cox regression yielded adjusted hazard ratios (HRs) to breast cancer risk.
Results: Most women were parous (98.7%) with means of number of livebirths 2.3 (1.3), age at firth birth at 23.4 (3.2) years and total breastfeeding 34.8 (24.7) months. After adjustment of various confounders, parity significantly reduced breast cancer risk, with a 19% (11-25%) reduced risk for every one more childbearing (adjusted HRs of 1.00 (0.85, 1.17), 0.85 (0.78, 0.92), 0.65 (0.55, 0.78) and 0.54 (0.42, 0.69) for women with one (reference), two, three and four or more livebirths, respectively). No material change on the association was found in subgroups defined by area and women's menopausal status. A slightly J-shaped association was observed between age at first birth and breast cancer risk. Parous women who ever breastfed her children had 25% (3-41%) lower risk of breast cancer than those who never done so. The adjusted HRs of breast cancer were 1.20 (0.94, 1.54), 1.00 (0.86, 1.16), 0.99 (0.89, 1.11), 0.90 (0.78, 1.03), 0.87 (0.71, 1.06), 0.88 (0.70, 1.11) for women never breastfed, total breastfed duration of <1, 1, 2, 3 and ≥4 years, respectively.
Conclusion: The more children women having or the longer women breastfeed, the more they are protected against breast cancer.

Risk of Cancer Mortality from Occupational Exposure to Ionising Radiation: Results of the International Cohort Study of Radiation Workers (INWORKS)

AUSRELE KESMINIENE, INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, FRANCE
RICHARDSON D. [2] , LEURAUD K. [3] , CARDIS E. [4] , DANIELS R. [5] , GILLIES M. [6] , O'HAGAN J. [6] , HAMRA G. [7] , HAYLOCK R. [6] , LAURIER D. [3] , MOISSONNIER M. [1] , SCHUBAUER-BERIGAN M. [5] , THIERRY-CHEF I. [1]

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[6] *Public Health England Centre for Radiation, Chemical and Environmental Hazards (PHE-CRCE), Chilton, UK*
[7] *Department of Environmental and Occupational Health, Drexel University School of Public Health, Philadelphia, P.A. USA*

Purpose
The carcinogenic effects of ionising radiation (IR) have been studied for decades. While the moderate to high exposure effects are well characterized, the low-level, chronic exposure effects remain a subject of continued debate. An International Nuclear Workers Study (INWORKS) was therefore established to further improve the precision of estimates of cancer risk following protracted low doses of IR and to strengthen the scientific basis of radiation protection standards.
Methods
INWORKS is built upon the previous 15-country study of nuclear industry workers and includes 308,297 workers with individual monitoring data for external exposure from France, the United Kingdom, and the United States of America. Excess relative rate (ERR) per gray (Gy) of radiation dose for mortality from

cancer and haematological malignancies was estimated after ascertaining vital status and cause of death through linkage with national and regional death registries and other sources.
Results
We observed 66,632 deaths, including 17,957 deaths from solid cancers and 1,791 deaths from haematological cancers. Statistically significant associations were seen between red bone marrow dose and risk of leukaemia (excluding chronic lymphocytic leukaemia (CLL)), and between colon dose and risk of solid cancers. The ERR of non-CLL leukaemia mortality was 2.96 per Gy (90% CI 1.17–5.21) and for solid cancers - 0.47 per Gy (90% CI 0.18-0.79).
Conclusions
INWORKS provides some of the strongest evidence for an association between protracted low dose exposure to IR and cancer mortality. The risk per unit of dose in our study was similar to estimates derived from studies of Japanese atomic bomb survivors.
Funding source
Support from the US Centers for Disease Control and Prevention; Ministry of Health, Labour and Welfare of Japan; Institut de Radioprotection et de Sûreté Nucléaire; AREVA; Electricité de France; US National Institute for Occupational Safety and Health; US Department of Energy; and Public Health England.

Ethnic/Racial Differences In Visceral And Liver Fat Distributions In The Multiethnic Cohort

LOIC LE MARCHAND, UNIVERSITY OF HAWAII CANCER CENTER, UNITED STATES
LIM U. [1] , MONROE K. [2] , ERNST T. [3] , SHEPHERD J. [4] , WILKENS L. [1] , LE MARCHAND L. [1]

[1] *University of Hawaii Cancer Center*
[2] *University of Southern California*
[3] *University of Hawaii Medical School*
[4] *University of California San Francisco*

Since 1992-1995, the Multiethnic Cohort (MEC) Study has followed over 215,000 men and women of five ethnic/racial groups (Japanese Americans, Latinos, whites, African Americans and Native Hawaiians). The associations of BMI to cancer and diabetes vary markedly across ethnicities. Thus, we examined differences in body fat distribution in the cohort.

Healthy MEC participants aged 60-73 years were recruited among each sex/ethnic group to undergo a whole-body DXA and abdominal MRI and anthropometric measurements. Recruitment was stratified across six BMI level (18.5-40 kg/m2) within each sex/ethnic group to maximize comparability in total adiposity. Data analyses were completed on 300 subjects and are being conducted on 1,000 subjects (~100 by sex/ethnic groups).

By study design, mean BMI (28kg/m2) was similar for men and women and across ethnicities (p=0.80). Total percent body fat was higher in women (40%) than in men (27%), and differed by ethnicity only in women (p=0.007). Mean visceral fat area at L3/L4 in men, adjusted for total body fat and age, was largest for Japanese Americans (247cm2), followed by whites (207cm2), Latinos (198cm2), Native Hawaiians (194cm2) and African Americans (158cm2) (p-heterogeneity=0.0002). In women, differences were even greater in the following decreasing order: Japanese Americans (183cm2), Native Hawaiians (149cm2), whites (134cm2), Latinas (120cm2) and African Americans (90cm2) (p-het.<0.0001). Multivariate adjusted percent liver fat showed a 3.3-fold difference across ethnicities in both men (7.9%-2.4%) and women (9.5%-2.9%; both p-het.<0.0001) in a similar ethnic/racial order as with visceral fat, except that Latinas showed a higher percent liver fat than white women. Weight gain in adulthood (since age 21) among men, but not women, was associated with greater visceral fat (p=0.0004) and liver fat (p<0.0001) even after accounting for total fat.

The substantial differences in body fat distribution observed among ethnic groups may in part explain their differing metabolic disease burdens.

Mechanisms Of Ethnic/Racial Differences In Lung Cancer Susceptibilty Evaluated With Tobacco Smoke Toxicant And Carcinogen Biomarkers And Genetic Studies

STEPHEN HECHT, UNIVERSITY OF MINNESOTA, UNITED STATES
CARMELLA S. [1] , MURPHY S. [1] , PARK S. [3] , STRAM D. [2] , HAIMAN C. [2] , PATEL Y. [2] , LE MARCHAND L. [4]

[1] *Masonic Cancer Center, University of Minnesota, Minneapolis, MN, USA*
[2] *University of Southern California*
[3]

Results of the Multiethnic Cohort Study demonstrated that African Americans and Native Hawaiians have a significantly higher risk for lung cancer than European Americans while Latinos and Japanese Americans have a significantly lower risk. We are investigating the mechanistic basis for these remarkable differences with the expectation that the results will provide leads for identifying individuals highly susceptible to lung cancer. We analyzed urine samples from 300-700 subjects per group for urinary total nicotine equivalents (the sum of nicotine and six metabolites comprising 80% of the nicotine dose), total NNAL (a biomarker of the powerful tobacco-specific lung carcinogen NNK), phenanthrene tetraol and 3-hydroxyphenanthrene (biomarkers of uptake and metabolism of carcinogenic PAH), and the mercapturic acids of acrolein, crotonaldehyde, and benzene (volatile toxicants and carcinogens in tobacco smoke). The results demonstrated that African Americans, although smoking fewer cigarettes per day than any of the other groups except Latinos, had significantly higher levels of total nicotine equivalents, total NNAL, phenanthrene tetraol, 3-hydroxyphenanthrene, and the benzene metabolite S-phenylmercapturic acid compared to Whites while Japanese Americans had significantly lower levels of these biomarkers than Whites. The relatively low levels of total nicotine equivalents in the urine of the Japanese American smokers was related to low activity polymorphisms in CYP2A6, the major enzyme responsible for nicotine metabolism. The biomarker profiles of Native Hawaiians and Latinos did not fit this pattern, but Native Hawaiians had high levels of the acrolein biomarker compared to other groups while those of Latinos were low. These results provide compelling new data pertinent to the relatively high risk of African Americans and the lower risk of Japanese Americans for lung cancer. The results of this study may lead to new metrics for lung cancer susceptibility resulting in personalized approaches to smoking cessation and lung cancer prevention.

Socioeconomic status and delays diagnosis and treatment: are there influences on childhood cancer survival in Sao Paulo, Brazil?

RAFAELA NAVES, FACULDADE DE CIENCIAS MEDICAS DA SANTA CASA DE SAO PAULO, BRAZIL
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Purpose: This study aimed to evaluate the influence of socioeconomic status (SES) in the intervals first consultation-diagnosis and diagnosis-treatment among children with cancer living in the city of Sao Paulo, Brazil, as well as the impact of delays on 5-year overall survival (5y-OS). Methods: This is a retrospective cohort study including all first primary cancers diagnosed among individuals < 20 years, registered in the Central Hospital-based Cancer Registry of Sao Paulo State in the period 2000-2010. Patients were classified according to the Youth Vulnerability Index (YVI), based on the district of residence at diagnosis. Intervals categories for each tumor were defined based on median or percentile 75. Five-year OS was obtained through Kaplan-Meier method and curves were compared using log-rank test. Results: During the study period, 2,756 cases were registered. No significant differences on intervals first consultation-diagnosis and diagnosis-treatment according to YVI were observed. Children and adolescents from lower YVI strata presented worse outcomes (upper stratum, 5y-OS=69.2%; intermediate stratum, 5y-OS=66.4%; lower stratum, 5y-OS=61.7%, p=0.005). Disparities in survival according to delay in diagnosis (days) were found for patients with CNS tumors (<8: 5y-OS=52.7%, ≥8: 5y-OS=67.2%, p=0.013), neuroblastoma (<7: 5y-OS=35.9%; ≥7: 5y-OS=51.6%, p=0.033), retinoblastoma (<13: 5y-OS=96.8%; ≥13: 5y-OS=66.7%, p=0.016), germ cell tumors (<7: 5y-OS=89.2%; ≥7: 5y-OS=74.1%, p=0.041), and carcinomas (<12: 5y-OS=73.6%; ≥ 12: 5y-OS=84.4%, p=0.043). Disparities in survival according to delay in starting treatment (days) were observed for lymphomas (<18: 5y-OS=74.2%, ≥18: 5y-OS=84.4%, p=0.013), neuroblastoma (<7: 5y-OS=35.9%; ≥7: 5y-OS=51.6%, p=0.011), CNS tumors (<1: 5y-OS=63.9%; ≥1: 5y-OS=48.4%, p=0.022), bone tumors (<13: 5y-OS=40.6%; ≥13: 5y-OS=54.2%, p=0.022), and carcinomas (<13: 5y-OS=85.9%; ≥13: 5y-OS=71.1%, p=0.019). Conclusions: SES did not have influence in access to diagnosis and treatment for children with cancer in Sao Paulo, Brazil. However, survival rates were affected by both SES and delays in diagnosis and treatment. Funding source: FAPESP.

Genome-wide AFB1-induced mutational signature in cells, mice and human tumors – implications for molecular epidemiology

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Purpose: Aflatoxin B1 (AFB1), a mutagen and IARC Group 1 carcinogen, causes hepatocellular carcinoma (HCC). The mutagenic effects of AFB1 on TP53 and reporter genes have been studied experimentally and in HCCs. Here we present first-of-its-kind data on the extended, genome-wide AFB1 mutagenesis using human and mouse in vivo and in vitro experimental systems.

Methods/Results: We determined genome-wide mutation patterns induced by AFB1 in two human cell-lines and a mouse model of HCC. The cell-line mutational patterns were remarkably stable across replicates, but differed somewhat between cell lines. Mutational patterns in the mouse tumors were more variable across replicates, possibly reflecting variability in the physiological clearance of the toxin in mice or random events during tumorigenesis. However, the overall pattern was consistently dominated by G>T mutations with a preference for TGC>TTC and substantial mutation enrichment on the non-transcribed strand. We next integrated these results with publicly available human HCC data and newly generated genomic HCC data from a known region of aflatoxin exposure. Like the experimental systems, the human HCCs showed high rates of G>T mutations and strong transcriptional strand bias, providing evidence that the HCCs were direct consequences of AFB1 exposure. However, they differed from the experimental systems in that the most prominent mutations were GGC>GTC. This difference may be due to exposure to other aflatoxins, to other mutagens, or to differences in biochemical processing of AFB1.

Conclusions: The experimental cell-based systems and mouse models used in our study present innovative tools allowing to determine genome-wide mutational signatures of candidate mutagenic carcinogens. We propose that the described experimental, multi-system approach can be used more broadly in support of molecular epidemiology studies aimed at cancer prevention.

Funding source: IARC Regular Budget; ITMO CANCER – INSERM Plan Cancer 2015; NIH/NIEHS 1R03ES025023-01A1; Singapore A*STAR and MOH via Duke-NUS and NMRC/CIRG/1422/2015.

CONSORTIA, BIG DATA AND THE FUTURE OF POPULATION RESEARCH

Friday 10 June - 15:00-15:30

Elio RIBOLI
Director, School of Public Health, Imperial College London, United Kingdom

Professor Elio Riboli's career started at the Department of Epidemiology of the National Institute of Cancer, Milan (1978-1983). In 1983 Dr Riboli was appointed Medical Officer in Epidemiology at the International Agency for Research on Cancer (IARC). While at IARC he engaged in a novel area of research focusing on the role of diet, nutrition and endogenous hormones in cancer aetiology. In 1990 this materialized into the initiation of the european Prospective Investigation into Cancer and Nutrition (ePIC), and its subsequent funding by the "europe Against Cancer" programme of the European Commission, from 1992 onward. Over the past decade, Dr Riboli has led research contributing to the discovery of the role of metabolic factors (obesity, insulin resistance and other components of the so-called "metabolic syndrome") in cancer causation. These results have translated into worldwide public health guidance by international bodies such as the World Health Organization and the World Cancer Research Fund. While working at IARC, during the period 1990-2005, he received joint appointments as Adjunct Professor in the Department of Environmental Medicine at New York University and as Senior Visiting Scientist at the National Cancer Institute, National Institutes of Health, in the USA. In 2006 Dr Riboli was appointed Professor and Chair in Cancer epidemiology and Prevention and in 2008 Director of the School of Public Health. He is also Chair of the Interventional Public Health Clinical Programme group of the Imperial College Academic Health Science Centre (AHSC) and Director of Research in Public Health of the Imperial College National Health Service Healthcare Trust, providing a direct link between academic research, public health and clinical translation.

The role of large prospective cohort studies in cancer research

Over the past decades, a growing number of large population cohort studies with extensive exposure information and stored biosamples have been developed in different regions of the world. These studies include early cohorts with extensive follow-up of up to 30 years, as well as more recently established cohorts with shorter follow-up time but often with richer baseline phenotype and exposure information. The two largest European cohort studies are EPIC and the more recently established UK Biobank. Both cohorts have recruited over 500,000 participants. EPIC was initiated in the 1990s, coordinated by IARC in collaboration with 23 collaborating centre in 10 countries. After 20 years of follow-up EPIC has accrued over 80,000 incident cases of cancer, over 26,000 cases of CHD and stroke and over 16,000 cases of type 2 diabetes. The EPIC database has become a shared research infrastructure used by hundreds of researchers in Europe and across the world (http://epic.iarc.fr/). EPIC and a number of other European cohorts have built a collaboration network that has materialized in the “Large Population Cohort” FP7 programme of the BBMRI infrastructure (http://www.bbmri-lpc.org/).

Population cohorts have greatly contributed to the advancement of our scientific understanding of the causes of chronic diseases. The first historical example was the demonstration of the carcinogenicity of tobacco smoke by the British Doctors Cohort in the 1950s. The list of causes of cancer and other chronic diseases discovered thanks to cohort studies is very long and include environmental, occupational, behavioural, pharmacological, nutritional exposures as well as endogenous metabolic and hormonal characteristics. A more recent development is the unique role of cohorts in research focused on the interaction between genetic and epigenetic characteristics in combination with environmental exposures and endogenous/metabolic characteristics. By supporting the investigation of the biological interplay of inherited and acquired risk factors, cohort studies have the potential to help epidemiology to move beyond “associations” into the realm of “causation”.

SUCCESSES IN UNDERSTANDING THE CAUSES OF CANCER

Friday 10 June - 15:30-16:00

Richard PETO

Professor of Medical Statistics and Epidemiology and co-Director of the Clinical Trial Service Unit, University of Oxford, United Kingdom

Richard Peto is a Professor of Medical Statistics and epidemiology and a co-Director of the Clinical Trial Service unit at the University of Oxford. He studied natural sciences at Cambridge University and obtained his MSc in statistics at the University of London. Professor Peto's work has included studies of the causes of cancer in general, and of the effects of smoking in particular, and the establishment of large-scale randomized trials of the treatment of cancer and various other diseases. He has been instrumental in introducing combined "meta-analyses" of results from diverse studies. Dr Peto is one of the world's most cited medical researchers and he was knighted in 1999 for his services to epidemiology and cancer prevention. He devotes much of his energy to advising and providing information on "avoidable death". His work continues to have a direct influence on public policy and adult mortality in many countries.

PARALLEL SESSIONS

WEDNESDAY 8 JUNE

EPIDEMIOLOGY - Global burden of cancer and cancer registries

Resource Requirements For Cancer Registration: Comparative Cost Data From Five Countries

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Purpose: High quality population-based cancer registry data are critical for implementing cancer control policies. Data on the resources needed to support cancer registration are essential for increasing global capacity in cancer surveillance and control. The aims of this study are to (1) Engage global stakeholders to identify and quantify the resources needed to strengthen and expand existing registries or establish new registries where none exist to support the collection of high quality cancer data; and (2) Share estimates of the costs for establishing and maintaining cancer registries with stakeholders to guide policies and facilitate planning.

Methods: A tool was developed to collect activity-based cost data from cancer registries. Working with registry staff and in-country consultants, training webinars were conducted. Cost and resource use data were collected from 12 registries in India, Kenya, Uganda, Barbados and Colombia. All monetary and non-monetary contributions to registry activities were collected for a comprehensive assessment.

Results: Host institution contributions provide valuable support for registry activities and account for 42% to 79% of registry operating expenditures. The largest budget component incurred by cancer registries is labor costs and this contributes to over half the total cost. The cost per case for registries in low income and lower middle income countries ranged from $2.47 to $32.76. Registries that were largely supported by research activities incurred higher costs than the more established long-standing registries.

Conclusions: Based on our preliminary assessment, the collection of information on the cost of operating cancer registries in LMICs is feasible. Some of the approaches to reduce the cost of operating population-based registries are to partner with universities and hospitals as infrastructure and other high fixed cost expenditures can be shared or donated, and to streamline data collection activities to reduce labor cost (e.g. travel to data sources and time spent accessing medical records).

Building Capacity For Cancer Control Research: The Global Initiative For Cancer Registry Development (Gicr)

LES MERY, INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, FRANCE
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Purpose:
High quality cancer data is lacking in many parts of the world. In response, the Global Initiative for Cancer Registry Development (GICR) has been launched to improve the coverage, quality and accelerate the availability of population-based cancer registries. The presentation will focus on the progress of the GICR to demonstrate how activities relate to strengthening cancer research worldwide.
Methods:
IARC Regional Hubs for Cancer Registration are to provide localized programmes in training, support and advocacy. The concept of the Hub model is to develop a connected system arranged to link country-level needs with regional support mechanisms. Four Hubs are operational: a Regional Hub for South, East, and South-Eastern Asia, a Regional Network Hub for Sub-Saharan Africa in collaboration with the African Cancer Registry Network; a Regional Hub for North Africa, Central and West Asia; and a Regional Network Hub for

Latin America. Two additional Hubs in the Pacific Islands and in the Caribbean are being implemented.
Results:
Since the launch of the GICR at the World Cancer Leaders' Summit in November 2011, site visits to 61 countries have been conducted to assess opportunities to improve their level of cancer registration. 17 new agreements between IARC and countries have been signed, with several others in development. Training as a core component has resulted in 32 GICR-led or affiliated courses. An IARC Technical Publication has been produced in English, French and Spanish as a reference for health planners in LMICs (Bray, 2014), with the further development of support tools, regional databases and reports underway.
Conclusion:
A key focus of the GICR is to support the development of trained staff in population-based cancer registries and to increase the quality of cancer data. New opportunities in cancer control planning and in building cancer research capacity are being established through the GICR.

Prostate-Specific Antigen Testing For Prostate Cancer: Emptying A Pool Of Susceptible Individuals?

MORTEN VALBERG, UNIVERSITY OF OSLO, NORWAY
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Purpose: After the introduction of the prostate specific antigen (PSA) test in the 1980s, a sharp increase in the incidence rate of prostate cancer was seen in the United States. The age-specific incidence patterns exhibited remarkable shifts to younger ages, and declining rates were observed at old ages. Similar trends were seen in Norway. We investigate whether these features could be explained by the existence of subgroups of the populations that are especially susceptible to prostate cancer.

Methods: We analyzed incidence data from the United States' Surveillance, Epidemiology, and End Results program for 1973-2010, comprising 511 027 prostate cancers in men ≥40 years old, and national Norwegian incidence data for 1953-2011, comprising 113 837 prostate cancers in men ≥50 years old. We developed a statistical frailty model where only a proportion of the population can develop prostate cancer. The increased risk of being diagnosed with the cancer due to the massive use of PSA testing is taken into account.

Results: The proportion of men that were susceptible was 39.9% (95% confidence interval (CI): 38.2%, 41.6%) in the United States and 30.4% (95% CI: 28.9%, 32.0%) in Norway. The frailty model describes the changing age-specific incidence patterns across birth cohorts well.

Conclusion: The peaking cohort-specific age-incidence curves of prostate cancer may be explained by the underlying heterogeneity in prostate cancer risk. Furthermore, the introduction of the PSA test seems to have driven the peak in the incidence rate toward younger ages by inducing a larger depletion of a pool of individuals susceptible to this cancer.

Funding source: Morten Valberg was supported by the Norwegian Cancer Society, grant number 4493570.

Initiative For Semi-Automated Population Based Cancer Registry In Iran

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Cancer registries are essential elements for cancer control programs. Iranian government launched a nationwide cancer registry program since 2002. However, the program could not reach the reasonable level of completeness and validity. Only Golestan province succeeded to run a high quality registry program and publish the results in the IARC monograph “Cancer in Five Continents, Volume 10, 2013”. We initiated 10 regional cancer registries in different part of the country. A memorandum of agreement has been signed with the International Agency for Research on Cancer (IARC) to provide technical support the new registries. We established a registry office in each province and provided essential infrastructure to run cancer registry activities in the region. The hospital information system and laboratory information system was improved to submit electronic reports to the registry offices. Cancer registries will use Iranian Integrated Care Electronic Health Record (locally called SEPAS), a national system designed for creation and integration of health data regarding each Iranian citizen to obtain the reports of cancer patients from laboratories and hospitals. We translated CanReg5 software and added Farsi calendar to the program to use it in the cancer registries in Iran. The national center for cancer registry is located in the cancer institute of Iran and provides technical support, training, and consultation to the regional registries. With capacity building and providing proper training to the registry managers and staff of the regional centers, and performing regular monitoring and updates will lead to high quality registry programs in Iran. These semi-automated registries will cover about 40% of the Iranian population. Such data would be sufficient to estimate incidence and mortality rates of cancers for the entire Iran and use it for cancer control planning. We will report the details about the framework and progress of the program in the conference.

The Impact Of Diagnostic Changes On The Rise In Thyroid Cancer Incidence

SALVATORE VACCARELLA, INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, FRANCE
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Purpose: Thyroid cancer (TC) incidence is rising in many high-resource countries, but corresponding mortality is constant or declining. Incidence increases appear largely restricted to small papillary TC in young/middle-age individuals. We compared age-specific incidence rates across countries and time periods to estimate the fraction of TC possibly attributable to diagnostic changes and incremented surveillance of the thyroid gland.
Methods: We focused on high-resource countries: the United States, Denmark, Finland, Norway, Sweden, England and Scotland, France, Italy, Australia, Japan, and the Republic of Korea. Before the 1970s, TC incidence in Nordic Countries increased proportionally to the second power of age, consistently with the multistage model. Using this historical observation as reference, we attributed the progressive departure from linearity of the age-curves in each country to an increased detection of asymptomatic disease in young/middle-age individuals. The proportion of cases attributable to diagnostic changes was estimated from the difference between observed rates and those expected using the Nordic reference.
Results: Attributable proportions were higher in countries with largest incidence increases. Diagnostic changes may account for ≥80% of TC cases diagnosed in 2003-2007 in women aged under 80 in the Republic of Korea, ≥80% in the United States, France, Italy, Australia, and approximately 50% in other countries, except Japan (30%). Attributable proportions were consistent across sexes, although increases were smaller and delayed in men.
Conclusions: A large proportion of TC cases diagnosed in high-resource countries are likely to be due to increased detection of asymptomatic TC. This proportion has progressively increased over time and it is likely to grow further in the future. Since there is evidence of harm but not benefit from the intense scrutiny of the thyroid, the possibility of overdiagnosis and overtreatment of TC should be urgently addressed.
Funding source: None.

Esophageal Cancer Case-Control Study In Western Kenya – Do Alcohol And Tobacco Contribute?

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Purpose: In Kenya, esophageal squamous cell carcinoma (ESCC) is the most common cancer among men and third most common in women. In Eldoret, Western Kenya, we have commenced an ESCC case-control study to investigate the environmental, behavioral, nutritional and genetic aetiology. We report on the influence of 2 strong risk factors from other settings: alcohol and tobacco.
Methods: We recruited cases, defined as histologically confirmed ESCC patients diagnosed at Moi Teaching and Referral Hospital between August 2013-October 2014, and age and frequency-matched hospital-based controls. Participants were interviewed using a pre-tested e-questionnaire. Odds ratios (OR) minimally adjusted for age and gender and 95% confidence intervals (CI) were computed using logistic regression
Results: Mean age of the 132 cases was 58.4 and of 158 controls 56.7 years. Amongst cases, the male:female ratio was 2:1; 61.3% were of Kalenjin ethnicity, 23% Luhya and 8% Luo. Ever consumption of alcohol (prevalence 75% in cases) and tobacco (61%) were each associated with ESCC (ORs 1.8 (1.0-3.2) and 2.3 (1.4-3.9) respectively). ORs were greatest in consumers of both habits (OR 2.4 (1.3-4.6) compared to non-drinkers non-smokers, which were largely driven by tobacco smoking rather than snuff/chewing and by drinking local brews/spirits busaa and chang'aa. These effects were independent of fresh fruit and traditional vegetables consumption which were protective for ESCC (p=0.008 and p=0.014). We will also present initial findings for oral health, oral health, biomass fuels, and blood group.
Conclusion: This study supports the concept of multifactorial etiology for ESSC. Initial results point to modifiable behavioral factors concerning alcohol and tobacco. Continued recruitment is needed to confirm results and to disentangle the specific effects of these co-present habits to better enlighten the most effective primary prevention strategies.
Funding Source: US NIH R21CA191965

The Fraction Of Breast Cancer Attributable To Smoking In Norway In 2012. The Norwegian Women And Cancer Study 1991-2012.

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Purpose: We utilized the Norwegian Women and Cancer Study, a nationally representative prospective cohort study to estimate the fraction of breast cancer attributable to passive and active smoking and the number of breast cancer cases that could have been avoided in the absence of smoking in Norway in 2012.

Methods: We followed 130 503 women, aged 34 to 70 years, who completed a baseline questionnaire between 1991 and 2007, through linkages to national registries through December 2012. We used Cox proportional hazards models to estimate hazard ratios (HRs) with 95% confidence intervals (CIs), while adjusting for confounders. We estimated attributable fractions (AF's) in smokers and in the population (PAF's) with 95% CIs.

Results: During a mean follow-up of 13 years, 4 293 women developed invasive breast cancer, confirmed by histology. Compared with never smokers, passive and ever (former and current) smokers had an overall risk of breast cancer that was 18% (HR=1.18, 95% CI 1.05 to 1.33) and 21% (HR=1.21, 95% CI 1.08 to 1.34),

respectively. Compared with parous never, excluding passive, smokers, women who had smoked five or more years before giving birth had an overall risk of breast cancer that was 29% (HR=1.29, 95% CI 1.14 to 1.46). The AF for breast cancer was 17.3 (7.4-25.4) for active smokers. The PAF of breast cancer for active smoking was 11.9 (5.3-18.1) overall, and 18.2 (0.9-32.5) for women diagnosed before age 50.

Conclusions: Our study shows that the number of breast cancer cases that may be prevented worldwide is huge. In smokers, one in six and in the population, one in nine breast cancer cases could have been avoided in the absence of smoking. Our findings support the notion that the global cancer burden due to smoking is substantially underestimated.

Funding Sources: None

Life-Course Trajectories Of Tobacco And Alcohol Consumption And Risk Of Head And Neck Cancer; Does Human Papillomavirus Play A Role? – An International Multi-Center Study.

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Purpose: To compare tobacco and alcohol life-course trajectories between two countries with different burden of head and neck cancers (H&NC), and to assess the role of the human papillomaviruses (HPV) in this relationship.

Method: We used data from a hospital-based case-control study conducted in Canada (460 cases, 458 controls) and India (350 cases, 371 controls). We recruited subjects newly diagnosed with primary squamous cell H&NC and non-cancer controls frequency-matched to cases according to age and sex. Semi-structured interviews using a life-grid technique collected information on several life-course exposures, including a detailed history of tobacco smoking and alcohol consumption. HPV was detected and genotyped in oral mucosal samples from brush biopsies using Linear Array.
Country specific trajectories of intensity of exposures were estimated as flexible functions of age and years since habit initiation using regression splines.

Results: Cases and controls had different life-course trajectories of smoking and alcohol in both countries. Canadian cases initiated and achieved their highest intensity of tobacco and alcohol consumption 2-5 years earlier than Indian cases. However, the latter consumed higher intensities of both throughout their life. Interestingly, 41% and 0% of cases tested positive for HPV infection in Canada and India, respectively. Trajectories of smoking and alcohol clearly showed considerable difference by HPV status. Among HPV negative subjects, controls had higher cumulative exposure before 30 years of age compared to cases. Trajectories did not differ between HPV positive cases and controls. Life-course tobacco and alcohol trajectories in the Indian sample were strikingly similar to those of HPV negative Canadians.

Conclusion: Life-course trajectories of major H&NC risk factors differ in specific characteristics between Canada and India. HPV may modify the effect of these trajectories. Cross population life-course studies may lead to new prevention avenues.

Funding source: Canadian Institutes of Health Research.

Smoking and risk of epithelial ovarian cancer subtypes in three prospective cohort studies

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Purpose
Based on three cohorts, the main purpose of this prospective study was to examine the impact of smoking on the risk of epithelial ovarian cancer according to histological subtypes and invasiveness.
Methods
We followed 300,398 Norwegian women, born between 1899 and 1975, recruited from 1974-2003, by linkage to national virtually complete registries through December 2013. The three cohorts included the Norwegian Counties Study (1974–1988), the 40-Years Study (1985–1999), and the Cohort of Norway Study (1994–2003). We used multivariable Cox proportional hazard models, stratified by birth cohort and study cohort to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between smoking characteristics and epithelial ovarian cancer (EOC) histological subtypes.
Results
During >5.9 million person-years, with a median follow-up of 19 years, 2,336 primary epithelial ovarian cancers were identified, of which 1,647 (71%) were invasive and 689 (29%) borderline. In our study, 38% of women were current, 21% former and 41% never smokers. Current smokers had an increased risk of EOC of 11% (HR=1.11 95% CI, 1.01-1.22) compared to never smokers. When stratifying according invasiveness, the risk of invasive-EOC (HR=0.97 95% CI, 0.86-1.08) in current smokers was significantly different from the corresponding risk of borderline-EOC (HR=1.55 95% CI, 1.29-1.85) ($p_{heterogeneity}$<0.0001). Compared with never smokers, current smokers had more than doubled risk of mucinous epithelial ovarian cancer (HR=2.09 95% CI, 1.67-2.62). When stratified according invasiveness, the corresponding figure was 78% increased risk of 78% [HR=1.78 95% CI, 1.20-2.64] for invasive-mucinous epithelial ovarian cancer and more than 100% increased risk [HR=2.26 95% CI, 1.71-2.97] for borderline-mucinous epithelial ovarian cancer ($p_{heterogeneity}$=0.34).
Conclusions
Independently of invasiveness status, smoking increases the risk of mucinous epithelial ovarian cancer.

Funding source
This research is supported by grants from the Norwegian Cancer Society.

Relevance of alcohol and tobacco to high premature mortality rate in Russia: Prospective study of 200,000 adults

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Purpose: To assess the joint effect of alcohol and tobacco on the high premature mortality in Russia.
Methods: In 3 west Siberian cities, 200,000 healthy adults aged 30-74 were interviewed during 1999-2008 and followed up for cause-specific mortality. Participants completed questionnaires about drinking, smoking and other lifestyle factors and had physical measurements taken. Almost all heavy drinkers smoke, so analyses of alcohol hazards are only in smokers; conversely, analyses of tobacco hazards are only in those who drink <1 bottle of vodka per week. Analyses exclude all with previous disease at entry
Results: Alcohol hazards – Among 57,361 male smokers, estimated 20-year risks of dying at ages 35-54 years were 16% (95% CI 15–17) for those who reported at baseline consuming less than a bottle of vodka

per week, 20% (18–22) for those consuming 1-2.9 bottles per week, and 35% (31–39) for those consuming ≥3 bottles per week; trend p<0·0001. The corresponding 20-year risks of death at ages 55-74 years were 50% (48–52), 54% (51–57), and 64% (59–69); trend p<0·0001. Tobacco hazards – Among 59,829 healthy adults who reported drinking <1 bottle of vodka per week, current smoking was associated with elevated all-cause mortality (RR=1.53 vs never smoking, CI 1.43-1.63). Starting young (<14 years) and smoking heavily (≥20 cigarettes/day) were both associated with even higher all-cause mortality (RR=1.97, 1.81-2.15 and RR=1.70, 1.63-1.77 respectively vs never smoking). Ex-smokers who quit before age 45 appeared to avoid most of the excess risk associated with continuing to smoke (RR=1.02 vs never smoking, 0.91-1.15). Conclusion: These risk ratios, together with retrospective study findings and national mortality trends, suggest that about 2/3 of all Russian male deaths in middle age are caused by tobacco and alcohol. Funding: UK MRC, British Heart Foundation, Cancer Research UK, WHO IARC

MECHANISMS - Systems perspectives of the exposome

Wednesday 8 June - 14:40-15:00

Invited speaker: Paolo Vineis
Chair in Environmental Epidemiology, Centre for Environment and Health, School of Public Health, Imperial College London, United Kingdom

Paolo Vineis is a leading researcher in the fields of molecular epidemiology and exposomics. His latest research activities mainly focus on examining biomarkers of disease risk, complex exposures and intermediate biomarkers from omic platforms (including metabolomics and epigenetics) in large epidemiological studies as well as studying the effects of climate change on noncommunicable diseases. He has more than 700 publications (many as leading author) in journals such as Nature, Nature Genetics, The Lancet and The Lancet Oncology. He is a member of various international scientific and ethics committees (including the Committee of the United States National Academy of Sciences on 21st Century Risk Assessment) and Vice-Chair of the Ethics Committee at the International Agency for Research on Cancer. He has been a member of the Scientific Council of IARC. Professor Vineis has extensive experience in leading international projects. He is currently the coordinator of the European Commission-funded Exposomics project (valued at €8.7m, started in 2012) and the Horizon 2020-funded project Lifepath (valued at €6m, started in 2015). He is a Principal Investigator/Co-investigator of numerous international research projects, such as the European Commission-funded GENAIR, ECNIS2, Envirogenomarkers, Hypergenes, ESCAPE and Transphorm networks, in which he has led Work Packages. In addition, he has attracted grants from the Leverhulme Trust, MRC, Cancer Research UK, HuGeF Foundation and the United States National Cancer Institute. He is the director of the Unit of Molecular and Genetic Epidemiology, HuGeF Foundation, Turin, Italy and leads the Exposome and Health theme of the MRC-PHE Centre for Environment and Health at Imperial College.

ABSTRACT:
Systems biology has been driven by technology (the development of omics) and by statistical modelling and bioinformatics. It is time to bring biological thinking back. We need to make at least three traditions of thought compatible: (a) causality in epidemiology, e.g. the “sufficient-component-cause framework”, and causality in other sciences, e.g. the Salmon and Dowe approach; (b) new acquisitions about disease pathogenesis, e.g. the “branched model” in cancer, and the role of biomarkers in this process; (c) the burgeoning of omic research, with a large number of “signals” that need to be interpreted. To address the new challenges of epidemiology, the concept of the “exposome” has been proposed, initially by Wild [2005], with more recent detailed development in relation to its application to population-based studies [Wild, 2012]. The original concept was expanded by others, particularly Rappaport and Smith [2010] who functionalized the exposome in terms of chemical signals detectable in biospecimens. The canonical exposome concept refers to the totality of exposures from a variety of sources including chemical agents, biological agents, radiation, and psychosocial components from conception onward, over a complete lifetime [Rappaport and Smith, 2010; Wild, 2012]. I will try to offer a unifying framework to incorporate omic data into causal models, referring to a position called “evidential pluralism”, according to which causal reasoning is based on both “difference-making” and the underlying biological mechanisms (Russo and Williamson). I will show examples from recent projects in the field, namely: new omic approaches such as adductomics; new long-term methylation biomarkers (in relation to smoking and air pollution); markers related to early life exposure and the role of socio-economic differentials. In particular, Illari and Russo suggest to conceptualize the detecting and tracing

of signals in terms of information transmission, which is a development of Salmon's and Dowe's mark transmission theory. One advantage of information transmission is that it is potentially widely applicable and capable of explaining how heterogeneous factors such as micro and macro – biological and social – are linked; this is arguably a pressing issue in the light of results of omic studies and also for the design of public health policies.

A Systematic Comparison of Linear Regression-based Statistical Methods to Assess Exposome-Health Associations

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The exposome constitutes a promising framework to better understand the effect of environmental exposures on health by explicitly considering multiple testing and avoiding selective reporting. However, exposome studies are challenged by the simultaneous consideration of many correlated exposures.

Objectives: We compared the performances of linear regression-based statistical methods in assessing exposome-health associations.

Methods: In a simulation study, we generated 237 exposure covariates with a realistic correlation structure, and a health outcome linearly related to 0 to 25 of these covariates. Statistical methods were compared primarily in terms of false discovery proportion (FDP) and sensitivity.

Results: On average over all simulation settings, the elastic net and sparse partial least-squares regression showed a sensitivity of 76% and a FDP of 44%; Graphical Unit Evolutionary Stochastic Search (GUESS) and the deletion/substitution/addition (DSA) algorithm a sensitivity 49 of 80% and a FDP of 33%. The environment-wide association study (EWAS) underperformed these methods in terms of FDP (average FDP, 86%), despite a higher sensitivity. Performances decreased considerably when assuming an exposome exposure matrix with high levels of correlation between covariates.

Conclusions: Correlation between exposures is a challenge for exposome research, and the statistical methods investigated in this study are limited in their ability to efficiently differentiate true predictors from correlated covariates in a realistic exposome context. While GUESS and DSA provided a marginally better balance between sensitivity and FDP, they did not outperform the other multivariate methods across all scenarios and properties examined, and computational complexity and flexibility should also be considered when choosing between these methods

DNA adductomics for the investigation of alcohol-related DNA damage

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Alcohol consumption increases the risk of head and neck and esophageal cancers. Despite this clear association, the underlying mechanisms of alcohol-induced carcinogenesis remain unclear. Alcohol–derived acetaldehyde seems to play a role in this process. Acetaldehyde is a genotoxic and carcinogenic compound that induces DNA modifications. If not eliminated or repaired, these modifications can result in miscoding events that can lead to misregulation of normal cellular growth control mechanisms and ultimately may result in cancer formation. Traditionally, the standard LC-MS methodology used for DNA adduct measurement

focuses on the investigation of small numbers of anticipated DNA adducts based on a priori assumptions regarding their formation from specific exposures or chemicals. This approach does not account for the complexity of in vivo DNA adduct formation resulting from endogenous sources such as oxidative stress, lipid peroxidation or aberrant metabolism, or as a result of exposure to complex mixtures of chemicals which cannot be completely anticipated or predicted. To address this limitation, we have developed a high resolution/accurate mass data dependent-constant neutral loss-MS^3 methodology for DNA adductomics using ion trap-orbital trap technology, to screen for all DNA modifications simultaneously. We have successfully tested our method on mixtures of standards and applied it to oral cell DNA samples collected from individuals exposed to 0.07% blood alcohol level and compared to controls. Our method allowed for the detection of the expected DNA adducts resulting from acetaldehyde but also of a number of unknown DNA adducts that have not been previously identified and investigated, confirming the ability of our DNA adductomic approach to characterize the DNA damage deriving from alcohol exposure. Our comprehensive DNA adductomic approach contributes to the development of new tools needed to investigate alcohol-related carcinogenesis, elucidate its mechanisms and ultimately generate instruments to help prevention.

The pathogenesis of increased cancer risk due to tobacco smoking

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Tobacco smoking is a recognised cause of multiple cancer types including lung, oral cavity, pharynx-larynx, esophagus, bladder, cervix, liver, kidney, stomach, pancreas, colorectum and bone marrow (AML). More than 60 chemicals in tobacco smoke are carcinogenic. A major mechanistic hypothesis underlying tobacco-smoke induced carcinogenesis is that some of these chemicals damage DNA in somatic cells resulting in an increased somatic mutation burden which increases the chance of a cell converting into a neoplastic clone. To investigate this hypothesis, we analysed 12 cancer types with elevated risks due to tobacco smoking. Our examination included single base mutations, small insertions and deletions, copy number variations, chromosomal rearrangements, and methylation profiles derived from the cancer genomes of 2,231 smokers and 1,023 lifelong non-smokers. Lung adenocarcinoma and larynx-pharynx cancer, both arising from tissues directly exposed to tobacco smoke, show markedly increased mutation burdens in smokers compared to non-smokers of a mutational signature that arises as a result of DNA damage caused by tobacco smoke mutagens. However, other cancer types caused by tobacco smoking, many arising in tissues not directly exposed to tobacco smoke, do not show evidence of this signature. Across all cancer types, other mutational signatures are influenced by smoking. In some cancer types, there was no elevation in somatic mutations or changes in methylation profiles between smokers and non-smokers. The results indicate that the pathogenesis of tobacco smoking induced elevated cancer risk is complex, differs between cancer types and in some cancer types is enigmatic.

MECHANISMS - Mechanisms in carcinogen evaluation

Wednesday 8 June - 16:00-16:20

Invited speaker: Martyn Smith
Professor of Toxicology, Division of Environmental Health Sciences, School of Public Health, University of California, Berkeley, USA

Martyn Smith received his PhD in Biochemistry from St. Bartholomew's Hospital in London and did postdoctoral training in toxicology at the Karolinska Institute in Stockholm. Dr Smith has expertise in molecular epidemiology, toxicology and genomics, and his research is aimed at finding the causes of chronic diseases, including cancer and diabetes. He currently teaches Advanced Toxicology and mentors graduate students and postdoctoral scholars in the Molecular Toxicology, Epidemiology and Environmental Health programmes. Since 1987, he has been the Director of the NIEHS-funded UC Berkeley Superfund Research Program. The goals of this programme are to improve understanding of the relationship between exposure and disease; improve risk assessments; and develop prevention and remediation strategies to improve and protect public health and the environment. Dr Smith's current research is in the emerging field of exposomics, but he is perhaps best known for his research on benzene and blood cancers. He also works with international collaborators on using mechanistic data in the identification of human carcinogens. Dr Smith is a Fellow of the American Association for the Advancement of Science. He received the 2010 Children's Environmental Health Network Award, became an Elected Fellow of the Collegium Ramazzini in 2012, and received the Alexander Hollaender Award from the Environmental Mutagenesis and Genomics Society in 2014.

ABSTRACT: The Key Characteristics of Human Carcinogens
Mechanistic data can provide biological plausibility to support epidemiological and animal toxicology findings in identifying cancer risks. However, there is a need for a broadly accepted systematic method for identifying, organizing, and summarizing mechanistic data for the purpose of decision-making in cancer hazard identification. An international Working Group of experts convened by IARC identified 10 key characteristics, one or more of which are commonly exhibited by established human carcinogens. These characteristics provide the basis for an objective approach to identifying and evaluating evidence from pertinent mechanistic studies (Smith et al. Env. Health Perspect. 2015, Nov24). The ten characteristics are distinct from the hallmarks of cancer in reflecting carcinogenic mechanisms rather than the properties of cancer cells, namely the abilities to: (1) act as an electrophile either directly or after metabolic activation; (2) be genotoxic; (3) alter DNA repair or cause genomic instability; (4) induce epigenetic alterations; (5) induce oxidative stress; (6) induce chronic inflammation; (7) be immunosuppressive; (8) modulate receptor-mediated effects; (9) cause immortalization; and (10) alter cell proliferation, cell death, or nutrient supply. The 10 key characteristics are used to systematically search the literature for evidence on relevant endpoints, and support objective evaluation of the overall strength of mechanistic information. Recent IARC monograph evaluations demonstrate the applicability of the approach for mechanistically diverse agents. For some compounds, there was strong evidence for only one (2,4-D) or no (parathion) key characteristics. Interestingly, strong evidence for two key characteristics (genotoxicity, oxidative stress) was found for glyphosate, diazinon and malathion, with malathion additionally showing three others (chronic inflammation, receptor-mediated effects, alters cell proliferation). DDT and TBBPA had strong evidence for a different set of key characteristics (receptor-mediated effects, immunosuppression, and oxidative stress). These developments lay the groundwork for future evaluations, where mechanistic data may fill important gaps in evidence of carcinogenicity.

Wednesday 8 June - 16:20-16:40

Invited speaker: Sarah Lewis
Senior Lecturer in Genetic Epidemiology, University of Bristol, United Kingdom

Sarah Lewis obtained a BSc in Genetics at the University of Sheffield in 1995 and then went on to complete a PhD in Genetic Epidemiology at the University of Manchester in 1999. She then had a series of short postdoctoral positions, including a post at the International Agency for Research on Cancer. She joined the School of Social and Community Medicine in January 2004 as a Lecturer in Genetic Epidemiology and was promoted to Senior Lecturer in 2009. Her research interests are in using Mendelian randomization to understand risk factors for cancer and also to identify key nutrients required for in utero development. She is involved in a large United Kingdomwide cohort study of cleft lip and palate, and a large birth cohort in which she is looking at the role of nutrition during pregnancy on childhood IQ and behaviour. She co-leads a work package on Mendelian randomization for the Integrative Cancer Epidemiology Programme, which is funded by Cancer Research UK. She is a Principal Investigator on a project to develop a framework for systematic reviews of mechanistic studies of diet and cancer in collaboration with the World Cancer Research Fund (WCRF). She also holds a grant from the WCRF to apply the above framework and Mendelian randomization to understanding the role of diet in prostate cancer.

ABSTRACT: Linking diet, nutrition and physical activity to cancer: a systematic review framework for integrating evidence from human, animal and other mechanistic studies

Background: Many laboratory experiments are performed to identify causal pathways and in doing so inform human health. These mechanistic studies complement epidemiological findings and can offer insights into biological plausibility and pathways between exposure and disease. Systematic reviews are the most robust way to synthesise data which have addressed a common question. Methods for conducting and reporting rigorous systematic reviews of epidemiological studies are well established. However, such methods are lacking for mechanistic studies. We were commissioned by the WCRF to develop a protocol for conducting systematic reviews of mechanistic studies which underpin epidemiological associations between exposures and cancer.
Methods: A multidisciplinary team with expertise in informatics, statistics, epidemiology, systematic reviews, cancer biology and nutrition was assembled and a series of 5 one-day workshops took place involving presentations, group work and discussions, along with smaller meetings and research being carried out in the intervening periods.
Results: We have developed a template for carrying out rigorous systematic reviews of mechanistic studies, which includes guidance on; a two stage search strategy, (the first stage of which is a mechanisms discovery search, followed by a targeted search for studies on a specific mechanism), formulating a research question, applying inclusion/exclusion criteria, assessing the relevance of retrieved studies to the research question, assessing the quality of individual studies (using appropriate risk of bias tools), synthesizing the data from individual studies, assessing the strength of the overall body of evidence from human and animal studies separately and integrating the human and animal studies to reach a conclusion
Conclusion: The above template will be available to researchers in the future who wish to conduct robust systematic reviews of the mechanisms which underpin associations between exposures and cancer.
Funding: World Cancer Research Fund (WCRF)

Use of high throughput screening data in IARC monograph evaluations

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Purpose: Evaluation of carcinogenic mechanisms serves a critical role in IARC monograph evaluations, and can lead to “upgrade” or “downgrade” of the carcinogenicity conclusions based on human and animal evidence alone. Three recent IARC monograph Working Groups (110, 112, and 113) pioneered analysis of high throughput in vitro screening data from the U.S. Environmental Protection Agency’s ToxCast program in evaluations of carcinogenic mechanisms.
Methods: For monograph 110, ToxCast assay data across multiple nuclear receptors were used to test the hypothesis that PFOA acts exclusively through the PPAR family of receptors, with activity profiles compared to several prototypical nuclear receptor-activating compounds. For monographs 112 and 113, ToxCast assays were systematically evaluated and used as an additional data stream in the overall evaluation of the mechanistic evidence. Specifically, ToxCast assays were mapped to 10 “key characteristics of carcinogens” recently identified by an IARC expert group, and chemicals' bioactivity profiles were evaluated both in absolute terms (number of relevant assays positive for bioactivity) and relative terms (ranking with respect to other compounds evaluated by IARC, using the ToxPi methodology).
Results: PFOA activates multiple nuclear receptors in addition to the PPAR family in the ToxCast assays. ToxCast assays offered substantial coverage for 5 of the 10 “key characteristics,” with the greatest coverage for modulation of receptor-mediated effects. The patterns of bioactivity observed in ToxCast assays provided additional support to Working Group evaluations of the mechanistic evidence.
Conclusions: High throughput in vitro screening data such as those from ToxCast provide a useful resource for evaluating both specific mechanistic hypotheses as well as the overall strength of the mechanistic evidence. However, ToxCast is limited or absent in its coverage of 5 of the 10 key characteristics of carcinogens that form the framework for current IARC mechanistic evaluations.
Funding source: None

Mechanical induction of the tumorigenic β-catenin pathway by tumour growth pressure

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The tumour microenvironment may contribute to tumorigenesis due to mechanical forces such as fibrotic stiffness or mechanical pressure caused by the expansion of hyper-proliferative cells. Here we explore the contribution of the mechanical pressure exerted by tumour growth onto non-tumorous adjacent epithelium. In the early stage of mouse colon tumour development in the Notch+Apc+/1638N mouse model, we observed mechanistic pressure stress in the non-tumorous epithelial cells caused by hyper-proliferative adjacent crypts overexpressing active Notch, associated with increased Ret and beta-catenin signalling. We thus developed a method that allows the delivery of a defined mechanical pressure in vivo, by subcutaneously inserting a magnet close to the mouse colon. The implanted magnet generated a magnetic force on ultra-magnetic liposomes, stabilized in the mesenchymal cells of the connective tissue surrounding colonic crypts after intravenous injection. The magnetically induced pressure quantitatively mimicked the endogenous early tumour growth stress in the order of 1,200 Pa, without affecting tissue stiffness, as monitored by acoustic strain imaging and shear wave elastography. Exertion of pressure mimicking that of tumour growth led to rapid Ret activation and downstream phosphorylation of beta-catenin on Tyr654, which impairs its interaction with the E-cadherin in adherens junctions, and which was followed by beta-catenin nuclear translocation after 15 days. As a consequence, elevated expression of beta-catenin-target genes was observed at 1 month, together with crypt enlargement accompanying the formation of early tumorous aberrant crypt foci. Mechanical activation of the tumorigenic beta-catenin pathway, which is conserved from early embryos beta-catenin dependent mechanical induction of developmental patterning genes expression, suggests unexplored modes of tumour propagation based on mechanical signalling pathways in healthy epithelial cells surrounding the tumour, which may contribute to tumour heterogeneity.

Fernandez-Sanchez, Barbier et al, Nature 2015, Jul 2;523(7558):92-5. doi: 10.1038/nature14329. Epub 2015 May 11

PREVENTION & MORTALITY REDUCTION - Challenges in primary prevention

Wednesday 8 June - 14:40-15:00

Invited speaker: Adèle Green
Senior Scientist at QIMR Berghofer Medical Research Institute, Brisbane, Australia and Senior Research Scientist at Cancer Research UK Manchester Institute, United Kingdom

Adèle Green is a Senior Scientist at QIMR Berghofer Medical Research Institute in Brisbane, Australia (www.qimrberghofer.edu.au) and is a Senior Research Scientist at Cancer Research UK Manchester Institute (www.cruk.manchester.ac.uk) and Professor of Epidemiology at the University of Manchester (www.manchester.ac.uk). She trained in medicine, and her research career has focused on the causes, management and prevention of cancer, especially melanoma and other skin cancers, ovarian cancer and cancer in Aboriginal and Torres Strait Island people, for which she has received various awards. Her current research program includes studies of prevention of skin cancers in organ transplant recipients and survival and quality of life of patients with high-risk primary melanoma, as well as collaborative studies of gynaecological cancer, cancer risk prediction and clinicopathologic studies of melanoma. She has served on many IARC committees, including the Scientific Council, and is currently a member of the International Commission on Non-Ionizing Radiation Protection (ICNIRP), Chair of Cancer Australia's Research and Data Advisory Group, and a Member of the Australian Paediatric Cancer Registry Advisory Committee and the Australian Radiation Health and Safety Advisory Council.

ABSTRACT: Challenges in primary prevention of cancer
Effective primary prevention of cancer requires
1) identification of likely causal or protective agents that potentially can be modified in the target population;
2) demonstration of likely benefit from appropriate intervention; and
3) that cultural, social, political or economic barriers to preventive activities can be surmounted. Each of these steps presents challenges.
1) For some common cancers eg certain haematological cancers, prostate cancer, few if any modifiable causal factors have been identified by epidemiologic studies, though future collaborations with molecular biologists /epigeneticists may extend current knowledge.
2) In various populations, studies of attributable and preventive fractions of cancer show a sizable proportion may be prevented each year if exposure to common causal factors were avoided. However these studies have been limited by lack of international consensus about various causal associations and inadequate prevalence data for candidate exposures. Also the unknown but lengthy latent periods between exposure and disease means that optimal timing for preventive intervention is uncertain.
3) Even when causal agents are known or strongly suspected, ingrained socio-cultural traditions eg dietary customs, and lifestyle habits eg smoking and sunbathing, resist change. Far greater investment in prevention research is required to improve knowledge about effective implementation of preventive strategies, while political will for long-term primary prevention also needs evidence that such programs are economically sound investments compared with the cost-effectiveness of late-stage cancer treatment. Finally wide cooperation between governments, not-for-profit and other non-communicable disease (diabetes, heart disease) organisations is needed to sustain the concerted action needed to lower the incidence rates of common cancers.

Long-term risk of upper digestive cancer in people with different baseline characteristics and supplementation with various combinations of multivitamins and minerals: 27-year Follow-up Results from the Linxian Nutrition Intervention Trial

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- **Purpose:** To investigate the long-term risk of upper digestive cancer in people with different baseline characteristics and supplementation with various combinations of multivitamins and minerals, and to provide suggestions for primary prevention of cancers.
- **Methods:** The Nutrition Intervention Trial was a randomized, double-blind, placebo-controlled trial conducted in Linxian, China. 29,584 Chinese residences without cancer initially aged 40-69 years old were randomly assigned, accepting nine nutrients in combination into four factors based on a one-half 24 fractional factorial design. The intervention began from March 1, 1986 to May 31, 1991, and follow-up through March 31, 2013. Risk factors and demographic information were interviewed for by a questionnaire, and physical examination was performed to each participant; Mortality of different diseases was collected through village doctors and Cancer Registry.
- **Results:** During 27.08 years follow-up, there were 18,210 subjects died, including 5443 from cancer. Male, elder age, smoking, and low BMI was associated with an increased risk of esophageal cancer (EC), and goiter was associated with a high risk of gastric cancer. Though the intervention group D had lower overall mortality, cancer mortality, and EC mortality within 10 years after cessation of the intervention, it disappeared at longer period of follow-up. The benefits were mostly attributable to subjects younger than 55 years at baseline, and was still evident on gastric cancer mortality (HR= 0.85, 95%CI= 0.75 to 0.97) and cardiac cancer mortality at 27-year follow-up (HR= 0.80, 95%CI= 0.69 to 0.93), but was not significant for the old group.
- **Conclusions:** Appropriate lifestyles are recommended for the long-term cancer prevention. Younger-age, long-term supplementation with selenium, vitamin E, and beta-carotene is essential to keep the sustained effects on the reduction of gastric cancer and other cancer mortality in poor nutrient population.
- **Funding Source:** National Cancer Institute contracts (HHSN261201200034C to Cancer Hospital, Chinese Academy of Medical Sciences)

Development and validation of a synthetic risk model for stratified disease prevention for breast cancer

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The risk-benefit balance of disease prevention strategies largely depends on the underlying risk of developing the disease. Therefore, risk prediction tools that can accurately stratify a population into categories with sufficiently distinct risks are critical to identify those most likely to benefit. With the increasing relevance of genetic testing for assessment of disease it is important for these tools to integrate information on genetic and environmental risk factors for disease. We developed a flexible risk model-building tool (iCARE) and used it to build a synthetic risk model for prediction of breast cancer risk in the general population. The model included information on age, reproductive and hormone use history, benign breast disease, lifestyle, family history and a polygenic risk score (PRS) based on 77 single nucleotide polymorphisms (SNPs). Predictions were based on estimates of risk factor relative risks reported in the

literature, and risk factor frequencies in the UK population. UK age-specific incidence and mortality rates were used to obtain estimates of absolute risk. Model calibration for relative and absolute risk predictions was assessed in a UK cohort of 106,637 women with a median age of 48 years who were included in the Breakthrough Generations Study. During an average follow-up period of 6.1 years, 1,420 women developed invasive breast cancer. The synthetic model showed good calibration for 5-year risk and had an AUC of 68% (95%CI 63-71%) for women 50 years of age or younger and 66% (95%CI 63%-69%) for women older than 50 years. This level of risk stratification could have utility to better inform decisions on risk reduction strategies for breast cancer. The flexible modelling approach we developed can be easily extended to include additional risk factors or to build models for other diseases

Worldwide Hpv Vaccination Coverage For Cervical Cancer Prevention

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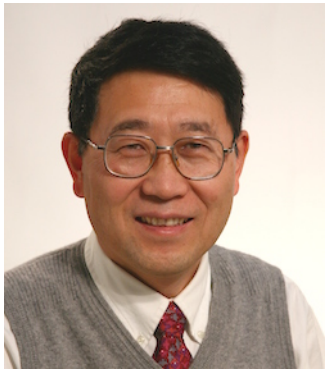
Purpose:
Since their licensure in 2006, HPV vaccines have been progressively introduced in many countries. By 2015, 64 countries have implemented national HPV vaccination programs and 37 have conducted demonstration projects. However, the national guidelines, targeted ages, financing and delivery strategies differ considerably between countries and even within countries at regional level. We aim to describe and estimate actual global coverage considering all these variations.
Methods
Compilation of the most comprehensive database to date on publicly-funded National HPV Immunization Programmes, including: conversion of all retrieved coverages from multiple sources into birth cohort specific coverages, design of an imputation algorithm to treat missing data, and the use of global population estimates and projections. These procedures allow continuous monitoring and production of vaccination coverage trends, together with the use of cancer statistics to approximate the expected reduction on cervical cancer in vaccinated cohorts.
Results
About 118 million women have been targeted through these programmes, but only 1% from low or lower-middle income countries. 47 million (95%CI:39-55) women received the full course of vaccine and 59 million (95%CI:48-71) at least one dose. In more developed regions 33·5%(26·0-42·1%) of girls aged 10-20 years received the full-course, but only 2·7%(1·8-3·7%) in less developed regions. We estimated a reduction of about 380,000 future cervical cancer cases in these vaccinated cohorts. The expected impact will be higher for Latin American girls, despite a lower number vaccinated (13 million) compared to high income countries (32 million).
Conclusions
Despite the high number of girls successfully vaccinated between 2006 and 2014 worldwide (47 million), there are still many populations that have not yet had the possibility to be vaccinated. The monitoring of the worldwide HPV vaccination coverage will provide a critical tool to assess the expected impacts and benefits of this important prevention strategy.
Funding: PATH (USA); ISCIII, AGAUR(Spain)

PREVENTION & MORTALITY REDUCTION - Screening and early detection

Wednesday 8 June - 16:00-16:20



Invited speaker: You-Lin Qiao

Professor and Director, Department of Cancer Epidemiology, National Cancer Center, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Before returning to China in 1997, You-Lin Qiao, MD, PhD, trained for 11 years at Johns Hopkins University School of Hygiene and Public Health and Cancer Prevention Studies Branch, NCI/NIH, USA. He is also Director of the International Collaboration Department, Cancer Foundation of China, and Deputy Director of the National Expert Committee for Cancer Screening and Prevention of the Ministry of Health in China. He is an author on over 480 peer-reviewed publications in both English and Chinese. As an expert in cancer prevention and control, he served in the WHO Director-General's Cancer Control Advisory Committee and WHO Cancer Technical Advisory Groups, helping to promote cancer prevention and control programmes in developing countries. He is involved in many national and international projects to study the etiology, primary intervention, and early detection of a variety of cancers through multidisciplinary and global collaborations. He was awarded the IARC Medal of Honour in 2011

ABSTRACT: Experience with careHPV implementation in China

China like all countries faces many challenges in providing universal, high quality, affordable healthcare to its people. During the year 1988-2008, the morbidity and mortality of cervical cancer among Chinese women increased continuously, especially for rural women which the crude mortality in 2008 was almost five times higher than 1988. The average age of women diagnosed as cervical cancer was five years younger. Effective preventive measures were imminently needed to curb the deterioration.

By a grant support from Bill Gates Foundation, in 2007, careHPV was successfully proved to be accurate, fast, reproducible, and low-cost by our team cooperated with PATH, IARC, CICAMS and QIAGEN Inc. Personnel with limited laboratory experience could perform it correctly after simple training procedure, which is promising for use in LMICs. Besides, the following study implied that careHPV 16/18/45 might be used in LMICs for triaging HPV-positive women.

Inspired by the experience from China, more implementing studies were conducted in LMICs, such as Nicaragua, Uganda, India and Laos. We believe more women from developing countries would be benefited after careHPV test get the pre-qualification from WHO.

HPV testing is now recommended in the WHO guidelines as primary. In 2015, a nationwide implementing demonstration program of HPV testing as the primary screening was launched, aiming at evaluating the real world performance by local health providers with fundamental infrastructures. The clinical utility, health economic effectiveness, and acceptability of careHPV test among screened women, health providers, and government officials will be evaluated. The final results of the 3-years study are expected to provide more convincing evidence and practical advice for policy maker in future population-based HPV screening programs in whole China. It is the most promise candidate for HPV as primary screening of cervical cancer among 5 million women in next fiscal year.

The mortality for lung cancer is reduced in a Low Dose CT Scan Screening program compared with conventional public health surveillance for former workers exposed to asbestos

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Purpose
To evaluate, in the area of the largest Italian shipyard, whether participation in a Low Dose CT Scan Screening (LDCT) (ATOM002 Study) is effective in reducing mortality for lung cancer in asbestos-exposed former workers, compared with conventional health surveillance program, often provided without a strict protocol and based on physician–expert's opinion.
Methods
Within a cohort of 2,433 occupationally asbestos-exposed men, enrolled in a public health surveillance program, we compared mortality and survival between participants in a screening program based on LDCT (n=926) and non-participants (n=1,507). For external comparison, we estimated the standardized mortality rate ratio (SMR) using Friuli Venezia Giulia regional standard rates (SMR_FVG) and Italian standard rates (SMR_ITA). For internal comparisons we performed Cox proportional hazard models to assess survival for all causes, all cancers, lung cancer and malignant neoplasm of the pleura. Final models were adjusted for smoking habits, age at start of follow-up, level of exposure to asbestos and Charlson-Quan comorbidity index.
Results
A reduction in mortality for lung cancer was found among subjects who participated in the ATOM002 study: SMR_FVG=0.55 IC95% 0.24-1.09, SMR_ITA=0.51 IC95% 0.22-1.01. In the group of other workers exposed to asbestos who did not participate in the ATOM002 study the SMR_FVG was respectively 2.07 (IC95% 1.53-2.73) and 1.98 (IC95% 1.47-2.61). Internal comparisons show a significant reduction in mortality for lung cancer in ATOM002 participants (HR=0.41 IC95% 0.17-0.96). Mortality was also reduced for all causes (HR=0.61 IC95% 0.44-0.84), but not for all cancers (HR=0.97 IC95% 0.62-1.50) and malignant neoplasm of the pleura (HR=0.86 IC95% 0.31-2.41).
Conclusions
In our cohort, health surveillance carried out with a strict 2-year protocol based on LDCT screening was more effective in reducing mortality for lung cancer than conventional public health surveillance
Funding source
This study was carried out with no external funding.

Factors Contributing to Delays in Diagnosis of Breast Cancers in Ghana, West Africa

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Late diagnoses of breast cancer are common throughout sub-Saharan Africa, resulting in many poor prognoses. To identify associated causes, we utilized data from a population-based case-control study conducted in three hospitals in Accra and Kumasi, Ghana in which cases comprised women presenting with suspicious breast lesions. Interviews focused on potential breast cancer risk factors as well as factors that might contribute to presentation delays. We calculated odds ratios (OR) and 95% confidence intervals (CI) for various factors comparing invasive breast cancers with masses larger than 5 cm. (61.7% of the 827 cases with measurable lesions) to smaller lesions. In contrast to at least one other study, distance from residence to a medical facility was only marginally associated with larger tumors, likely reflecting the restricted catchment area of study subjects. In analyses adjusted only for age and study site, factors significantly associated with larger masses were low levels of education, being widowed/separated/ divorced, lack of ownership of such items as a car or computer, practicing no or a traditional religion, not regularly seeing a doctor or nurse, financial problems in paying for medical care, frequent use of herbal medications/treatment, and delays in seeking care once symptoms arose. In multivariate analyses, independent predictors of larger masses were low levels of education (OR=2.17, 95% CI 1.42-3.31 no formal vs. >senior secondary education), being widowed/separated/ divorced (OR=1.71, 1.19-2.44 vs. currently married), frequent use of herbal medications/treatment (OR=1.73, 0.99-3.03 for >3x/day usage vs. none), and delays in seeking care (OR=1.50, 1.04-2.17 for >2 vs. <1 month). These findings suggest that additional communication, particularly among poorly educated women, should stress the importance of prompt medical attention for unusual breast symptoms. Given higher risks of larger tumors among women availing themselves of traditional medicine, the involvement of traditional healers in outreach programs would appear advantageous.

Comprehensive evaluation of promising biomarkers for lung cancer risk prediction

MATTIAS JOHANSSON, INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC), FRANCE
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[1] *International Agency for Research on Cancer*
[2] *University of Texas MD Anderson Cancer Center*
[3] *Imperial College, London, United Kingdom*

Background
Lung cancer will remain the number one cancer killer worldwide for the foreseeable future (Globocan 2012). Although low-dose CT screening has been shown to reduce mortality, there is an urgent need to improve risk prediction models to identify those subjects at high risk and most likely to benefit from screening in order its improve the screening efficacy (PMID: 23697514, 25372087).
Methods
We have assembled a panel of promising blood-based risk biomarkers for lung cancer that are currently being validated in two large prospective cohorts (EPIC and NSHDS) in order to identify a set of validated risk markers for use in lung cancer risk assessment. Biospecimens from these cohorts include pre-diagnostic plasma from 550 former and current smoking lung cancer cases that were diagnosed within 5 years of blood draw, along with 1,100 matched controls.
Results
Preliminary data indicate that blood-based biomarkers of lung cancer risk have a strong potential to improve on questionnaire-based risk prediction models for lung cancer (PMID: 26282655). In particular, based on a panel of 18 markers analyzed in the NSHDS study, we selected the 4 most risk informative markers and observed c-statistics of 0.80 using smoking history information alone, and 0.91 after incorporating additional the additional 4 risk markers. During the meeting we will present detailed results of the individual risk biomarkers and their associations with lung cancer risk up to 2 years prior to diagnosis, as well as an assessment of the extent to which they can improve traditional risk prediction models.

PARALLEL SESSIONS

THURSDAY 9 JUNE

EPIDEMIOLOGY - Nutrition, obesity and exercise

Thursday 9 June - 11:00-11:20

Invited speaker: Christine Friedenreich
Cancer epidemiologist, Department of Cancer Epidemiology and Prevention Research, Cancer Control Alberta, Alberta Health Services. Adjunct Professor, Faculties of Medicine and Kinesiology, University of Calgary, Canada

Dr Friedenreich is a cancer epidemiologist with the Department of Cancer Epidemiology and Prevention Research (CEPR) of CancerControl Alberta, Alberta Health Services and an Adjunct Professor in the Faculties of Medicine and Kinesiology of the University of Calgary. She holds a Health Senior Scholar career award from Alberta Innovates-Health Solutions and in 2012 was named the Alberta Cancer Foundation's Weekend to End Women's Cancers Breast Cancer Chair at the University of Calgary. Dr Friedenreich is the Scientific Director for CEPR and the Division Head for the Division of Preventive Oncology, Department of Oncology, Faculty of Medicine, University of Calgary. Dr Friedenreich completed her doctorate in Epidemiology at the University of Toronto in 1990 and postdoctoral work at the International Agency for Research on Cancer (IARC) in Lyon, France and at the University of Calgary between 1990 and 1994. In 2004–2005, Dr Friedenreich was a Visiting Scientist at IARC. In 2013, Dr Friedenreich was a co-recipient of the Canadian Cancer Society's O. Harold Warwick Prize. Dr Friedenreich's research is focused on understanding the role of physical activity in reducing the risk of developing cancer and in improving quality of life and survival after cancer diagnosis. She has conducted over 35 observational epidemiologic and randomized controlled intervention trials in this area.

ABSTRACT: Physical Activity and Cancer Control: From Observational to Experimental Evidence
Substantial evidence exists for a beneficial effect of physical activity across the cancer continuum. To date, nearly 400 studies have examined some aspect of physical activity and how it is related to cancer risk and about 40 studies have investigated the role of activity in cancer survival. There is "convincing" evidence that physical activity reduces the risk of breast, colon and endometrial cancers. In total, 80 out of 111 studies in breast cancer have demonstrated, on average, about a 20-25% risk reduction when comparing the least to most physically active participants in these studies. In addition, evidence of a dose-response effect of decreasing risk with increasing activity levels exists in 53 of 88 studies on breast cancer. For colon cancer, 79 out of 100 studies have found reduced risks of about 25-30% and a dose response in 43 of 56 studies. The evidence for endometrial cancer is also consistent with 27 out of 32 studies observing 25-30% decreased risks and a dose-response in 14 out 23 studies. Physical activity done before and after diagnosis also appears to reduce the risk of recurrences and deaths associated with breast, colon and prostate cancers with reductions in cancer-specific mortality around 25-30%. Randomized controlled exercise intervention trials have found that the main mechanisms involved in the association between physical activity and cancer risk and survival are effects on adiposity, endogenous sex steroids, insulin resistance and inflammation. Other possible pathways involve effects on genomic instability, DNA methylation and oxidative stress. On-going cohort and randomized controlled trials are specifically addressing some of the limitations in previous studies by incorporating objective measurements of activity, sedentary behaviour, health related fitness. Future priorities in this field include more molecular epidemiologic studies that target the underlying biologic pathways as well phase III randomized controlled trials of exercise in cancer survivors.

Thursday 9 June - 11:20-11:40

Invited speaker: Michael Leitzmann
Chair of the Department of Epidemiology and Preventive Medicine, University of Regensburg, Germany

Michael Leitzmann received an MD from the University of Berlin and completed an MPH and a DrPH at the Harvard School of Public Health. He subsequently joined the Division of Cancer Epidemiology and Genetics of the United States National Cancer Institute as investigator. In 2008, he was appointed Professor and Chair of the Department of Epidemiology and Preventive Medicine at the University of Regensburg, Germany. He leads an interdisciplinary team of scientists on research related to epidemiology, biostatistics, bioinformatics, nutritional health, and sociology. A major focus is the relationship between energy balance and cancer. This includes investigations of the independent and joint relations of body mass, physical activity, sedentary behavior, and diet in relation to cancer incidence and survival. The energy balance research is characterized by the development and application of methods to validly measure body composition and energy expenditure in large populationbased cohorts. Professor Leitzmann has published more than 200 research articles, serves as editorial board member and reviewer to numerous biomedical journals, and acts as scientific consultant to several national and international advisory boards and research institutions. He is a member of the International Epidemiological Association, the American College of Epidemiology, and the Society for Epidemiologic Research.

ABSTRACT: Recent Findings on Diet, Nutrition, Physical Activity and Cancer: the WCRF/AICR Continuous Update Project

Objective: Evidence suggests that diet and lifestyle affect cancer incidence and survival. The WCRF/AICR Continuous Update Project comprehensively summarizes published epidemiologic data regarding such relationships.
Methods: Data are summarized/meta-analyzed using standard methodology and are subsequently independently evaluated by a panel of international scientists.
Results: Liver cancer: based on 34 studies and 24,600 liver cancer cases, there is strong evidence for increased liver cancer risk with overweight/obesity and intakes of alcohol and aflatoxin-contaminated foods. In contrast, there is strong evidence for decreased liver cancer risk with drinking coffee, and limited evidence for decreased liver cancer risk with consuming fish and engaging in physical activity. Gallbladder cancer: data from 14 studies and 8,300 gallbladder cancer cases reveal strong evidence for increased gallbladder cancer risk with overweight/obesity. Prostate cancer: a review of 104 studies and 191,000 cases of prostate cancer shows strong evidence that overweight/obesity are associated with increased risk of advanced prostate cancer. By comparison, consuming beta-carotene is unlikely to substantially affect prostate cancer risk. Also, there is limited evidence for increased prostate cancer risk with high intakes of dairy products and calcium. Stomach cancer: based on 89 studies and 77,000 stomach cancer cases, there is strong evidence for increased risk of stomach cancer with consumption of alcohol and foods preserved by salting. Also, processed meat intake is associated with increased risk of non-cardia stomach cancer, whereas being overweight or obese is related to increased risk of cancer of the cardia. There is limited evidence that consuming grilled or barbecued meat and fish is associated with increased risk of stomach cancer. In addition, there is some evidence to suggest that consuming little or no fruit is related to increased risk of stomach cancer, and that consuming citrus fruit decreases the risk of stomach cardia cancer. Breast cancer survivorship: based on data from 85 studies and 164,416 women, a healthy body weight, physical activity, and greater consumption of fiber and soy are related to increased survival, whereas a diet high in fat and saturated fat before diagnosis is associated with decreased survival. However, the latter findings may be confounded by limitations in the quality of the studies reviewed, which precludes making specific recommendations.
Conclusions: The presentation concludes with a brief summary of future research priorities in the area of diet, nutrition, physical activity and cancer.

Risk Factors For Premenopausal Breast Cancer Among Latin American Women: The Precama Study

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-Purpose
Breast cancer (BC) is the most common cancer among Latin American (LA) women with a high proportion of cancer occurring among premenopausal women. Little is known about risk factors, especially for aggressive phenotypes. Therefore we are conducting a multicenter population-based case-control study to evaluate the etiology of molecular subtypes of premenopausal BC in LA.
-Methods
Cases and controls (aged 45 years or less) are recruited in Chile, Colombia, Costa Rica and Mexico, and matched on age and center. Standardized protocols are used to collect clinical and exposure data (reproductive history, lifestyle, anthropometry, diet, and environment), biological specimens, and tumor samples. Molecular subtypes are defined by immunohistochemistry analyzed at a central laboratory (FHCRC). Statistical analyses were conducted using logistic regression models adjusting for potential confounding factors.
-Results
To date, the study includes 466 subjects (268 cases and 198 controls). Sixty-one percent of tumors are luminal A, and 23% are triple negative. Parity, younger age at first or last pregnancy, breastfeeding , body mass index, waist and hip circumferences have a significant protective effect on BC risk. Intake of processed food (OR=1.43; 1.00- 2.05 per 1 portion/day increase), milk products, carbohydrates and fruits are associated with an increased risk of breast cancer, while vegetable intake (OR=0.88; 95% CI: 0.83-0.93 per 1 portion/day) is protective. Moderate physical activity is protective while sedentary behavior increases breast cancer risk (OR=1.10 95% CI 1.02-1.18 per 1hr/week).
-Conclusions
These preliminary results suggest that lifestyle factors are involved in the incidence of premenopausal breast cancer in LA women. A larger number of cases and controls in the near future will allow determining risk factors for specific phenotypes and support target prevention and control of the disease.
-Funding source
Union for International Cancer Control; Pan American Health Organization; and International Agency for Research on Cancer.

Diet and Cancer in a U.S. Cohort Containing Many Vegetarians

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PURPOSE: The purpose of this study is to evaluate associations between dietary patterns, foods, nutrients and minerals, and risk of common cancers.

METHODS: Adventist Health Study-2 is a cohort of 96,000 subjects from the U.S. and Canada, established between 2002-7. About half are vegetarians and the others eat meat at least weekly. This provides a wide range of dietary habits, and many cohort members represent a region of intake of certain foods/nutrients uncommonly found in other studies. Dietary habits were measured by a validated food frequency questionnaire at study baseline. A calibration study of 1100 representative subjects also completed 6 structured 24 hour recalls. Incident cancers were ascertained by matching with state and provincial cancer registries. Analyses used Cox proportional hazard analyses with energy-adjustment, and where appropriate regression calibration for measurement error correction.

RESULTS: Adventists have substantially lower incidence rates of several common cancers. Vegan

vegetarians only, have 1/3 lower incidence of prostate cancer compared to non-vegetarians. Dairy consumption is significantly positively, but consumption of cooked tomatoes also intake of alpha linolenic acid are negatively, associated with risk of prostate cancer. Despite a very low average intake of processed red meat, a significant association is found with risk of colorectal cancer with a much stronger slope than reported from meta-analyses of other studies. Calcium consumption is significantly negatively associated with colon (but not rectal) cancer, and dairy kcals are significantly negatively associated with rectal (not colon) cancer. For breast cancer there is a negative association with intake of soy isoflavones (half of this population eat at Asian levels) and an apparent advantage of substituting these for dairy foods.

CONCLUSIONS: In this special population prostate, colorectal and breast cancers are associated with diet in ways that often have known plausible biological mechanisms.

FUNDING: National Cancer Institute, World Cancer Research Fund

EPIDEMIOLOGY - Occupation

Thursday 9 June - 14:30-14:50

Invited speaker: Jack Siemiatycki
Professor of epidemiology, Université de Montréal, Canada

Jack Siemiatycki has a PhD in epidemiology and is currently Professor of epidemiology at Université de Montréal. He has held a Canada Research Chair and is currently the Guzzo-SRC Chair in Environment and Cancer, and is a Fellow of the Canadian Academy of Health Sciences. He has served on over 100 national and international boards and expert advisory bodies for academic and government agencies in Canada, the USA and Europe, such as the National Cancer Institute of Canada, the Canadian Institutes of Health Research, the National Cancer Institute (USA), the Institut de Recherche en Santé publique (France), INSERM (France), the American College of Epidemiology, IARC and WHO. He has served on the editorial board of the American Journal of Epidemiology and other journals, and has chaired many grant review panels. Most of his research has been in the area of environmental and occupational etiology of cancer. He is known for having developed novel and influential design and exposure assessment methods in the occupational etiology of cancer, and for results from a variety of case-control studies concerning a wide variety of possible environmental carcinogens. Professor Siemiatycki has been an invited speaker at over 150 meetings or seminars throughout the world, including for President Clinton's Cancer Panel, and as a Distinguished Lecturer at the United States National Cancer Institute. He has authored or co-authored over 200 peer-reviewed articles, 50 scientific reports, and 150 invited presentations or posters. He was the principal expert witness in the largest ever successful class action lawsuit against the tobacco industry

ABSTRACT: Occupation and Cancer
Until recently, occupational studies represented one of the most active and fruitful domains of research in cancer epidemiology. Nearly half of known human carcinogens were discovered because of observations or research among workers. It is estimated that in developed countries, as much as 5%-10% of cancers may be attributable to known occupational risk factors. The identification of occupational carcinogens is not only important for occupational health, but many of the identified carcinogens find their way into the general environment. We will review the current state of knowledge regarding occupational cancer. We will explore the causes and consequences of the recent decline in research activity on occupational causes of cancer, and some of the methodological challenges in this area.

Pesticide use and cancer incidence among spouses of pesticide applicators in the Agricultural Health Study

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[5] Yale University School of Public Health, New Haven, CT, USA

Objectives: Pesticides have been linked to cancer risk in some epidemiologic studies; however most evaluations have been conducted in predominantly male populations. We evaluated personal use of specific pesticides, including organophosphate insecticides (OPs) and cancer incidence among female spouses of pesticide applicators in the prospective Agricultural Health Study cohort.
Methods: At enrollment (1993-1997) spouses provided information about ever use of specific pesticides, demographic information, reproductive health history, and other potential confounders. We used Poisson regression to estimate relative risks (RRs) and 95% confidence intervals (95% CIs) for all cancers diagnosed through 2010 for North Carolina and 2011 for Iowa.
Results: Among 30,003 women, 60% reported personally using any pesticides. Among the 25.9% who reported OP use, 718 OP were diagnosed with cancer. Any OP use was associated with an elevated risk of breast cancer (RR = 1.20, 95% CI: 1.01, 1.43). Malathion, the most commonly reported OP, was associated with increased risk of thyroid cancer (RR = 2.04, 95% CI: 1.14, 3.63) and decreased risk of non-Hodgkin lymphoma (RR = 0.64, 95% CI: 0.41, 0.99). Diazinon use was associated with ovarian cancer (RR = 1.87, 95% CI: 1.02, 3.43).
Conclusions: This first comprehensive analysis of OP and other pesticide use in relation to cancer risk among women showed increased risks with OP use and several hormonally-related cancers. Further work evaluating other routes of exposure among farm women is needed for OPs and other chemicals.

Exposure Response Analyses of Asbestos and Lung Cancer Subtypes in a Pooled Analysis of Case-Control Studies in Europe and Canada

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Background: The evidence is limited regarding risk and the shape of the exposure-response curve at low levels of asbestos exposure. We estimated the exposure-response for occupational exposure to asbestos and assessed the joint effect of asbestos exposure and smoking by sex, and lung cancer subtypes (adenocarcinoma, squamous cell lung carcinoma, small cell lung carcinoma) in general population studies.
Methods: Fourteen case-control studies conducted between 1985 and 2010 from Europe and Canada were pooled, including 16,901 lung cancer cases (13,605 men, 3296 women) and 20,965 controls (16451 men, 4514 women) with detailed information on tobacco habits and lifetime occupations. A quantitative job-exposure-matrix (SYN-JEM) was developed to estimate job-, time period-, and region-specific exposure levels. Fiber years (ff/ml-years) were calculated for each subject by linking SYN-JEM with individual

occupational histories. Unconditional logistic regression models were fitted to estimate odds ratios (OR), 95% confidence intervals (CI), and trends.
Results: The OR for the highest quartile of cumulative asbestos exposure (>2.8 ff/ml-years) was 1.38 (95%CI 1.27-1.50) in men and 1.22 (95% CI 0.84-1.78) in women. In men, increasing lung cancer risk was observed with increasing exposure to asbestos in all smoking categories; and for all major subtypes of lung cancer. In women, the asbestos related lung cancer risk was increased for all subtypes in current smokers with ORs approximately 2-fold. The interaction between asbestos exposure and smoking was more than additive among men and women for all lung cancer types, although not statistically significant for all combinations of subtype and gender; moreover the interaction between asbestos and smoking among men did not significantly deviate from multiplicativity.
Conclusions: Our results in men showed an excess risk of lung cancer and its subtypes at low levels of cumulative exposure, with an exposure-response slope steeper in this exposure range than at higher previously studied levels.

Bladder cancer and occupational exposure to diesel and gasoline engine emissions among Canadian men

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Purpose: IARC has classified diesel engine emissions (DEE) as a carcinogen and gasoline engine emissions (GEE) as a possible carcinogen based on evidence for lung cancer. The purpose of this study was to investigate the effect of exposure to DEE and GEE on bladder cancer in occupationally exposed men using data from the Canadian National Enhanced Cancer Surveillance System.
Methods: This analysis included 658 cases and 1360 controls recruited from seven Canadian provinces (1994-97). Lifetime occupational history, including job title, status and duties, and information on possible cancer risk factors was obtained by self-reported questionnaire. Concentration and frequency of occupational exposure to DEE and GEE, and a measure of the reliability of exposure assessment, was assigned for each job using a job-exposure matrix supplemented by expert review. Exposure metrics were modeled as ever-never, highest attained concentration, highest attained frequency, duration, and cumulative exposure. Logistic regression was used to calculate adjusted odds ratios and 95% confidence intervals.
Results: Relative to unexposed, men ever exposed to high concentrations of DEE were at an increased risk of bladder cancer (OR=1.64, 95%CI=0.87–3.08), and those with >10 years of exposure to DEE at high concentrations had a greater than twofold increase in risk (OR=2.45, 95%CI=1.04–5.74). Increased risk of bladder cancer was also observed with >30% of work time exposed to GEE (OR = 1.59, 1.04–2.43) relative to the unexposed, but only among men that had never been exposed to diesel engine emissions.
Conclusions: Our results suggest that occupational exposure to high concentrations of diesel engine emissions may increase the risk of bladder cancer.
Funding source: This research was funded by the Workplace Safety and Insurance Board (Ontario), WSIB#10011, with support from the Ontario Occupational Cancer Research Center and Health Canada. MÉ Parent received funds from Fonds de recherche du Québec-Santé (FRQS).

EPIDEMIOLOGY - Radiation

Thursday 9 June - 16:00-16:20

Invited speaker: Shunichi Yamashita
Trustee and Vice-President, Nagasaki University and part-time Vice-President, Fukushima Medical University, Japan

Shunichi Yamashita graduated from the Nagasaki University School of Medicine in March 1978 and spent almost three years from July 1984 to March 1987 as the first endocrine research fellow at the Cedars-Sinai Medical Center, Los Angeles. In October 1990, Dr Yamashita became Professor of Molecular Medicine and International Radiation Health at the Atomic Bomb Disease Institute, Nagasaki University School of Medicine. He has been deeply involved in Chernobyl and Semipalatinsk medical aid and research projects for 25 years. Professor Yamashita is the Adviser to the Governor of Fukushima Prefecture on Health Risk Management immediately after the Fukushima Nuclear Power Plant (NPP) accident. He was dispatched from Nagasaki University to Fukushima for two years after the Fukushima NPP accident. Since April 2013, he has been mainly in Nagasaki University but partly in Fukushima Medical University. He is still in charge of the Fukushima Health Management Survey, especially for the thyroid examination as a part-time Vice-President of Fukushima Medical University. Professor Yamashita is the Director of the WHO collaborating centre for research on Radiation Emergency Medical Preparedness and Response Network, council member of the Science Council of Japan and a member of the Nuclear Disaster Expert Group of the Prime Minister's Office in Japan. He is the former President of the Japan Thyroid Association.

ABSTRACT: Radiation and Health Effects: a gap between understanding of real radiation health risk and public risk perception, beyond the accumulated scientific knowledge

In terms of basic data on radiation and health, the Radiation Effects Research Foundation's (RERF) long-term survey study of the atomic bomb survivors is the most precise for assessing the consequences of external radiation exposure and cancer death rates. The painfully tragic atomic bombing, as well as other data related to radiation exposures, contributed to the accumulation of scientific knowledge and the creation of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), which reviews the sources and effects of ionizing radiation every few years. In addition, the atomic bomb survivor follow-up studies have formed the bedrock of the International Commission on Radiological Protection's (ICRP) activities. The ICRP has been working since late 1920-es toward the standards and policy proposals for nuclear safety, such as workplace regulations regarding radiation exposure. The International Atomic Energy Agency (IAEA) formulated its Basic Safety Standards (BSS) based on both the scientific knowledge and policy proposals. Each country, including Japan has devised, on the basis of these recommendations, nuclear safety measures according to their individual circumstances.
However, listening to the discussions and debates on radiation exposure risks since the Fukushima Nuclear Power Plant accident to date, it appears that the international standards, which use the linear no-threshold (LNT) cancer risk model, established from the standpoint of radiation protection do not reflect the real health risks themselves. In particular, the meaning of LNT model and biological effects of low dose radiation exposure have been unsatisfactorily understood. Thus, an inadequate understanding stemming from insufficient knowledge of radiation biology and molecular epidemiology has been exposed.
There is an urgent need in narrowing the gaps between our scientific understandings and public risk perception, which sometimes manifests in fear and anxiety, and even in an anger toward radiation and radioactivity. Here, the current situation and relevant problems of Fukushima will be introduced focusing on the Fukushima Health Management Survey results.

New Results from the UK-NCI Pediatric CT scans study

AMY BERRINGTON, NCI, UNITED STATES
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Purpose: CT scans save lives and avoid unnecessary surgery. However, they may also be associated with an increased risk of cancer, particularly in children who are more sensitive to radiation exposure. We published the first evidence of the potential risk of cancer from pediatric CT scans in our UK cohort. Here we present results from analyses using new data on underlying conditions, dose uncertainty and the first results for lymphomas.
Methods: Retrospective record linkage cohort study of approximately 180,000 patients who underwent CT scans between before 2002 aged <22 years in the UK. We collected and reviewed clinical information to assess potential bias from underlying conditions and a set of 1000 CT films to assess the impact of dose uncertainty. We analysed the risk of leukemia/MDS (n=74), brain tumors (n=135) and lymphomas (n=119) in relation to estimated organ dose from CT scans using Poisson regression.
Results: Underlying conditions that pre-dispose to cancer did not bias the risk estimates for leukemia or brain tumors, but did introduce some bias for lymphomas. Previous cancers that had not been reported to the cancer registry were a source of bias, particularly for brain tumors. However, significant dose-response relationships remained even after exclusion of these previous cancers for leukemia/MDS and brain tumors. The CT films provided new information on trends in doses showing a decrease starting in the mid-1990s and age-adjustments becoming more common. Assessment of the impact of dose uncertainty and lymphomas will be completed early 2016.
Conclusions: Our new findings, based on additional clinical data, still support a relationship between pediatric CT scans and subsequent leukemia/MDS and brain tumors. These results have clinical and public health importance as they re-inforce the need to avoid unnecessary CT scans in children, and also provide direct evidence of cancer risks in the low-dose range (<100mGy).

Radon Exposure And Cancers Other Than Lung Among Ontario Uranium Miners

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Lung cancer mortality risks have been well studied among radon-exposed uranium miners. However, the dose-response relationship between radon exposure and other cancers has seldom been examined. The Ontario Uranium Miners' cohort is one of the largest cohorts with detailed quantitative radon exposure estimates, cancer incidence data, and lengthy follow-up. The recent update was funded by the Canadian Nuclear Safety Commission. The associations between occupational radon exposure and incidence of leukemia, stomach and kidney cancer, chosen a priori based on some evidence in the literature, are presented.

The cohort of mines and mills workers was created using data from Canada's National Dose Registry and the Ontario Mining Master File (work history collected during annual chest x-rays). The cohort consists of men, who worked for at least one week in the mines, with follow-up for cancer incidence (1969- 2005) and vital status ascertainment (1954-2007). Poisson regression was used to estimate relative risks and their 95% confidence intervals with levels of cumulative radon exposure, measured in Working Level Months (WLM).

The cohort consisted of 28,546 male miners with a mean cumulative exposure of 21.0 WLM. We found no evidence for an increasing dose-response association with incidence of leukemia, stomach, or kidney cancer. The relative risks in the highest exposure category compared to the unexposed group were: stomach cancer (>30 WLM): RR=0.86, CI:0.52-1.43, kidney cancer (>15 WLM): RR=0.66, CI:0.40-1.10, or leukemia (>30 WLM): RR=1.25, CI:0.77-2.02. There were no appreciable differences found when different latency intervals were modeled.

This study found no increased incidence of leukemia and of stomach and kidney cancer, at low levels of cumulative respiratory radon exposure. Other exposure scenarios including ingestion of radon progeny, for stomach cancer, and acute moderate to high dose radon exposure, for leukemia, may be relevant to examine when assessing other cancer effects from radon exposure.

Age at first indoor tanning use and melanoma risk: a prospective, population-based cohort study

GHIASVAND REZA, UNIVERSITY OF OSLO, NORWAY
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Purpose: We assessed melanoma risk and age at melanoma diagnosis in relation to age at initiation of indoor tanning.
Methods: We used data from the Norwegian Women and Cancer study, a large, prospective, population-based cohort study established in 1991. Host characteristics and history of UV exposure (sunburns, sunbathing, and indoor tanning) were recorded by questionnaire at inclusion and updated with follow-up questionnaires every 4-6 years. Multivariable relative risks (RRs) and 95% confidence intervals (CIs) were estimated by Poison regression. Multivariable linear regression analysis was used to study age at diagnosis in relation to age at initiation of indoor tanning. Models were adjusted for birth-cohort, year at inclusion, ambient UV of residence, hair colour, skin colour, cumulative sunburns, and sunbathing.
Results: During follow-up of 141 045 women through December 2012 (mean follow-up 13.7 years), 861 incident melanoma were diagnosed. We found an increased risk of melanoma for women with age at initiation <30 years compared to never-users (adjusted RR=1.34, CI 1.05-1.66). Moreover, a significant interaction between cumulative exposure of indoor tanning and age at initiation was found (PInteraction=0.01), with a higher risk of melanoma among women initiating <30 years than those initiating ≥30 years. Compared to never-users of indoor tanning, mean age at diagnosis was 2.15 years (CI 0.87-3.37) lower among women with age at initiation<30 years and 1.18 year (CI 0.21-2.07) lower among women with initiation at ≥30 years of age.
Conclusions: This study provides strong support for the declaration by the IARC that indoor tanning increases melanoma risk with greater increase in risk among women starting indoor tanning before age 30 years. Furthermore, indoor tanning leads to melanoma at a younger age.
Funding sources: The Norwegian Extra Foundation for Health and Rehabilitation through Extra funds and the Norwegian Cancer Society.

MECHANISMS - DNA damage, repair and mutagenesis

Thursday 9 June - 11:00-11:20

Invited speaker: Hitoshi Nakagama
President, National Cancer Center (NCC), Tokyo, Japan

Hitoshi Nakagama graduated from the University of Tokyo in 1982 and received his MD from the University of Tokyo in 1991. He then moved to the USA and joined the Center for Cancer Research, MIT, and worked as a postdoctoral fellow on the functional analysis of the tumour suppressor gene, WT1, with Professor David Housman. After returning to Japan in 1995, he took up a position as Section Head, Carcinogenesis Division, National Cancer Center Research Institute (NCCRI), and then became Chief, Biochemistry Division (1997), Deputy Director (2007), and Director of NCCRI in 2011. From April 1, 2016, he now serves as President of the National Cancer Center. He has long been working on animal cancer models of colon carcinogenesis induced by various environmental carcinogens and on the DNA adductome to elucidate genetic and epigenetic modifications which play pivotal roles in driving cancer development. He also identified several tumour suppressive microRNAs regulating cell cycle arrest and/or apoptosis after exposure to environmental damage, and proved that these tumour suppressive microRNAs are inactivated during colon carcinogenesis, including in the phase of liver metastasis. He is currently working on the application of exosomal microRNA in the early detection of various cancers.

Novel Regulatory Role of BRCA2 in Endothelial Cell Function and Survival Following Genotoxic Stress

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Background: Germ-line mutations in the tumor suppressor gene BRCA2 (breast cancer 2, early onset) predispose carriers not only to breast cancer, but also to other cancers. BRCA2 plays crucial role in the genome integrity maintenance and is central to DNA-damage repair. BRCA2-associated DNA-damage responses are not only specific to cancer syndromes but also represent a pathophysiological basis for diverse cardiovascular diseases (CVDs). We hypothesize that BRCA2 is an essential regulator of endothelial function and apoptosis following genotoxic stress.
Methods: BRCA2 was silenced using siRNA and DharmaFECT-4 in human umbilical vein endothelial cells (ECs). Key indices of EC function; tube formation and proliferation, DNA-damage/repair and apoptosis were measured by Matrigel™ assay, MTT assay, qPCR, immunoblotting and immunofluorescence following doxorubicin (DOX) treatment.
Results: Basal BRCA2 expression and its successful silencing in ECs were confirmed at transcript and protein levels by qPCR and immunoblotting, respectively. Genotoxic stress in the form of DOX exacerbated DNA-damage in BRCA2-silenced ECs, evident by increased expression and activation of DNA double-stranded breaks (DSBs) marker H2A.X and reduced RAD51-foci formation, an essential regulator of DSB repair. Increased DSBs were associated with significantly increased expression and activation of p53, and p53-upregulated modulator of apoptosis PUMA. Elevated levels of DNA-damage and p53 were further associated with significantly increased DOX-induced apoptosis in BRCA2-silenced ECs as measured by immunoblotting for cleaved-caspase-3 and TUNEL-staining. Key indices of endothelial function, including tube formation and proliferation, were significantly reduced following DOX-treatment in BRCA2-deficient ECs, which was accompanied with significantly increased expression of cell cycle inhibitor, p21 at transcript and protein levels and decreased nitric oxide levels.
Conclusion: Our data for the first time, demonstrate an entirely novel role of BRCA2 as a regulator of endothelium function, and provide important clues regarding a potential susceptibility of BRCA2 mutation carriers to anthracycline-induced CVDs, a cornerstone of cancer chemotherapy.

Exposure of hepatocellular carcinoma cells to low-level As_2O_3 causes an extra toxicity pathway via L1 retrotransposition induction.

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Various mechanisms have been proposed for toxicity and carcinogenesis pattern of arsenic, a naturally occurring metalloid. The extent to which the long interspersed element-1 (LINE-1) retrotransposon, an ubiquitous retroelement with autonomous mobility, can be influenced upon exposure to low-level arsenic remains to be elucidated. The aim of this study was to evaluate the possible effect of low-level As2O3 on L1 retrotransposition alteration in human hepatocellular carcinoma cells (HepG2). L1 retrotransposition in HepG2 cells was performed by the in vitro retrotransposition assay using an EGFP-tagged L1RP. Following determination of non-cytotoxic concentrations of arsenic by a MTT assay, the cells were transfected with pL1RP-EGFP and then exposed to 0.25, 0.50 and 0.75 μM of As2O3. The amount of EGFP and its copy number in retrotransposed cells were evaluated by FACS and qPCR analysis in treated vs. control cells, respectively. Significant increase in retrotransposition frequency was found after 12 days exposure to 0.50 and 0.75 μM of As2O3 by FACS analysis ($P<0.05$). Obtained results were further confirmed by real time PCR, which showed significant induction of retrotransposition in all mentioned concentrations. Our findings indicate that low-level long-term As2O3 exposure may pave activation of L1 retrotransposon.

The Joint Value Of Microsatellite Instability And The Braf V600e Mutation In Colorectal Cancer Prognosis

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Purpose: While microsatellite instability (MSI) is a favorable prognostic marker in colorectal cancer (CRC), the BRAF V600E mutation may predict worse survival in microsatellite stable (MSS) and MSI tumors. We aimed to replicate and summarize associations between MSI/BRAF status and mortality in literature.
Methods: Cox regression analyses were adjusted for clinically relevant covariates and included 530 CRC cases from the Netherlands Cohort Study, diagnosed during 1989–1993, with follow-up until December 31, 2009. 366 cases died, including 207 of CRC-related deaths. We pooled mortality hazard ratios with those from previous studies and made three different comparisons (model 1–3). $P <0.05$ indicated statistical significance.
Results: The first model included MSI/BRAF combinations and showed, compared to MSS BRAF wild type tumors, an increased CRC-specific mortality risk for MSS BRAF mutated tumors [pooled HR (95% confidence interval, CI) = 1.59 (1.34 to 1.89)], while risk was decreased for MSI BRAF wild type and mutated tumors [pooled HRs (95% CIs) = 0.43 (0.29 to 0.63) and 0.64 (0.49 to 0.85), respectively]. Comparison of BRAF mutated with wild type tumors within MSS tumors (the second model) and MSI tumors (the third model) showed increased CRC-specific mortality risks, although these were nonsignificant within MSI tumors [pooled HRs (95% CIs) = 1.55 (1.30 to 1.86) and 1.43 (0.88 to 2.32), respectively]. Associations extended to overall mortality within MSS tumors.
Conclusions: MSI overrides BRAF status in prognosis, but the BRAF mutation was associated with worse survival within MSS and, possibly, MSI tumors. This justifies research on interventions that could benefit MSI/BRAF subgroups.
Funding source: World Cancer Research Fund; Health Foundation Limburg.

The role of PARP inhibitors to radiosensitize liver tumours

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As over 50% of all cancer patients will receive radiotherapy there is considerable interest in the development of radiosensitisers that could replace chemotherapeutic agents without the associated dose-limiting toxicities. Small molecules inhibitors of poly(ADP-ribose) polymerases (PARPs), key proteins in the DNA damage response (DDR), are one example of this drug class that are entering into clinical trials. Based on this strong rational and the fact that radiotherapy has been shown to be a promising approach for hepatocellular carcinoma (HCC) treatment we are assessing this combined treatment strategy in HCC cell lines. In a first series of experiments 4/7 HCC lines were sensitive to the PARP inhibitor ABT-888 given as a single 2 hour exposure, with the two cell lines tested showing enhanced radiosensitivity when irradiated in its presence (Guillot et al., BMC Cancer, 14 (2014) 603). As Hepatitis B virus (HBV) infection is a major cause of HCC and HBV proteins modify the DNA damage response, these studies have now been extended to examine radiation sensitivity in cell models expressing or not HBV viral proteins. Greater radiation sensitivity was seen in two HBV expressing lines compared to the parental line and these lines also showed a greater gain in sensitivity when irradiated in the presence of ABT-888. In parallel studies the variation in expression of PARP proteins in liver cancers of different etiology is being examined. Paradoxically in the light of the in vitro results PARP-1 mRNA levels were found to be highest in the panel of HBV-HCC compared to HCV or alcohol associated HCCs and increased relative to the peritumour tissue. Studies are underway to identify which viral proteins contribute to this cellular phenotype and to dissect the impact on the DDR.

Financial support of La Ligue Nationale du Cancer Comité du Rhône is gratefully acknowledged.

MECHANISMS - Genetics and (epi)genomics

Cross-cancer genome-wide pleiotropy analysis based on GAME-ON and GECCO across five common cancers: lung, ovary, breast, prostate and colon cancer

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[1] Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, Toronto, Canada.
[2] Harvard T.H. Chan School of Public Health, Boston USA, on behalf of Discovery, Biology, and Risk of Inherited Variants in Breast Cancer (DRIVE)
[3] University of South California, Los Angeles, USA, on behalf of (a) The Elucidating Loci in Prostate Cancer Susceptibility (ELLIPSE), African American Breast Cancer Consortium (AABC), African Ancestry Prostate Cancer Consortium (AAPC), Japanese American Prostate Cancer Consortium (JAPC), Latino American Breast Cancer Consortium (LABC), Latino American Prostate Cancer Consortium (LAPC); (b)on behalf of Colorectal Transdisciplinary (CORECT) Study
[4] University of Cambridge, Cambridge, UK, on behalf of (a) Ovarian Cancer Association Consortium (OCAC); (b) Breast Cancer Association Consortium (BCAC)
[5] Institute of Cancer Research, London, UK, on behalf of The PRACTICAL Consortium
[6] National Cancer Institute, Bethesda, USA.
[7] Replication and eQTL studies: (a) deCODE genetics, Amgen, Reykjavik, Iceland. (b) Nanjing Medical University School of Public Health, Nanjing, China. (c) Division of Genome Biology, National Cancer Center Research Institute. Tokyo, Japan. (d) Institut universitaire de cardiologie et de pneumologie de Québec, Department of Molecular Medicine, Laval University, Québec, Canada. (e) University of British Columbia Centre for Heart Lung, Innovation, St. Paul's Hospital. Vancouver, Canada. (f) Dana-Farber Cancer Institute, Boston, USA.

[8] *Fred Hutchinson Cancer Research Center, Seattle, USA, on behalf of Genetic Epidemiology of Colorectal Cancer Consortium (GECCO)*
[9] *Geisel School of Medicine, Dartmouth College, Lebanon, USA, on behalf of the Transdisciplinary Research for Cancer of Lung (TRICL)*
[10] *Moffitt Cancer Center, Tampa, USA, on behalf of Transdisciplinary Cancer Genetic Association and Interacting Studies (FOCI)*

Background: Identifying genetic variants with pleiotropic associations can uncover common pathways influencing multiple cancers and further understanding of cancer susceptibility. **Method:** We conducted a genome-wide cross-cancer pleiotropy analysis across five common cancers: lung, ovary, breast, prostate and colon cancer from the GAME-ON/GECCO Network with a total of 61,851 cases, 61,820 controls of European ancestry using the association analysis based on subsets (ASSET) method, and validated the results in additional independent studies from Harvard, deCODE and Collaborative Oncological Gene-Environment Study (iCOGS) with a total of 55,789 cases and 330,490 controls of European ancestry. We have also evaluated the generalizability in Chinese, Japanese, Latinos and African Americans. **Results:** We identified a novel pleiotropic association at 1q22 with a variant associated with breast and lung squamous cell carcinoma (overall P-value for both cancers combined=8.9 x 10-8) in European descendants and the results were validated in the replication set. The eQTL analysis of this region showed a consistent association with ADAM15/THBS3 gene expression in lung tissues in three independent studies. New pleiotropic associations were also found at previously known cancer loci: variants at a known BRCA2 locus for lung and breast cancer were associated with serous ovarian cancer (overall p-value=4.0 x 10-8); a known breast cancer locus, CASP8/ALS2CR12, with a variant associated with prostate cancer (overall P-value=1.9 x 10-8), and a known breast cancer locus, CDKN2B-AS1, where one variant was associated with lung adenocarcinoma (overall P-value=1.0 x 10-5) and a second was associated with prostate cancer (overall P-value=9.5 x 10-7). **Conclusions:** Our results provide important insights into common carcinogenesis across multiple major cancers and highlight the value of pleiotropy analysis.

The value of large international consortia in characterizing genetic susceptibility to breast cancer
DAVID GOLDGAR, HUNTSMAN CANCER INSTITUTE, UNITED STATES

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It has long been recognized that having a close relative with the disease is one of the strongest risk factors for developing breast cancer. Many studies over the last two decades have focused on identifying the specific genetic and environmental factors responsible for this familial clustering. Initially these methods were linkage analysis in large high-risk families followed by positional cloning (responsible for the discovery of BRCA1 and BRCA2) and then in the last decade has seen Genome-Wide Association (GWAS) studies and most recently, whole exome and whole genome sequencing. Given that the initial discoveries were of the most common effects associated with the largest effect sizes, the discovery of additional loci implicated in contributing to the familial risk of breast cancer requires very large sample sizes and thus is most suitable to international collaboration. In this presentation, I will describe the progress that has been made in identifying such loci/genes and describe a number of ongoing international collaborations/consortia that have been instrumental in these successes. These include the iCOGS and OncoArray efforts, the BCAC consortium, COMPELXO and ENIGMA consortia and the IBCCS study. In addition I will describe some collaborations geared towards looking at the effects of life-style factors in modifying risks conferred by genetic predisposition. Other consortia have been focusing on interpretation of the large amount of sequence variants discovered through both research-based and clinical sequencing of known breast cancer genetic predisposition genes. Lastly, I will describe means by which additional progress can be made in our understanding of the familial component of breast cancer.

Genome-Wide Study Of Head And Neck Cancer

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Purpose: We sought to investigate novel genetic head and neck cancer (HNC) susceptibility loci in a large scale genome-wide association study (GWAS).
Methods: 6,034 cases and 6585 controls from 12 epidemiological studies including individuals from Europe, North and South America. Genotyping was carried out using the Illumina OncoArray a cancer-specific platform followed by genome-wide imputation of >7 million genetic variants. Overall HNC and site-specific, oral cancer (OC) and oropharyngeal cancer (OPC) associations were explored with multivariate unconditional logistic regression models adjusted for covariates and eigenvectors within geographical regions followed by fixed-effects meta-analysis.
Results: We detected 8 novel genetic loci ($P<5 \times 10^{-8}$) associated with HNC and/or OC and OPC. HNC was associated with 5p14.3 (rs79767424, *RP11-124N3*), a deletion at 10q26.13 (rs201982221, *LHPP*) and 11p15.4 (rs1453414, *OR52N2/TRIM5*). We also detected a large signal at 6p21.3 in the HLA class II associated with HNC and more strongly with OPC. For oral cancer, we identified genome-wide associations at 2p23.3 (rs6547741, *GPN1*) and 9q34.12 (rs928674, *LAMC3*). Additionally, two known neoplastic disease susceptibility regions 9p21.3 (*CDKN2B-AS1*) and 5p15.33 (*CLPTM1L*) were associated with oral cancer. Lastly, we confirmed previously described alcohol-related HNC susceptibility locus, *ADH1B* (4q23) that reached the significance threshold in the overall and site-specific analyses.
Conclusions: This large GWAS provides further genetic susceptibility associations for head and neck, oral and oropharyngeal cancer and highlights a strong effect of the HLA region in susceptibility to these cancers. Additional work is required to uncover biological mechanisms behind these findings.
Funding source: NIDCR 1X01HG007780-01, GWA study of oral and pharyngeal cancer based on the Oncochip. NCI 2R01CA092039-04A1, Genetics of tobacco and alcohol related cancers. Genetic Associations and Mechanisms in Oncology (GAME-ON) Initiative. IARC Fellowship Programme, partially supported by the European Commission FP7 Marie-Curie Actions (COFUND).

Epigenetic Markers Of Smoking-Induced Lung Cancer: Screening And Risk

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Purpose: Lung cancer represents the first cause of death from cancer worldwide, despite advancements in therapies and imaging. Survival improvement remains hampered by the lack of understanding of the molecular mechanisms driving lung carcinogenesis. Building upon recent studies identifying differential dynamics in the epigenetic response to exposure to tobacco smoke, we propose here to explore the contribution of these DNA methylation markers to smoking-induced lung cancer profiles and assess the

benefit of their use compared to classical smoking-related metrics in a predictive context.
Methods: We performed a nested case-control study within two prospective cohorts: the Italian component of the European Prospective Investigation into Cancer and Nutrition (EPIC) and the Norwegian Women and Cancer cohort (NOWAC). For each of the participants (N=377 from Italy and N=249 from Norway), genome-wide methylation profiles were acquired from blood samples collected at enrolment using the Illumina-HM450 DNA methylation array. Full-resolution association studies used logistic regressions controlling for technical variations and a set of confounders. The discriminatory performances of the logistic models were subsequently characterized by the area under the receiver operating characteristic curve (AUC). Disease-relevant biomarkers were subsequently explored with respect to their association to smoking exposure, and we investigated the persistence of these signals after smoking cessation.
Results: The methylation at 9 CpG sites was associated with lung cancer risk (FDR5%). Of these, 5 were classified as persistent, 1 as reversible markers of smoking. Comparison of the predictive abilities of these 6 biomarkers with smoking status showed that the inclusion of disease-associated CpG sites moderately but systematically improved discriminatory performances of the logistic models (AUC for smoking=76.3%; AUC for CpGs =83.9%, AUC total=84.4%).
Conclusions: Our work provides leads to possible epigenetic markers related to tobacco induced lung cancer.

Funding sources: COLT foundation, EU FP7-Exposomics grant, EU-ERC advanced grant (ERC-2008-AdG-232997)

Identifying Epigenetic Precursors Of Childhood Cancer And Associated Early-Life Exposure Factors

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Childhood cancer, though rare, remains the first cause of disease-related death in children, with increasing incidence worldwide. Its risk factors are largely unidentified but could be predetermined during in utero development. During embryogenesis, a global redistribution of DNA methylation occurs to enable tissue differentiation. Hence, DNA methylation is a potential sensor of environmental exposures during development and may persist later in life. We profiled the genome-wide methylation levels in cord blood samples from the International Childhood Cancer Cohort Consortium (I4C), the largest mother/child birth cohort of childhood cancer.
Starting with one of the largest I4C cohorts, the Norwegian Mother and Child Cohort (MoBa), DNA methylation levels of more than 450,000 cytosines were compared (using HM450-BeadChip) between nested cases of childhood cancer (n=80, representing similar proportions of leukemias, central nervous system tumors and other tumors) and control subjects followed-up for the same time period (n=160). We identified a differentially methylated 200-bp region in leukemias relative to controls (FDR<0.05). A mean difference of 5-10% methylation was consistently found across 8 CpG sites in this region and was validated using bisulfite pyrosequencing. The observed association was not influenced by covariates such as blood cell subtype distribution, gender or birth weight. This potential epigenetic signature of childhood leukemia is currently being replicated and analyzed in relevance to early-life exposure factors in other I4C cohorts, in neonatal blood spots from a Californian birth cohort focusing on leukemia, and in the Pregnancy And Childhood Epigenetics consortium. Preliminary findings suggest a role for early-life infection, maternal smoking during pregnancy and maternal use of hormone contraception preceding pregnancy.
These findings may place DNA methylation in the causal pathways linking early-life exposures and childhood leukemia and may contribute to a ‘leap forward’ in deciphering mechanistic precursors of childhood cancer.
[Acknowledgement: INSERM/INCA grant and the IARC Postdoctoral Fellowship-Marie-Curie-Actions-People-COFUND].

Thursday 9 June - 16:00-16:20

Invited speaker: Roland Eils
German Cancer Research Center (DKFZ), Heidelberg, Germany

Roland Eils received his PhD in Mathematics from the University of Heidelberg, Germany, in 1995. He is currently a Professor at the University of Heidelberg and holds a joint appointment as division head at the German Cancer Research Center (DKFZ) in Heidelberg. He is founding and managing Director of BioQuant, the Center for Quantitative Analysis of Molecular and Cellular Biosystems at the University of Heidelberg. His research focuses on the integration of tools from mathematical modeling, image analysis and informatics into life science research and he is a leading figure in systems biology and bioinformatics. In his research, he is applying various methods on issues related to human health, such as viral infection, cellular death pathways and cancer genomics. He has published more than 280 papers in peer-reviewed journals over the past 10 years and received a total of more than 10 000 citations from them. He is co-editor of the book Computational Systems Biology (Elsevier) and is the Editor-in-Chief of systembiologie.de, the magazine for systems biology research in Germany. Professor Eils is coordinating the several systems biology and systems medicine consortia and is the coordinator of HD-HuB, the Heidelberg Center for Human Bioinformatics. He is a member of the International Society for Systems Biology (ISSB). In 1999 he was awarded the BioFuture Prize, the most prestigious prize for young researchers in Germany, and in 2014 he received the Heidelberg Molecular Life Sciences (HMLS) Investigator Award.

ABSTRACT: Big Data in Cancer: Curse or Cure?
Recent developments in DNA sequencing technology now enable sequencing of the human genome for less than US$1,000 facilitating applications in basic and translational cancer research. These cost reductions have spurred initiatives such as the UK-based 100,000 Genomes Project, the International Cancer Genome Consortium to pursue sequencing and analysis of large numbers of patient genomes. Hundreds of thousands of patient genomes will become sequenced in the next few years, and in Germany alone we expect completion of >25,000 genomes by 2018. While those estimates are made on the basis that for each tumor only one sample is sequenced it has become very clear that averaging over millions of cells in a given tumor sample may hide subtle, but clinically important genomic alterations that are only present in a small fraction of cells. Sequencing of many individual cells per sample will lead to a further, massive explosion of genome sequencing data in the next few years. Thus, an unprecedentedly rich set of “big data” will emerge in cancer and other diseases with the promise to improve patient stratification, diagnostics and personalized medicine. These promises are, however, accompanied by significant threads and challenges: First of all, the fact that whole genome sequences are unequivocally connected to only one individual, ethical and legal considerations for generation, storage, analysis and distribution of genome sequences need to be taken into account. Further, no single institution has the necessary infrastructure to perform analyses of hundreds of thousands of genomes, to store and access them securely and to utilize these data for research and translation. Furthermore, the diversity of analysis pipelines renders data processed in different institutions largely non-comparable. I will present in my presentation recent advances in single cell genomics of patient derived cells. Further, I will discuss promises and challenges of big data in oncology and will outline potential avenues to overcome some of the most pressing hurdles in the field of personalized genomics.

Comprehensive Analysis Of A:T>T:A Mutational Signatures In Human Cancers

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Purpose
Exposure to the genotoxic compound Aristolochic Acid (AA), an IARC Group 1 carcinogen, leads to renal disease and urological and hepatobilliary cancers. AA-related tumors carry specific types of mutations caused by AA mutagenesis which are characterized by a high prevalence of A:T>T:A transversions in a 5'-Py-A-Pu-3' sequence context with transcriptional strand-bias. The presence of this mutational signature may thus inform of exposure to AA. However, the specificity of the signature towards AA has not been fully demonstrated. In order to address this question and to characterize the general landscape of A:T>T:A mutations in human cancers, we performed a systematic screen of A:T>T:A-based mutational signatures present in publicly available cancer genome data.

Method
Somatic mutation data from TCGA, ICGC and COSMIC repositories were analysed for mutational signatures using the non-negative matrix factorization (NMF) algorithm applied solely to A:T>T:A mutations. Tumors from patients with documented AA exposure were analysed as positive controls. Signature comparisons were performed using the cosine similarity method.

Results
From 253,292 samples available in public repositories, we identified 1,814 samples passing a minimum threshold number of A:T>T:A mutations. In these samples and 44 samples from AA-exposed cases, we identified six A:T>T:A-based mutational signatures. Four of these signatures matched with the A:T>T:A profiles of previously published signatures, including one that matched both signature 22 (AA) and the A:T>T:A component of signature 4 (smoking). The remaining two signatures, one observed in some esophageal tumors and the other in a subset of skin cancer, were new.

Conclusions
Our preliminary analyses revealed that the sequence context of A:T>T:A mutations caused by AA is not specific to AA, and that other distinct A:T>T:A signatures contribute to the mutation load in specific cancer types, for which the causative agents or processes remain to be identified.

Funding sources
International Agency for Research on Cancer

MR-Base: an online platform for Mendelian randomization using summary data

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Background: Mendelian randomization (MR) is an increasingly important tool for appraising causality in hypothesized exposure-disease pathways but requires specialist knowledge and access to large genetic datasets. We have created an online platform called MR-Base (www.mrbase.org) that greatly simplifies the implementation of MR for non-specialists.
Methods: We have collated and harmonized summary genetic data from 34 genome-wide association study (GWAS) consortia, dbGAP and the GWAS catalog, corresponding to >1,200,000 individuals, 141 diseases and 1946 biomarkers, and have automated the MR pipeline through a web-based interface and R package. Implementation of MR through MR-Base involves the following stages: i) selecting instruments for target exposures; ii) choosing statistical methods and iii) specifying outcome traits. In the first stage, the user defines their genetic proxies either through manual upload or selecting exposure from the MR-Base

repository. In the second stage, the researcher selects their statistical methods for implementing MR, which currently allows 10 different methods including standard approaches and sensitivity analyses. The user also specifies their preferred method for dealing with correlated genetic proxies as well as strand ambiguity arising from palindromic SNPs. In the third stage, the user selects the outcome of interest from the MR-Base outcome repository. In the fourth and final stage, the analysis is implemented and results are returned in the form of text files and a variety of plots. MR-Base also allows hypothesis-free techniques, such as phenome-wide MR.
Results: MR-Base enables fast and automated application of MR to assess the causal relationship between any known exposure and outcome/disease of interest by combining summary results from hundreds of GWASs and consortia. MR-Base is currently being utilised in a hypothesis-driven context to assess associations of hypothesised risk factors with a variety of outcomes, including lung, prostate and renal cancers, in addition to investigating other risk factors with a hypothesis-free approach.

Prioritizing Chemicals for Risk Assessment Using Chemoinformatics: Examples from the IARC Monographs on Pesticides

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Identifying cancer hazards is the first step towards cancer prevention.The IARC Monographs Programme, which has evaluated nearly 1000 agents for carcinogenic potential since 1971, typically selects agents for hazard identification on the basis of public nominations, expert advice, published data on carcinogenicity, and public health importance. PURPOSE. Here we present a novel and complementary strategy for identifying agents for hazard evaluation using chemoinformatics, database integration and automated text mining. METHODS. To inform selection among a broad range of pesticides nominated for evaluation, we identified and screened nearly 6000 relevant chemical structures. RESULTS. We systematically compiled information on 980 pesticides, creating chemical similarity network maps that allowed cluster visualization by chemical similarity, class, and the number of publications concerning epidemiology, cancer bioassays, and carcinogenic mechanisms. For the IARC Monograph meetings that took place in March and June 2015, this approach supported high priority evaluation of glyphosate, malathion, parathion, tetrachlorvinphos, diazinon, DDT, lindane, and 2,4-D. CONCLUSIONS. This systematic approach, accounting for chemical similarity and overlaying multiple data sources, can be used by risk assessors as well as researchers to systematize, inform and increase efficiency in selecting and prioritizing agents for hazard identification, risk assessment, regulation or further investigation. This approach could be extended to an array of outcomes and agents, including occupational carcinogens, drugs, and foods.FUNDING. US National Cancer Institute (Cooperative Agreement 2U01CA033193-34);National Institute of Environmental Health Sciences (Cooperative Agreement LAC/IMO/2015/01).

The proportion of cancer attributable to major modifiable lifestyle and environmental factors in China, 2011

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Introduction: Several studies have used population attributable fractions (PAF) to estimate the proportion of cause-specific deaths attributable to individual risk factors at the global or regional levels. However, very few similar up-to-date analyses by cancer site are available at the country level. In this study, we estimated the proportion of cancer deaths attributable to four major potentially modifiable risk factors in China in 2011 (age ≥30 years) for common cancers.
Methods: The list of potentially modifiable risk factors was abstracted from the International Agency for Research on Cancer (IARC) Monographs and the World Cancer Research Fund / American Institute for Cancer Research (WCRF/AICR) expert reports on food, nutrition and physical activity. We abstracted the distribution of risk factors mainly from the China National Nutrition and Health Survey 2002 and information on the magnitude of the association of risk factor with cancers from published reports of the WCRF/AICR, meta-analyses, pooled analyses, and some cohort studies in China. For infection, we used prevalence of infections in cancer cases abstracted from published epidemiological studies. The source of mortality data was the Chinese National Cancer Registry Program, 2011.
Results: Overall, 40.0% of cancers deaths (~832,000 deaths) in China in 2011 attributed to four major risk factors: smoking (active, secondhand), alcohol drinking, body mass index ≥25 kg/m2, and infections. Tobacco was the main cause of cancer death (active smoking, ~372,000 and passive smoking, ~99,000 deaths), followed by infection with hepatitis B virus (~242,000) and helicobacter pylori (~97,000), alcohol drinking (~73,000), excess body weight (~34,000), and infection with hepatitis C virus (~40,000), human papilloma virus (~24,000), and Epstein Barr virus (~22,000).
Conclusion: Nearly half of all cancer deaths in China were related to four potentially modifiable major risk factors, underscoring the importance of preventive measures in the country, particularly tobacco control and hepatitis B virus infections.

The Global Burden Of Cancer In 2012 Attributable To Alcohol

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Purpose: Alcohol consumption is a leading risk factor in the growing global cancer epidemic, thus information on the cancer incidence and mortality attributable to alcohol is vital for public health planning. The aim of this study is to estimate the global burden of cancer incidence and mortality attributable to alcohol in 2012.
Methods: The proportion of new cancer cases and cancers deaths attributable to alcohol were estimated using Population Attributable Fractions (PAFs), under the theoretical minimum risk of lifetime abstention. All PAFs were estimated by age, sex, country and cancer subtype. Data on alcohol consumption were obtained from the Global Information System on Alcohol and Health. Relative risk estimates were obtained from recent meta-analyses. Data on cancer incidence and mortality were obtained from the GLOBOCAN database, held at IARC. Population data were obtained from the UN Population Division.
Results: Globally, an estimated 662,000 incident cancer cases (4.7% of all cancer incidence), and 373,000 cancer deaths (4.8% of all cancer mortality) were attributable to alcohol in 2012. The burden was much greater in men, with respective proportions of 65.0% and 75.7% of all alcohol-attributable cancer incidence and mortality occurring in men. Colorectal cancer contributed the largest proportion of alcohol-attributable cancer cases (22%), while oesophageal cancer contributed the largest proportion of cancer deaths (24%). As with alcohol consumption, the age-standardized burden of alcohol-attributable cancer exhibited large geographical variation; the age-standardized incidence rates were greatest in Central Europe, while corresponding mortality rates were highest in Eastern Europe.
Conclusions: The burden of cancer caused by alcohol consumption is considerable and preventable and

varies by sex and geographical region, thus giving rise to health inequities. Accordingly, cost-effective policies are required to stem the rising number of alcohol-related cancer cases and deaths worldwide.
Funding source: none

Estimates of the fraction of several cancers attributable to occupational exposure to certain carcinogens in France

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Purpose:
The aim of this work is to produce the estimates of the fraction of several cancers attributable to occupational exposure to four carcinogens that are classified by the International Agency for Research on Cancer as Group 1 carcinogens: asbestos, silica, benzene, and trichlorethylene. This work also gives an estimate of the rate of recognition as occupational disease.
Methods:
The attributable fraction was calculated from the Levin's formula, according to two scenarios. Relative risks were identified in the national and international scientific literature. The job-exposure matrices (developed through the Matgéné program) were linked to a representative sample of work histories of the French population in order to estimate the lifetime prevalence of occupational exposure to each agent. The number of cases attributable was calculated for each cancer and compared to the number of compensated of carcinogen-related occupational diseases.
Results
The results for each of the 4 carcinogens will be presented. For example, globally, the number of cases (pleural mesothelioma, lung, larynx and ovarian cancer) attributable to occupational exposure to asbestos is estimated, in 2012, between 2439 and 6184 in men and between 250 and 437 in women; based on the total number of cases for these four cancers, 7.7% to 19.4% of these cancers are attributable to occupational exposure to asbestos among men and 1.5% to 2.6% in women. Moreover, 27% to 73% of the lung cancer cases and 24.5% to 44% of the mesothelioma cases from the French general employees social insurance fund are not compensated as an occupational disease.
Conclusion
Notwithstanding the methodological limitations inherent to this exercise, these estimates are important to improve occupational health and public health knowledge. They confirm the substantial burden of occupational exposures in the occurrence of several cancers in the French population and hence the importance of under-recognition of the attributable cancers.

Burden of cancer attributable to physical inactivity in Brazil

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Purpose: To estimate the number of cancer cases attributable to physical inactivity in Brazil. **Methods**: We estimated the number of cancer cases attributable to physical inactivity using population attributable fraction (PAF). PAF was estimated using the following equation: PAF=P(RR-1)/P(RR-1)+1 where P is the prevalence of physical inactivity, obtained from the National Health Survey in Brazil (PNS 2013), and RR the relative risk of each cancer site (bladder, breast, colon, endometrial, esophageal, gastric, kidney, lung, ovarian, pancreas, prostate) from published meta-analysis showing evidence of association. An individual was considered physically inactive if s/he did not reach the World Health Organization physical activity guideline (≥150 minutes/week) in the following domains: commuting (to work and habitual activities), occupational, and leisure-time. We collected the number of incident cases estimated from the Brazilian National Cancer Institute for 2014 in order to obtain the absolute number of cases attributable to physical inactivity. **Results**: In 2013, the prevalence of physical inactivity reached 46% in Brazil (men 39.8% and women 51.5%). In a hypothetical scenario in which the whole Brazilian population were physically active, we estimated the following number of cancer cases that could be avoided: 7.6% of bladder cancer (n=684), 6.7% of breast cancer (n=3,841), 12.7% of colon cancer (n=4,135), 11.4% of endometrial cancer (673), 11.0% of

esophageal cancer (n=1,191), 9.2% of gastric cancer (n=1,874), 6.1% of kidney cancer (data not available), 13.2% of lung cancer (n=3,602), 5.8% of ovarian cancer (n=331), 3.5% of pancreas cancer (data not available), and 4.2% of prostate cancer (n=2,886). **Conclusion**: Physical inactivity has a significant role on the burden of cancer in Brazil. Interventions aimed to reduce physical inactivity are important to cancer prevention strategies in Brazil.
Funding source: Leandro Fórnias Machado de Rezende receives funding for his PhD, grant #2014/25614-4, São Paulo Research Foundation (FAPESP).

Global burden of cancer attributable to infections
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Purpose. Infections with certain viruses, bacteria, and parasites have been identified as strong risk factors for specific cancers. The aim of this study is to quantify the impact of these infections on the global burden of cancer.

Methods. We considered infectious agents classified as carcinogenic to humans by IARC. We calculated the number of cancers attributable to infections by country by combining statistics on estimated cancer incidence in 2012 with estimates of population attributable fraction for the infectious agents. Incidence estimates were obtained from GLOBOCAN 2012. Attributable fraction calculations were based on the prevalence of infection in cancer cases combined with the relative risk for the infection. Estimates of infection prevalence and relative risk were obtained from reviews of published data.

Findings. Of the 14 million new cancer cases that occurred in 2012, 2.2 million were attributable to carcinogenic infections. The most important infectious agents were *Helicobacter pylori* (770 000 cases worldwide), human papillomavirus (640 000 cases), hepatitis B virus (420 000 cases) hepatitis C virus (170 000 cases) and Epstein-Barr virus (120 000 cases). Globally, 15.4% of all cancers were attributable to infections. The fraction of cancers attributable to infection varied by country from under 5% in the United States, Canada, Australia, New Zealand and some countries in Western and Northern Europe to over 40% in some countries in sub-Saharan Africa. The spectrum of infectious agents causing cancer also varied by development status as measured by the UN human development index.

Interpretation. Over 2 million cancer cases each year are caused by infectious agents. Application of existing public health methods for infection prevention, such as vaccination, safer injection practice, or antimicrobial treatments, could have a substantial effect on the future burden of cancer worldwide.

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Monitoring Hpv Vaccination Program Impact In Bhutan And Rwanda

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Background
Human papillomavirus (HPV) vaccination is expected to reduce the high number of cervical cancer deaths in low- and middle-income countries (LMIC), but not within 20 years. Hence, reliable early evidence of effectiveness is crucial to encourage national planners to implement and sustain programs. Bhutan (2010) and Rwanda (2011) were the first countries in Asia and Africa to introduce national, primarily school-based, vaccination (HPV6/11/16/18) programs. These target 12 year-old girls and included catch-up campaigns up to 18 years. Approval of long-term protocols to monitor HPV prevalence in both settings, offers an opportunity to demonstrate HPV vaccine effectiveness in LMIC.
Methods and Results
Firstly, baseline HPV prevalence was characterized among unvaccinated population-based female cohorts, by collecting cervicovaginal samples from ~2,500 women aged 18-69 years in both Bhutan [Tshomo, BMC Infect Dis, 2014] and Rwanda [Ngabo, submitted], of whom 18% and 22%, respectively, were infected with high-risk HPV. Women under 25 years (22% and 32% HR HPV prevalence, respectively), were oversampled to establish a robust sample with which to compare future vaccinated cohorts.
Secondly, to obtain earliest indicators of vaccine impact, we piloted school-based surveys of HPV testing from urine. 973 and 912 female students in Bhutan and Rwanda, respectively (mean age=19 years), self-collected first-void urine samples [Franceschi, Int J Cancer, 2016]. 92% and 43% reported vaccination, respectively, and HPV6/11/16/18 prevalence was lower in vaccinated than in unvaccinated (vaccine effectiveness = 68% and 88% respectively).
We also monitor HPV types in CIN2/3 and cervical cancer, and are evaluating HPV testing as a primary screening test, both to anticipate reductions in cervical cancer mortality in older women, and to facilitate long-term monitoring of HPV prevalence.
Conclusions
Recent findings mark the beginning of demonstrating HPV vaccine impact in Bhutan and Rwanda, and support the feasibility of urine HPV surveys for this purpose.

The impact of HBV vaccination on B-cell non-Hodgkin lymphoma

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Purpose: To evaluate the risk of B-cell non-Hodgkin lymphoma (NHL) associated to HBV infection and the fraction of cancer preventable through vaccination.

Methods: We conducted a case-control study in Italy in 1999-2014, enrolling 513 incident, histologically confirmed B-cell NHLs. Controls were 997 cancer-free patients hospitalized for diseases unrelated to infectious and auto-immune diseases. Controls were matched to cases according to study centre, period, sex and age group. Study subjects provided serum for HBV and HCV screening (HCV and HBV serology, HCV viral load). Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were estimated by logistic regression, adjusting for potential confounders.

Results: Chronic HBV infection (HBsAg+) was reported in 20 NHL cases (3.9%) and 17 control (1.7%). No patients were coinfected with HCV. Compared to people susceptible to HBV infection (HBsAg–, antiHBc–, antiHBs–), those with chronic HBV infection had a two-fold higher risk of B-cell NHL (95% CI: 1.07-4.15).

Accordingly, 2.9% (95% CI: 1.5-4.2%) of B-cell NHL cases were attributable to chronic HBV infection. No excess of B-cell NHL risk emerged in people with serological evidence of past/immune HBV infection (HBsAg–, antiHBc+, antiHBs+; OR=0.79; 95% CI: 0.58-1.10) or vaccination (HBsAg–, antiHBc–, antiHBs+; OR=0.87; 95% CI: 0.58-1.31). The effect of vaccination was consistent across sex (OR=0.91 among men and 0.86 among women) and age groups (OR=0.78 and 1.04 among people aged <50 or ≥50 years).

Conclusions: Our results lend additional support to the role of chronic HBV infection in the development of B-cell NHL. The primary prevention of HBV infection through vaccination and the promotion of safe behaviors may reduce the incidence of B-cell NHL of approximately 3%. HBV vaccination could have greater impact on the reduction of B-cell NHL cases in endemic areas where prevalence of HBV is much higher.

Funding source: Italian Association for the Research on Cancer

Expression Of E6 Oncoprotein And Incidence Of High Cervical Precancerous Lesions Among Hpv Infected Women: 5 Year Follow Up Results In A Chinese Cohort

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Purpose: To evaluate the correlation of expression of E6 oncoprotein and incidence of the cervical precancerous lesions caused by HR-HPV infection in 5 years among a Chinese rural screening cohort.
Methods: The screening cohort with 1997 women aged 35-45 was built in 1999 and followed up in 15 years by cytology and HR-HPV testing every 5 years. The expression of E6 oncoprotein and incidence of the cervical precancerous lesions with CIN2+ were analyzed in the year of 2005 and 2014. The risk of CIN2+ incidence and E6 expression were estimated by HPV infection status and times of HPV positive testing.
Results: The positive rates of HPV, E6 oncoprotein and CIN2+ of the followed population were 17.6%, 1.3% and 1.3% respectively. A significant higher expression of E6 oncoprotein after 5 years was observed in HR-HPV positive women than in the women with HR-HPV negative (4.2% vs. 0.6%, RR=6.7, 95%CI: 3.4-13.2). The incidence risk of CIN2+ in HR-HPV positive women after 5 years was significantly higher than that of women with HR-HPV negative (5.9% vs. 0.3%, RR=21.9, 95%CI: 9.1-52.5). Compared to HPV negative women, the incidences of CIN2+ were higher in women with once HPV positivity (RR=6.8) and in women with twice HPV positivity (RR=92.3) in 5 years. When stratified by E6 oncoprotein expression, the incidence risk of CIN2+ in women with twice HPV positivity and E6 positive expression were 228.7 times higher than that of women with double negative in HPV and E6 oncoprotein (95%CI: 63.7-821.4).
Conclusions: Our data indicate multiple times of HPV infected events and expression of E6 oncoprotein elevate the risk of CIN2+ development. HPV infection history and E6 oncoprotein could assist the triage of HPV positive women in cervical screening.
Funding source: Our work was supported by the National Natural Science of Foundation of China (No 81322040).

High Incidence Of A Hepatitis B Virus Pres2 Deletion In West Africa Among Hbv Chronic Carriers : Association With Hepatocellularcarcinoma

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Hepatitis B virus (HBV) is endemic in Sub-Saharn Africa driving high rates of related cirrhosis and Hepatocellularcarcinoma (HCC). PROLIFICA (EU-FP7) aims to prevent HCC by treating HBV chronic carriers in West Africa. Demographic data project confirm early (30-40 yr) development of cirrhosis and HCC in Gambia. We aimed to evaluate the contribution of HBV genetic variability for progression of liver diseases in West Africa.
Population based screenings of HBV were done on more than 6500 people. Quantification of HBV DNA, HBsAg and HBV genotyping were performed to know the genotypes and mutational profile. Further in-vitro characterization of mutant HBV strains were done in vitro.
We further tested 195 HBsAg positive cases in the community (HBV viral load > 150 IU/ml) and 121 HBsAg positive HCC cases. Finally we sequence 217 samples. 80% of them were genotype E and rest genotype A. 40% were carrying in frame deletion in PreS2 region, subsequently affecting overlapping polymerase gene. Deletion mutants proportion was significantly higher in cirrhosis (35%) and HCC (55%) as compared to chronic hepatitis (22%). Presence of 2-4 types of preS2 deletion mutant were observed along with the wild type (WT) in same samples. In-vitro study in Huh7 cells shows PreS2 mutant strains have significantly reduced release of HBsAg and retention within cells as compared to WT. Our data suggest that HBeAg (-) hepatitis with PreS2 deletion and a complex quasispecies formation among treatment naive individuals may have influence progression to cirrhosis and HCC. Our hypothesis is the retention of HBsAg within hepatocytes may exert ER stress. Immunohistochemistry for HBV antigens in liver biopsies are ongoing to explore further. Also pyrosequencing studies are ongoing to better understand the quasispecies complexity. This study highlighted the underestimated genetic complexity among the HBV genotype E strain and potential role of PreS2 deletion in HCC.

HPV burden in HPV related lesions

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Purpose: To estimate the HPV prevalence and type distribution in HPV-related cancers: cervix, vulva, vagina, anus, penis, oral cavity, oropharynx and larynx.

Methods: Paraffin embedded tissue blocks from primary cancers of the cervix, vulva, vagina, anus, penis, oral cavity, oropharynx, and larynx were collected from collaborating centers. The network of collaborating institutions includes more than 85 centers located in more than 45 countries in Europe, Africa, Asia, America and Oceania. After a thorough pathology evaluation, HPV/DNA detection was performed using SPF-10 PCR/DEIA/LiPA25. Detection of E6*I mRNA, p16INK4a, and other markers was also performed.

Results: Number of analyzed cancer cases were: cervical-10575, anal-496, vaginal-408, penile-1010, vulvar-1709, oral cavity-1264, oropharyngeal-1090 and laryngeal-1042. HPV DNA positivity was 85%, 88%, 74%, 33%, 29% 7%, 25%, and 6%, respectively. HPV multiple infections varied from a less than 1% identified in oropharyngeal cancers to a 9% in penile cancers. HPV 16 was the most common type identified in all cancer sites. The next types in frequency varied by anatomical site. HPV16/18 accounted from a 59% in laryngeal cancers to a 85% in oropharyngeal cancers, among HPV DNA positive cases. When considering the 9 types included in the recently approved 9-valent HPV vaccine the figures varied from 82% in the oral cavity to a 95% in the anal cancers.

Conclusions: The observed HPV type distributions reinforces the potential benefit of current and new HPV vaccines in the reduction of HPV-related cancers.

Funding source: Spanish public grants from the Instituto de Salud Carlos III, the Agència de Gestió d'Ajuts Universitaris i de Recerca, the Marató de TV3 Foundation, the Stichting Pathologie Ontwikkeling en Onderzoek (SPOO) foundation, the Lilly Foundation, Asociación Española Contra el Cáncer, the European Commission (HPV AHEAD) and unrestricted grants from GlaxoSmithKline Biologicals and Sanofi Pasteur MSD & Merck & Co, Inc.

Disparities in cancer survival between Indigenous and non-Indigenous adults in Canada: Results from linkage of the 1991 Census Mortality Cohort and the Canadian Cancer Registry

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PURPOSE: A lack of ethnic identifiers in Canadian cancer registries limits understanding of cancer burden in ethnic subgroups. We use a census-registry linkage to compare cancer survival of First Nations, Métis and non-Indigenous adults in Canada.
METHODS: The cohort comprises a 15% sample of the Canadian population derived from the 1991 Long Form Census. Cohort members are followed for cancers and deaths from 1992 to 2009. We measured site-specific age-standardized 5-year relative survival using age-, sex-, ethnicity- and calendar time-specific life tables. Flexible parametric modeling was used to estimate the excess mortality rate ratio (EMRR) for First Nations (FN) and Métis compared to their non-Indigenous peers.
RESULTS: Cancer survival was significantly poorer for FN than for non-Indigenous Canadians for 9 of 15 cancers examined. EMRRs ranged from 1.00 (95%CI: 0.68-1.47) for multiple myeloma to 2.39 (95%CI: 1.63-3.50) for prostate cancer. Taking rurality and income into account reduced EMRRs slightly but they remained elevated for 7 out of 15 cancers. Among Métis, there was a consistent trend toward poorer survival for all 4 cancers examined, with the greatest disparity for prostate cancer.
CONCLUSIONS: Indigenous people in Canada experience poorer survival than their non-Indigenous peers, even after accounting for differences in income and rurality, supporting the need for: 1. additional research to understand why; 2. additional investments in culturally appropriate initiatives to reduce cancer burden; and 3. creation of databases for ongoing monitoring of cancer burden. This will require novel methodologies and appropriate data sharing, collaboration and capacity-building arrangements with Indigenous organizations.
FUNDING SOURCE: Canadian Institutes for Health Research

Determinants Of Late Stage Breast Cancer Diagnosis In The Multi-Country African Breast Cancer – Disparities In Outcome (Abc-Do) Study

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Purpose: Breast cancer (BC) survival rates in sub-Saharan Africa (SSA) are low, in part due to advanced stage at diagnosis. The African Breast Cancer – Disparities in Outcomes (ABC-DO) study is an m-Health technology-implemented study of breast cancer survival in multiple SSA settings and includes a detailed assessment of the pre-diagnostic journey. This journey and determinants of late stage at diagnosis are examined.
Methods: Newly diagnosed women with BC presenting at ABC-DO hospitals are being enrolled since September 2014. Face-to-face baseline interviews were conducted at first hospital visit to obtain data on socio-economic and cultural factors, healthcare access and beliefs. Clinical data were extracted from medical records. Logistic regression was used to estimate odds ratios (OR) of late stage at diagnosis (stage III/IV vs 0/I/II), adjusted for country and age.

Results: From a total of 756 women enrolled in Namibia, Nigeria and Uganda, information on stage at diagnosis has so far been extracted for 626 women. Median age at diagnosis was 49 years (IQR: 41-61) and time from first symptom to diagnosis was 7.8 months (IQR: 3.5-21.1). Over half of the cohort was diagnosed at late stage (60% overall; Namibia 55%; Nigeria 75%; Uganda 62%). Late stage at presentation was strongly associated with time from first symptom to diagnosis (5.3, 8.9 and 14.7 months for stage 0/I/II, III, and IV, respectively), living in rural areas (OR 1.68, 95% CI: 1.17-2.40), not having tertiary education (OR 2.67, 1.75-4.08), and being uninsured (OR 4.76, 2.89-7.83).
Conclusions: Long delays from symptoms to breast cancer diagnosis are present in these SSA settings, and were correlated with advanced diagnostic stage. This lengthy period, and its determinants, indicate windows of time and opportunity to target improvements in early presentation and diagnosis using context-specific and culturally-appropriate strategies.
Funding source: Susan G. Komen.

Effect of prostate cancer investigation and treatment intensity on reported long term physical condition and health related quality of life: a two country study

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Introduction
Ireland has since 1994, higher levels of PSA testing and Prostate Cancer (PCa) in Republic of Ireland (ROI) compared with N. Ireland (NI). We investigate, health effects of different intensities of PCa investigation and treatment.
Method
Postal questionnaires to PCa survivors 2-18 years post diagnosis on physical symptoms and Health Related Quality of Life (HRQoL) at questionnaire completion. Survivors were analysed separately for ROI and NI, for categories at diagnosis 'late disease' defined as stage III/IV and any Gleason Grade (GG) and 'early disease' defined as stage I/II and GG 2-7. Data were weighted by age, jurisdiction and time since diagnosis. Univariate and multivariate results are presented.
Results
3,348 (54%) men responded. ROI responders were younger (average age diagnosis 65.3 vs 67.1 years); more likely to present asymptomatically (66% vs 41%); without comorbidities (45% vs 58%) and with early disease. Urinary incontinence was (16%) similar in early and late group for NI and ROI, impotence similar for NI and ROI, lower in early than late disease (56% vs 67%). In early disease, only bowel problems (NI=21%, ROI=12%) and fatigue (NI=29%, ROI=17%) were significantly different. Multivariate modelling explained fatigue as treatment related.
In late disease NI vs ROI men reported higher levels of breast changes (23% vs 9%) and hot flashes (41% vs 19%) which remained in multivariate modelling however, when men on ADT were analysed separately no significant differences remained. Differences in HRQoL were minimal.
Conclusion
Similar health outcomes were reported however the increased intensity of investigation has resulted in additional men with ongoing incontinence and/or impotence in ROI.

Cancer Survival Disparities In New South Wales, Australia Over 30 Years

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Purpose: Public concerns are commonly expressed about widening health gaps due to social inequities. This study examines variations and trends in cancer survival by geographical remoteness, socio-economic disadvantage and country of birth in an Australian population over a 30-year period.

Methods: Cancer diagnoses from the largest Australian state, New South Wales (NSW), for 1980-2008, were extracted from the population-based NSW Cancer Registry (n=651,245). Remoteness was measured using the Accessibility/Remoteness Index of Australia. Socio-economic disadvantage was measured using the Index of Relative Socio-Economic Disadvantage, based on data for Census Collection Districts (approximately 200-300 dwellings), and categorised into equal-population quintiles. Country of birth was categorised as Australia, other English speaking, non-English speaking, and unknown. Competing risk regression models, using the Fine & Gray method, were used to compute sub-hazard ratios (SHRs) with 95% confidence intervals (CIs) for comparative analyses.
Results: After adjusting for sex, age, diagnostic period, cancer site, degree of spread (summary stage) and other study variables, a higher risk of cancer death was associated with living in the most socio-economically disadvantaged areas compared with the least disadvantaged areas (SHR 1.15, 95%CI 1.13-1.17), and in outer regional areas compared with major cities (SHR 1.05, 95%CI 1.03-1.06). People born in other English speaking countries had a similar risk (SHR 0.99, 95%CI 0.98-1.01) and those born in non-English speaking countries had a lower risk of cancer death (SHR 0.91, 95%CI 0.90-0.92) than the Australian-born. SHRs for cancer mortality were observed to increase over time by socio-economic disadvantage (comparing the most with the least disadvantaged areas): SHR 1.07 (95%CI 1.04-1.10) for 1980-1989; SHR 1.14 (95%CI 1.12-1.17) for 1990-1999; and SHR 1.24 (95%CI 1.21-1.27) for 2000-2008.
Conclusions: The contributions of co-morbidity and treatment access and practices need investigation to explain the cancer survival disparities detected in NSW.
Funding source: The NHMRC Program Grant (no. 0631946).

Factors associated with survival in individuals diagnosed with head and neck cancer in a public institution of reference in Rio de Janeiro, Brazil

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Objective: To analyze the factors associated with survival in individuals diagnosed with head and neck cancer. **Methods:** Cohort study in a public institution of reference in Rio de Janeiro. We excluded individuals with cancer in the nasopharynx, glands and thyroid; those diagnosed for more than 6 months and those who didn't contribute to the follow-up. 504 individuals were eligible. A descriptive analysis was conducted. Survival analysis using the Kaplan-Meier method was performed. To identify differences between the categories we used the log-rank test. In univariate analysis, the variables with $p<0.20$ were selected. The Cox regression by forward stepwise method was performed to estimate the risk to different factors. The variables with $p<0.05$ were retained in the final model. This study is part of a larger project called "Head and Neck Cancer Study in Brazil". **Results:** The mean age of the population was 61 years (SD = 10.48). Most are male, white, low education, overweight or obese, have a reasonable/poor oral health, smokers or former smokers and currently drink or had in the past, and uses both types of beverages. Most consumes few vegetables and fruit, but included in their daily meals rice and bean. The mate consumption was very low (0.8%). Overall survival at 2 years was higher for larynx cancer ($p=0.347$). There were 171 deaths (33.9%). Survival was higher in younger individuals (59.6%), female (71.8%,), white (62.0%), overweight or obese (68.6%), higher education (66.8%), with daily intake of vegetables (66.6%), fruit (60.2%), bean (59.1%) and rice (59 6%). For those with good oral hygiene survival was greater (75%). After multiple analyzes, BMI (HR = 1.59; $p = 0.007$) and oral hygiene (HR = 1.89; $p = 0.013$) were retained in the model. **Conclusion:** The survival rate in this population is associated with BMI and oral hygiene.

PARALLEL SESSIONS

FRIDAY 10 JUNE

EPIDEMIOLOGY - Environmental exposures

Friday 10 June - 11:00-11:20

Invited speaker: Manolis Kogevinas
Co-Director, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain

Professor Manolis Kogevinas is co-Director of the Centre for Research in Environmental Epidemiology (CREAL). He graduated from the Medical School of Athens, Greece and did his PhD in Epidemiology at the University of London (1989). He worked at the International Agency for Research on Cancer (IARC), Lyon, at the Municipal Institute of Medical Research (IMIM) in Barcelona and was Professor of Epidemiology at the Medical School in Heraklion, Crete and at the National School of Public Health in Athens. His major research interest relates to the evaluation of environmental and occupational exposures in relation to cancer, respiratory diseases and child health. He served on several WHO and other expert committees evaluating the toxicity of chemicals such as dioxins and drinking-water contaminants. He is the Director of the European Educational Programme in Epidemiology (EEPE-Florence course). He is President (2016–2017) of the International Society for Environmental Epidemiology (ISEE).

ABSTRACT: Environment and cancer
Global climate change is the most important threat for humans in the next decades both regarding direct (e.g. heat waves and mortality), and indirect effects (e.g. long term availability of food and drinking water, disruption of communities due to disasters). In relation to cancer, environmental epidemiology has focused on proximal causes of health and disease and has shown clear effects of numerous exposures. These include outdoor and indoor air-pollution and lung cancer, exposure to radon, exposure to UV light and skin cancer, water contaminants such as arsenic in well-water in relation to bladder and other cancers, exposure to food contaminants such as dioxins and several cancers, environmental exposure to asbestos and erionite. For several widespread exposures there is still no consensus concerning the degree of evidence including endocrine disruption, pesticides, exposure to non-ionising radiation, exposure to water disinfection by-products and nitrates or effects of circadian disruption and environmental light-at-night. Serious difficulties in evaluating widespread low-level exposure, particularly when repeated sampling is necessary, and exposure to mixtures rather than single chemicals has hindered epidemiological research. In several areas, for example research on endocrine disruption, we have not made major breakthroughs in methodological approaches for several years. Major advances will come through the development of new technologies on exposure assessment including the use of personal devices (e.g. smartphones), use of massive population data, together with extended use of Geographic Information Systems. Understanding of mechanisms and use of biotechnology is the other main area of advance in studies evaluating environmental exposures. However, there exists extensive knowledge on major causes of cancer (e.g. air-pollution) that allows the prevention of prevalent cancers, particularly in many newly developed countries where high levels of exposure occur. The development of interventions will allow consolidation of the evidence and help application of preventive policies.

A detailed assessment of glyphosate use and the risks of non-Hodgkin lymphoma overall and by major histological sub-types: findings from the North American Pooled Project

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Purpose: Glyphosate is the most frequently used herbicide worldwide. The International Agency for Research on Cancer recently classified glyphosate as a probable carcinogen for non-Hodgkin lymphoma (NHL), but the epidemiological studies considered were limited by small sample sizes and a lack of exposure-response data for NHL sub-types. We evaluated potential associations between glyphosate use and NHL risk using detailed information from the North American Pooled Project (NAPP).
Methods: Data from NHL cases (N=1690) and population-based controls (N=5131), recruited from Canada and the Midwest U.S. during the 1980s-1990s for 4 different studies, were recently pooled for the NAPP. Self-reported glyphosate use information was used to assess possible associations with NHL overall and by histological sub-type (follicular lymphoma [FL], diffuse large B-cell lymphoma [DLBCL], small lymphocytic lymphoma [SLL], and other). Odds ratios (OR) and 95% confidence intervals (CI) were estimated with multiple logistic regression models adjusted for demographic and NHL risk factors.
Results: Unadjusted for other pesticides, subjects who ever used glyphosate (N=133) had a significantly elevated NHL risk (OR=1.43, 95% CI: 1.11, 1.83). Glyphosate use for >3.5 years increased SLL risk (OR=1.98, 95% CI: 0.89, 4.39). Handling glyphosate for >2 days/year was associated with significantly higher odds of NHL (OR=2.42, 95% CI: 1.48, 3.96) and DLBCL (OR=2.83, 95% CI: 1.48, 5.41). There were suggestive risk increases (p-value ≤0.02) for NHL, FL, and SLL with greater years*days/year of glyphosate use. Except for SLL, risks attenuated when adjusted for other pesticides.
Conclusions: This analysis suggested that glyphosate use was associated with increased NHL risk. Risk differences by histological sub-type were not consistent across glyphosate use metrics and may have been chance findings. Nevertheless, the NAPP's large sample size yielded more precise results than previously possible.
Funding source: Canadian Cancer Society Research Institute; U.S. National Institutes of Health Intramural Research Program, National Cancer Institute.

The role of oral hygiene in head and neck cancer: Results from International Head and Neck Cancer Epidemiology (INHANCE) Consortium

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Background: Poor oral hygiene has been proposed to contribute to head and neck cancer (HNC) risk although causality and independency of some indicators are uncertain. This study investigates the relationship of five oral hygiene indicators with incident HNCs.

Methods: In a pooled analysis of 8399 HNC cases and 9425 controls from 13 studies participating in the International Head and Neck Cancer Epidemiology Consortium, comparable data on good oral hygiene indicators were harmonized. These included: no denture wear, no gum disease (or bleeding), < 5 missing teeth, tooth brushing at least daily, and visiting a dentist at least once a year. Logistic regression was used to estimate effects of each oral hygiene indicator and cumulative score on HNC risk, adjusting for tobacco smoking and alcohol consumption.

Results: Inverse associations with any HNC, in the hypothesized direction, were observed for < 5 missing teeth (OR 0.78; 95% CI: 0.74, 0.82), annual dentist visit (OR 0.82; 95% CI: 0.78, 0.87), daily tooth brushing (OR 0.83; 95% CI: 0.79, 0.88), and no gum disease (OR 0.94; 95% CI: 0.89, 0.99), and no association was observed for wearing dentures. These associations were relatively consistent across specific cancer sites, especially for tooth brushing and dentist visits. The population attributable fraction for lacking at least 2 out of 5 good oral hygiene indicators was 8.9(95% CI: 3.3%-14%) for oral cavity cancers.

Conclusion: Good oral hygiene, as characterized by few missing teeth, annual dentist visits, and daily tooth brushing, may modestly reduce the risk of HNC.

Funding: This study and the INHANCE consortium are supported by NIH grants NCI R03CA113157 and NIDCR R03DE016611 as well as partially supported by government grants from each of the instituions of individual participating countries.

Exposure to ambient air pollution and global DNA methylation

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Outdoor air pollution is a complex mixture of particulate matter and gases. It has been associated with several adverse health effects and is carcinogenic to humans. Recent evidence suggests that exposure to air pollution induces changes in DNA methylation, but functional regions of the genome have not been studied yet.
We used data from 2 case-control studies nested in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. For each of the participants (N=457 from Italy; N=167 from the Netherlands), genome-wide methylation profiles were acquired from blood samples collected at enrolment using the Illumina-HM450 DNA methylation array. Long-term air pollution exposure estimates were calculated using exposure models developed within the European Study of Cohorts for Air Pollution Effects (ESCAPE). The association of DNA methylation per region with ambient air pollution was assessed using beta-regression controlling for technical and confounding factors.
Exposure to NO_2 and NO_x was associated with significant global hypomethylation on the CpG island's shores in Italy (β±se = -2.2E-04 ± 6.1E-05, p-value=0.0003, and β±se = -7.3E-05 ± 2.9E-05, p-value=0.0104 for NO_2 and NO_x, respectively) and in the Netherlands (β±se = -2.3E-03 ± 1.1E-03, p-value=0.0339 and β±se = -1.1E-03 ± 4.7E-04, p-value=0.0188 for NO_2 and NO_x respectively). Hypomethylation of theCpG island's shelves was also significantly associated with exposure to NO_2 and NO_x. The promoter regions were significantly more methylated in association to particles smaller than 10 µm in the Italian dataset.
We observed DNA hypomethylation at CpG island's shores and shelves with exposure to outdoor NO_x and NO_2 levels in healthy adults. DNA methylation is involved in genome stability which can be achieved through chromatin structure modelling. A hallmark of cancer is genome instability and as such lower DNA methylation resulting from exposure to NO_2 and NO_x can enable the development of cancers.

High-resolution metabolomics of occupational exposure to Trichloroethylene

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[9] *Tufts University, Department of Civil and Environmental Engineering*

Occupational exposure to trichloroethylene (TCE) has been linked to kidney cancer and is suspected to cause non-Hodgkin lymphoma and liver cancer. However, TCE's mode of action for development of these diseases in humans is not well understood. Non-targeted metabolomics analysis of plasma obtained from 80 TCE exposed workers and 95 controls were completed by ultra-high resolution mass spectrometry. Biological responses to TCE exposure was determined, with metabolic changes and plasma TCE metabolites evaluated by exposure-dose response and pathway enrichment. Metabolic features associated with TCE exposure included known TCE metabolites, unidentifiable chlorinated compounds and endogenous metabolites. Exposure resulted in a systemic response in endogenous metabolism, including disruption in purine catabolism and decreases in sulfur amino acid and bile acid biosynthesis pathways. Metabolic perturbations were consistent with immunologic alterations, hepatotoxicity, and nephrotoxicity. High-resolution metabolomics correlates measured occupational exposure to internal dose and metabolic response, providing insight into molecular mechanisms of exposure related disease etiology.

Associations Between Body Mass Index, Physical Activity And 145 Blood Metabolites: A Targeted Metabolomic Approach In The Epic Cohort

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Purpose: Metabolomics approaches are of main interest to better characterize metabolic phenotypes of lifestyle exposures. Obesity and physical inactivity have been associated with cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. The present study aimed to examine the associations of body mass index (BMI) and physical activity (PA) with 145 blood metabolites in EPIC.
Methods: Blood metabolites were measured with the Biocrates kit using tandem mass spectrometry and liquid chromatography in 392 men from the Oxford (UK) cohort (EPIC-Oxford) and in 327 individuals who were control subjects in a nested case-control study on hepatobiliary carcinomas (EPIC-Hepatobiliary). Measured metabolites included acylcarnitines, amino acids, biogenic amines, hexoses, phosphatidylcholines, and sphingomyelins. Associations between metabolites concentrations and BMI and PA were assessed using linear regression models, controlling for potential confounders and multiple testing.
Results: Of the 145 quantified metabolites, 40 and 45 individual metabolites showed significant differences according to BMI variations in the EPIC-Oxford and EPIC-Hepatobiliary sub-cohorts, respectively, of which 22 metabolites were common (kynurenine, glutamate, one sphingomyelin, and 19 phosphatidylcholines). Stratification of EPIC-Oxford individuals by diet group revealed that associations of metabolites with BMI were predominantly observed in meat eaters (2 acylcarnitines, serine, 8 phosphatidylcholines) rather than fish eaters (4 phosphatidylcholines), vegetarians (one phosphatidylcholine) and vegans (none). No metabolites were consistently associated with PA in the two sub-cohorts.
Conclusions: Our findings provide new knowledge on blood metabolic signatures of BMI in European

adults. These signatures made of phosphatidylcholines, sphingomyelins and kynurenine may help identifying novel mechanisms mediating the relationship of BMI with obesity-related diseases.

Funding source: International Agency for Research on Cancer; Fondation de France (project grant #2014-00050542); French National Cancer Institute (L'Institut National du Cancer; INCA) (grant number 2009-139; PI: M. Jenab); EPIC grants.

Serum Metabolomic Profiling Of Prostate Cancer Risk In The Plco Cancer Screening Trial

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Purpose
Two recent analyses conducted within the ATBC Study identified serum metabolites related to risk of aggressive prostate cancer up to 20 years prior to diagnosis, including glycerophospholipids, fatty acids, inositol-1-phosphate, alpha-ketoglutarate, and citrate. The present investigation re-examined those associations in another cohort.
Methods
A nested case-control study of prostate cancer in the Prostate, Lung, Colorectal and Ovarian Cancer Screening (PLCO) Trial cohort was conducted with 380 cases and 380 controls matched on age, race, study center, and date of baseline blood collection. Median time from baseline to prostate cancer diagnosis was 10.0 years (range, 4.4-17.0), and the majority of cases included here were diagnosed post-trial. Sera were analyzed on a high resolution accurate mass (HRAM) platform of ultrahigh performance LC-MS/GC-MS that identified 722 metabolites. Logistic regression estimated odds ratios (OR) of risk associated with a one standard deviation (1-SD) increment in metabolite concentration.
Results
Of the 27 metabolites associated with prostate cancer at $p<0.05$, 12 were amino acids or dipeptides, and amino acids as a chemical class was overrepresented among the top signals for stage 3-4 but not overall prostate cancer ($p=0.003$ and $p=0.08$). Pyroglutamine, gamma-glutamylphenylalanine, phenylpyruvate, N-acetylcitrulline, and stearoylcarnitine yielded the strongest metabolite prostate cancer risk signals (1-SD increment ORs 0.78, 0.76, 0.73, 0.80, and 1.25, respectively; $0.001 < p < 0.006$), including for aggressive disease. Our earlier findings of inverse associations for the lipid and energy metabolites, and positive associations for TMAO and thyroxine, were not replicated.
Conclusions
Amino acids, and not lysolipids or TCA cycle metabolites, were prominently associated with prostate cancer in the present study. Whether the PSA and digital rectal examination screenings in the trial, or the non-fasting status of the participants, contributed to the findings should be considered in future studies.
Funding source
Intramural research program of the US National Cancer Institute, NIH.

A Metabolome-Wide Association Study Of Alcohol Consumption And Smoking In The Epic Cohort

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Purpose: Alcohol consumption and smoking are among the main modifiable risk factors for cancer and many other chronic conditions worldwide. The exact biological mechanisms through which these lifestyle behaviors affect human health and metabolism need further investigation. Metabolomic approaches allow an agnostic exploration of novel associations of risk factors with human metabolites and metabolic pathways. Our aim was to study associations of alcohol consumption and smoking habits with concentrations of a set of 130 targeted blood metabolites.

Methods: The study population consisted of 327 control subjects from a nested case-control study on hepatocellular carcinoma within the European Prospective Investigation into Cancer (EPIC). Alcohol consumption and smoking habits were based on self-report assessments. The Biocrates AbsoluteIDQTM p180 kit and tandem mass spectrometry were used to measure serum concentrations of 11 acylcarnitines, 20 amino acids, hexose, 79 phosphatidylcholines, 14 sphingomyelins, and 5 biogenic amines. Multivariable linear regression analyses were performed to study confounder-adjusted associations of categories of alcohol consumption and smoking habits with metabolite concentrations, using false discovery rate correction for multiple testing.
Results: Study subjects (56% men) had a mean age of 59.6 years (5th-95th percentile: 47.5-72.7). In multivariable models, moderate-to-heavy alcohol consumption (>15 and >30 grams/day in women and men, respectively) compared to light alcohol consumption (0.1-15 grams/day and 0.1-30 grams/day, respectively) was statistically significantly associated (q-value<0.05) with higher concentrations of 2 lyso-phosphatidylcholines and 3 diacyl-phosphatidylcholines and lower concentrations of 3 acyl-alkyl-phospatidylcholines and 4 sphingomyelins. None of the metabolites were significantly associated with current or former smoking compared to never smoking.
Conclusions: Our results indicate that alcohol consumption may affect sphingo- and phospholipid metabolism. Replication of our findings together with research aiming at elucidating biological mechanisms will be key to relate sets of identified metabolites with the development of cancer and other chronic conditions.
Funding source: Dutch Cancer Society.

A nested case-control study of plasma microseminoprotein-beta and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition

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Purpose
Genome wide association studies have identified a common variant in the promoter region of the MSMB gene, rs10993994, as a risk factor for prostate cancer. MSMB encodes microseminoprotein-beta (MSP), a protein secreted by the prostate epithelial cells into the seminal fluid. There is uncertainty, however, about the role of MSP in the development of prostate cancer.

Methods
A nested case-control study was conducted in the European Prospective Investigation into Cancer and Nutrition (EPIC) with 1,871 cases and 1,871 matched controls to investigate the association of circulating MSP and rs10993994 genotype with prostate cancer risk. Odds ratios (ORs) for prostate cancer by fourths of blood plasma MSP concentration were estimated by conditional logistic regression and MSP association with prostate cancer by rs10993994 genotype was calculated from hierarchical Bayesian logistic regression.

Results
Plasma concentration of MSP was 67% higher for CC genotype when compared to the TT genotype. In a minimally adjusted model, MSP concentration was not significantly associated with prostate cancer risk (OR in the highest versus the lowest fourth = 1.01, 95% CI 0.84-1.22, Ptrend = 0.7). However, after adjusting for prostate-specific antigen (PSA) concentration, higher MSP concentration was associated with a reduced risk of prostate cancer (OR = 0.69, 95% CI 0.54-0.89, Ptrend = 0.004). No heterogeneity in this association was observed by time to diagnosis or tumour characteristics. For CC and CT genotypes, increase in MSP concentrations was associated with a reduced risk of prostate cancer (CC - OR = 0.42, 95% CrI 0.19-0.78; CT - OR = 0.44, 95% CrI 0.23-0.75), while no clear association was observed for TT (OR = 0.71 CrI 0.36-1.61).

Conclusions
The current study shows a significant inverse association of circulating MSP concentration with prostate cancer risk, but only after adjustment for total PSA concentration.

PREVENTION & MORTALITY REDUCTION - Implementation research

Friday 10 June - 11:00-11:20

Invited speaker: Mauricio Maza
Chief Medical Officer, Basic Health International, San Salvador, El Salvador

Dr Mauricio Maza is the Chief Medical Officer for Basic Health International, an organization dedicated to the eradication of cervical cancer. He received his MD from the Universidad Dr José Matías Delgado in El Salvador, and his Master's of Public Health from Harvard University with a concentration in Health Care Management and Policy. As a medical doctor, public health practitioner and researcher, Dr Maza's focus is cervical cancer prevention in low-resource settings, specifically with the use of novel technologies and treatment paradigms. He is a co-investigator in NIH-funded studies that include development of technologies for screening, triaging and treatment of pre-cancerous lesions. Dr Maza is currently leading a 3-phase demonstration project in El Salvador that will screen 30 000 women by 2016 with an HPV test developed specifically for use in low-resource areas. Dr Maza has presented programme results and implementation strategies at international conferences and meetings held in Brazil, China, Guatemala, India, Panama, Peru and the USA. He believes in the need to advocate for more clinical and implementation research, in order to support more evidence-based policies in limited-resource settings.

ABSTRACT: How Research can lead to Implementation in Limited Resource Settings: The Case of El Salvador

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INTRODUCTION: El Salvador has one of the Latin America's highest cervical cancer incidence and mortality rates, at 24.8/100,000 and 11.9/100,000, respectively. In an effort to improve cervical cancer screening in El Salvador, the Ministry of Health, in cooperation with Basic Health International, started the CAPE (Cervical Cancer Prevention in El Salvador), demonstration project, which integrates a low cost HPV test into the public health system of El Salvador.
OBJECTIVE: To outline the research projects which have led to decision making, for changes to the cervical cancer program in El Salvador.
METHODS: CAPE project goals were based on consensus amongst stakeholders from the Ministry of Health, the medical societies, international agencies, non-profits, and other public sector institutions that work on cervical cancer prevention. Research about cost-effectiveness, adherence to recommended screening, screening acceptability, and follow-up were conducted.
RESULTS: This project to date has provided population-based screening for over 20,000 women aged 30-59 living in the Paracentral Region of El Salvador. Studies have demonstrated good acceptability of self-sampling, strong adherence to screening based on a health promoter educational model, women who were HPV positive were more likely to follow up with a screen and treat modality than colposcopy management, and cost effectiveness was shown to be better with the use of the screen and treat. The Ministry of Health has changed its local guidelines, which now include HPV screening followed by cryotherapy. It is expected that the Ministry of Health includes HPV testing in their national program and have the test available nationwide by 2019.
CONCLUSION: Research in limited resource settings is feasible and valuable for decision maker in order to support evidence-based policies.

Clinical trial to implementation in India: Cost and effectiveness considerations for scaling up cervical cancer screening in low and middle income countries

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Background: There is a growing need to create the evidence-base for implementing and translating findings from clinical trials to make them operational and scalable. Several large and small clinical studies on cervical cancer screening have been conducted and lessons learned from these studies can be extrapolated to assess the cost and benefits of scaling up screening programs.
Methods: We developed a detailed framework to translate the benefits, harms and costs from clinical trials to the real world setting. We used data from two large scale screening trials in India, the Dindigul and Osmanabad district studies, to draw inferences on the benefits and cost of implementing large scale screening programs using visual inspection with acetic acid (VIA). Compliance with screening and follow-up recommendations anticipated to occur in the real world setting (based on the Tamil Nadu Health System pilot study) were used to assess potential benefits and costs during scale up. Detailed activity based cost data that were categorized into fixed and variable components were used to determine costs related to scaling up screening.
Results: The programmatic cost per women in the clinical trial was estimated to be $4-$6 while the screening delivery cost was about $11-$14. The cost per women with screen detected CIN or cervical cancer was $235-$314 in the screening trial; excluding programmatic costs it was $167-$223. Key issues in scaling up screening were related to compliance with diagnostic testing (56% in scale-up versus 98% in clinical trial) and ensuring high quality screens (requires systematic and ongoing training of providers).
Conclusions: Comparing total cost can be misleading as the resources expended on specific program activities impact access, quality and adherence to care and therefore overall program effectiveness. It is important to utilize activity-based costs and detailed performance indicators (provided in this study) to evaluate program effectiveness and cost-effectiveness.

A pilot randomised controlled trial examining the feasibility, acceptability and impact of giving information on personalised genomic risk of melanoma to the public, for motivating preventive behaviours

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Purpose: To evaluate the feasibility and acceptability of giving information on personalised genomic risk of melanoma to the public, and its impact on sun protection and skin examination behaviours, psycho-social and ethical issues.
Methods: We recruited 120 people (22-69 years); consent was 41% overall but differed by age and sex. Participants were randomised 1:1 to the intervention arm (personal genomic risk of melanoma based on variants in 21 genes, delivered as telephone-based genetic counselling and a personalised booklet; plus educational materials) or the waitlist arm (educational materials only, with genomic risk feedback at the end of the study), and followed-up after 3-months (to January 2016).
Results: 118 (98%) participants with complete baseline data were randomised. Most (88%) consented for a copy of their risk information to be sent to their primary care physician. Follow-up questionnaires were completed by 108 (92%) participants and UV dosimeters by 100 (85%). Comments from high-risk participants included that the risk information was “very valuable”, “information I needed to know”, and “reinforces [the] need to be vigilant about sun protection and screening”. One participant elected not to receive their risk information because of insurance concerns. Some participants reported undergoing skin checks as a result of receiving their genomic risk information; analysis is underway to compare the intervention and control groups.
Conclusions: The public expressed a strong interest in receiving their personalised genomic risk information for melanoma. Obtaining saliva samples, questionnaires and UV dosimeters by post, and telephone-based genetic counselling, was feasible and acceptable with minimal loss to follow-up. This pilot will inform a larger trial to evaluate the effectiveness and cost-effectiveness of this innovative melanoma prevention intervention in the general population.
Funding source: Sydney Catalyst Translational Cancer Research Centre, The University of Sydney, Fellowships to AEC from the NHMRC and the Cancer Institute NSW.

Implementation Research To Evaluate Scaling-Up Of Hpv-Self Collection In The Province Of Jujuy, Argentina

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Purpose: We carried-out implementation research to evaluate scaling-up of HPV self-collection offered by community health workers (CHW) during home visits in Jujuy, Argentina. In 2014 findings from previous mix-methods research (The EMA project) were used to expand HPV self-collection as a provincial strategy to increase HPV-testing among screening under-users. We report selected monitoring outcomes for the first year of the scaling-up phase.
Methods: We analyzed data program from the national online screening information system using the RE-AIM framework. Presented outcomes are Reach: percentage of screened under-users; Efficacy: positivity; detection of CIN2+; Adoption: percentage of CHWs with at least one woman with self-collected test; Implementation: percentage of trained CHWs, percentage of women with completion of follow-up. Maintenance: Number of women with self-collected tests during second year of the scaling-up (2015).
Results: Protocols, referral network and training components were developed; triage cytology was recommended for HPV+ women. In total 568/698 CHWs were trained to offer the strategy. In 2014, a total of 12780 women aged 30+ were HPV-screened in the Jujuy public health sector, 38% (n=4866) of them with self-collected tests. Among women with self-collected tests 85% (n=4133/4866) were screening under-users vs. 61% (n=4820/7914) of women with clinician-collected tests at health centers ($p<0.0001$). Of the total of trained CHWs, 75% (426/568) had at least one woman with self-collection. HPV positivity was 13%; 75% (473/633) of HPV+ women had triage follow-up, and among triage+ women 55% (80/146) had colposcopy results. The number of women with CIN2+ lesions was 22. In 2015, 4627 women had self-collected tests.
Conclusions: results indicate that programmatic implementation of HPV-self collection is effective to increase screening, especially among under-users. Triage of HPV+ women and colposcopy follow-up remain a challenge.
Funding source: National Cancer Institute, Argentina, in collaboration with Jujuy Ministry of Health.

POSTERS

EPIDEMIOLOGY

EPIDEMIOLOGY - Global burden of cancer and cancer registries

A-001 - Epidemiology And Survival Analysis Breast Cancers In Jordan, 2005-2010

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Background: Breast cancer is the most common cancer in women all over the world.; Breast cancer is the most common cause of death due to cancer in women and it ranks the fifth cause in both sexes. The objective of the study is to explain the epidemiology of breast cancer in Jordan 2005-2010 and to identify the observed five years survival for the years 2005-2006 .
Methods: All breast cancer cases that diagnosed and registered in Jordan during the period 2005-2010 for epidemiological analysis. Cases diagnosed in 2005-2006 were included for survival analysis.
Data were collected on all patient from Jordan cancer registry files, hospital medical record and histopathology reports. The status of all patients whether alive or dead were ascertained from Civil Registration System .
Data were entered and analyzed using SPSS. Survival obtained by using Kaplan Meier .
Results: Overall five years survival for breast cancer in Jordan regardless the stage or grade is 74%. 5 years survival rate was (60%) in the group less than 30 years and 70 years and above, while the best survival was seen in the age group40-49 years(78%) with significant association P value 0.01. no.For summary stage, 5years survival varied from 82% for localized and for regional 69%,while for distant metastasis 52% with significant association P value 0.001.
Conclusion: stage, age and were factors that significantly influenced cancer survival at univarite analysis, but with Cox regression analysis the most important factor that affect survival rate was stage. Effort should done to improve early diagnosis through early strengthening screening programs to high risk groups. Breast self examination and health education through media and campaign are very important to diagnose case early this will improve the survival of patients.
Key words: breast cancer, stage. Survival analysis,

A-002 - Evolution Of Cancer Registration In Sri Lanka

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Background: The first publication of cancer registry data was in 1990 publishing data of 1985.Since then publications were done for years, 1986,1987, 1990, 1995, 2000, 2001-2005, 2006, 2007, 2008 and 2009 named 'cancer incidence data' of Sri Lanka. The objective of the present research was to find out the evolution of cancer registration in Sri Lanka.
Methods: A desk review of all the publications of cancer incidence data from 1985 to 2009 and in-depth interviews of cancer registry staff.
Results: From 1985 to 2005, cancer incidence data were collected only from the Cancer Treatment Centres (CTC). Data from maxillo-facial units were included from 2006. Data from pathology labs (16) were incorporated from 2008 and publication, presented data collected from 40 sources. Cancer cases with behaviour codes 1, 2 and 3 were included in the registry but from 2006, only behaviour code 3 (malignant primary site) cases were included. Population-based cancer registry was initiated in 2012 in Colombo district, collecting data from death registrars and medical record officers of all hospitals. CanReg 4 software introduced in 2008 was replaced with CanReg 5 in 2012 for data entry. It has evolved from an active paper–based data collection system to a computer-based system in 2015 and plans are under way to make a web-based real-time data collection system.
Discussion and conclusion: 'Cancer incidence' term had been used in all publications with the assumption that all cancer patients come into contact with a CTC at least once as chemo radiation facilities were available only there and the denominator used for the calculation was the total population of Sri Lanka. Increasing the coverage of the registry has been achieved by collecting data from CTCs, pathology laboratories, medical registrars of hospitals and death registrars with the aim of establishing a true national population based cancer registry.

A-003 - Leading Causes Of Cancer-Specific Mortality In The Caribbean Region

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Objective: This study examined cancer-related mortality rates among the 21 Caribbean countries that submitted mortality data to the Caribbean Public Health Agency.

Design and Methods: We calculated proportions and age-standardized mortality rates (ASMR) by cancer site and sex for each country using the most recent 5 years of mortality data available from 2003 to 2013. Calculations were completed using SEER*Stat software and the World (Segi 1960) Standard Million population.

Results: ASMR for all cancers combined ranged from 46.1 to 139.3 per 100,000. Among males, prostate cancer was the most common cause of cancer deaths in all countries, accounting for 18.4–47.4% of cancer deaths, and an ASMR of 15.1 to 74.1 per 100,000; lung cancer (4.6-34.0 per 100,000) was the second or third leading cause of cancer deaths among males in most countries. Among females, breast cancer was the most common cause of cancer deaths in 16 of 18 countries (with >6 reported cases), accounting for 16.1–30% of cancer deaths and an ASMR of 10.0 to 27.3 per 100,000. The ASMR of cervical cancer was higher than the world average (6.8 per 100,000) in 11 countries, and accounted for 4.5–18.2% of cancer deaths.

Conclusion: There is great variability in cancer specific mortality rates within the Caribbean region; however, prostate and breast cancers are consistently the leading causes of cancer-related deaths among males and females, respectively. Lung and cervical cancers—cancers for which World Health Organization “best buy” interventions exist—are also important causes of mortality in many countries.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

A-004 - Cancer Mortality In A Rural Department Of Paraguay

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Purpose: Itapúa is a rural department in Paraguay lacking cancer diagnostics and treatment in the public health sector. We analyzed the cancer mortality in this region as a first step towards epidemiological data for cancer prevention and capacity building.
Methods: We calculated the age-adjusted mortality rates according to world standard (AMRWs) for the major cancer sites in both men and women between 2003 and 2012, and compared the capital city of Itapúa and adjacent central districts (3,968 km^2, population 232,800 in 2012) with remote districts (14,072 km^2, population 313,043 in 2012).
Results: There were about 2,000 cancer deaths in the decade studied, with AMRWs for all malignancies of 90.9/100,000 in men from central vs. 49.1/100,000 in remote districts and 69.0/100,000 vs. 45.0/100,000 in women. Cancer was documented on 12% of all death certificates and outweighed mortality from certain infectious and parasitic diseases (3.6%). However, the cause of death was ill-defined in nearly 20% of all certificates, especially from remote regions. The part of cancer located in the uterus or cell type of neoplasm of the lymphatic or hematopoietic system were frequently not specified (47.8% and 73.1%, respectively). The uterus (mainly the cervix) was the leading cancer site in women with AMRWs of 17.2/100,000 in central and 14.0/100,000 in remote districts, followed by the breast. Lung and prostate were the leading cancer sites in men. AMRWs for lung cancer were 19.3/100,000 in central and 9.5/100,000 in remote districts. Children comprised 36% of the population, but only 24 death certificates listed childhood cancer in this decade.
Conclusions: The results have been presented to the Ministry of Health to support the development of a national cancer plan. The cancer burden is likely underestimated, especially in remote regions and children. Lung and uterus are common cancer sites with high potential for prevention.

A-005 - One RB World Online: A Virtual Retinoblastoma Clinic

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Purpose: Retinoblastoma (childhood eye cancer) is curable, but outcomes remain poor in low-and-middle-income countries. Optimal resources and expertise for retinoblastoma management have been outlined in published clinical guidelines, and serve as a guide to inform health policy, at national, regional and institutional levels. We conducted a situational analysis of resources and expertise available at key retinoblastoma treatment centers worldhide, in an attempt to inform systems of patient referral, educational capacity initiatives, and enhance patient care.

Methods: We conducted a survey of Global Retinoblastoma Treatment Centers to identify and document expertise and resources available for the care of children with retinoblastoma worldwide. An online platform was developed to disseminate this information in an interactive and data-rich format (www.1rbw.org).

Results: The virtual clinic connects patient families to caregivers, and documents data on 166 centers in 56 countries. Survey functionality allows further data collection and updates. Knowledge of where and how retinoblastoma children are managed worldwide provides an efficient and rapid path for parents to access urgent care. The website indicates the closest expert center and all the contacts. Paths of referral and multicenter co-management aim to keep the children close to home while optimizing access to advanced therapies when needed. Estimated incidence vs location and capabilities of treatment centers reveals opportunities to increase capacity, collaboration and coverage in various regions.

Conclusions: The One Retinoblastoma World Virtual Clinic connects stakeholders and strengthens capacity to care for the global retinoblastoma population. This first-of its-kind collaboration promotes global standards of care, setting the stage for multicenter clinical trials and other research, thereby accelerating the translation of results from lab to clinic.

A-006 - Increased Colorectal Cancer Incidence In Iran: A Systematic Review And Meta-Analysis

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Purpose
Colorectal cancer is the third most common cancer in Iran. The increasing trend of colorectal cancer incidence in Iran and the close relationship with the geographical location are the underlying reasons for this study.
Methods
Eleven databases, including MEDLINE, EMBASE, SCOPUS, and four other databases, for articles in Persian were searched from April 2014 to October 2014. Additional data were obtained from an online survey of the Central Library of Tabriz Faculty of Medicine.
In this systematic review and meta-analysis, we included studies reporting different measures of incidence, age-standardized incidence rates, and crude incidence rates. All rates (per 100,000 person-years) were standardized to the world standard population.
A preliminary review of the title and abstracts of these articles was used to exclude any that were clearly irrelevant. The full text review determined whether the article was relevant to our topic. A total of 39 studies from different provinces and diverse areas of Iran, were analyzed in this study using comprehensive meta-analysis software. For accuracy studies, we used estimated rates for males and females with 95% confidence intervals.
Results
Age-standardized incidence rates were obtained based on the random effects model and were 8.16 (95%CI: 6.64 to 9.68) and 6.17 (95%CI: 5.01 to 7.32) for males and females, respectively. The random crude rates were 5.58 (95%CI: 4.22 to 6.94) for males and 4.01 (95%CI: 3.06 to 4.97) for females.
Conclusions
Colorectal cancer incidence rates rise due to individual and environmental risk factors as well as improvement in the registry system and increase in access to health services. A more executed organized and structured system for collecting cancer data, in all cities and rural areas of the country, is an essential priority.
Funding sources
Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
Key Words
Epidemiology; Incidence; Colorectal Cancer

A-007 - Coordinated Data Development Initiative: Enhancing The Access To And Use Of Standardized Treatment Data In Canada

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Purpose
In Canada, and internationally, many rich repositories of data exist, however reports have highlighted barriers to the meaningful use of this data, including less than adequate access, poor data linkages and privacy concerns. There are several types of data, including treatment data in particular, which are either unavailable or difficult to access, that would greatly enhance our ability to advance the cancer system. The Canadian Partnership Against Cancer (CPAC), which is an independent organization funded by the Federal Government of Canada to accelerate action on a national cancer control strategy, undertook an initiative (Coordinated Data Development Initiative) to enhance the access to and use of standardized cancer treatment data across Canada through the creation of linkage and/or data collection.

Methods
The initiative consists of developing and establishing a data standard for cancer treatment, determining what data sources currently exist that map to the standard, cataloguing data access policies, and through projects, testing the feasibility of accessing standardized treatment data on a small scale in multiple jurisdictions. The results of these projects may inform future programming with respect to data linkages in Canada.

Results
An expert validated data standard for cancer treatment has been developed which is inclusive of a core set of treatment data elements that are feasible to access/collect across Canadian jurisdictions. Projects are currently underway to test the feasibility of accessing standardized data.

Conclusions
The use of cancer treatment data for planning, management, policy development, research and monitoring population and public health is fundamental to advancing cancer control efforts. This initiative will accelerate the uptake and translation of the best evidence and knowledge into practice and policy as well as evidence-informed decision-making at all levels of the cancer control system.

Funding source
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A-008 - Changes In The Incidence Of Anal Cancer Cases In Canada: From 1971 To 2010 ñ A Population Based Study

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Purpose: Assess the change in incidence in men and women of HPV-related anal cancer in Canada and evaluate temporal and age specific trends.

Methods: National incidence data for HPV-related anal cancer were obtained from the Canadian Cancer Registry from January 1st, 1971 to December 31st, 2010. Age standardized incidence rates (ASR) per 100,000 person years were calculated. Trends in ASR were analyzed using the Joinpoint Regression Program. Average Annual Percentage Change (AAPC) was used to summarize trend changes over this period, rejecting the null hypothesis that AAPC equals 0 if the resulting p-value was <0.05.

Results: From 1971 to 2010, the ASR for anal cancer per 100,000 increased from 0.3 to 1.2 for males and from 0.5 to 2.3 for females. The AAPC for anal cancer was 4.3 (95% CI 2.7-5.6) p=0 and 3.8 (95% CI 3.0-4.6) p=0, in men and women respectively. The greatest ASR increase occurred prior to 1981 with a significant AAPC of 14.1 in men and 12.3 in women. In both men and women, nearly a quarter of overall anal cancer cases (27.9% and 23.1% respectively) were diagnosed between 65 and 74 years old. The peak ASR in men (2.2) occurred in the 65-74 age group between 1996 and 2000; and in women (2.9), in the 55-64 age group over the 2006-2010 period.

Conclusions: Anal cancer has increased over 40 years. There is no population based screening for this cancer. With HPV vaccination, incidence is expected to decrease by the next generation.

Funding source: None

A-009 - Changes In The Incidence Of HPV-Related Gynecologic Cancers In Canada: From 1971 To 2010 ñ A Population Based Study

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Purpose: Assess the change in incidence of HPV-related vulvar, vaginal, and cervical cancer over 40 years and evaluate temporal and age specific trends.

Methods: National Incidence Data for HPV-related vulvar, vaginal and cervical cancers were obtained from the Canadian Cancer Registry for January 1st, 1971 to December 31st, 2010. Age standardized incidence rates (ASR) per 100,000 person-years were calculated. ASR trends were analyzed using the Joinpoint Regression Program. The Average Annual Percentage Change (AAPC) was used to summarize trend changes over this period, rejecting the null hypothesis that AAPC equals 0 if the resulting p-value was <0.05.

Results: Per 100,000 the ASR for cervical and vaginal cancers decreased from 24.7 to 9.8 and 1.3 to 0.7 from 1971 to 2010 respectively. Correspondingly the AAPC for cervical cancer was -2.3 (95% CI -3.2; -1.3) p=0.0 and for vaginal cancer -1.8 (95% CI -2.5; -1.1) p=0.0. For vulvar cancer the ASR remained unchanged: 2.9 and its AAPC did not change significantly over this period. Almost a quarter of cervical (23.4%), vaginal (24.6%) and vulvar cancers cases (25.3%) were diagnosed in 35-44, 65-74 and 75-84 years old respectively. Compared to the earliest and most recent cohorts, the 1970-1980 birth cohorts show the highest ASR.

Conclusions: Mainly with the uptake of cervical cancer screening in Canada, cervical and vaginal cancer incidence has decreased from 1971 to 2010. As vulvar cancer is not directly linked with a screening tool, there has been no change in incidence. With the uptake of HPV vaccination, further decrease in rates of all the HPV related gynecologic cancers is expected in the coming years.

Funding source: None

A-010 - Colo-rectal Cancer Trends In Saudi Arabia, And The Need To Organize Nationwide Cancer Prevention Program

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COLO-RECTAL CANCER TRENDS IN SAUDI ARABIA, AND THE NEED TO ORGANIZE NATIONWIDE CANCER PREVENTION PROGRAM
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PURPOSE
Saudi Arabia is lacking an organized national Colo-rectal cancer(CRC) control program. Our aims are to figure out the magnitude, ASR, trends of CRC, and the need of cancer prevention program.
METHOD
We obtained CRC cases diagnosed between 1994-2011 from the National Cancer Registry database. We assessed trends of incidence rates over the past 18 years by calculating the Age Standardized Incidence Rate (ASR) in 13 administrative regions.
RESULTS
Between 1994-2011, there were 11,259 CRC cases ; 6,082 case (54 %) in men and 5,177 (46 %) in women with male to female ratio 117:100. The overall ASR was 7.8 per 100,000 (8.2 for males and 7.4 for women). The mean age at diagnosis was 58 years in men and 56 years in women. CRC ranked 1st in men and 3rd in women, nearly 1 % of patients presented with In Situ while up to 64 % distant or regional extension. Over years, the incidence rate increased steadily for both sexes; the ASR doubled from 4.1 in 1994 to 7.8 in 2011.There are substantial variations in CRC incidence between regions. The highest ASR reported in Riyadh and Eastern provinces while the lowest ASR reported in Jazan. In 1994 and 1998 CRC ranked 6th, years 1995-1997ranked 5th, year 2001 ranked 3rd, but after that from 2002-2011, it maintains the 2nd rank.
CONCLUSION
Although ASR among Saudis is low compared with other countries, but the age at diagnosis is lower, maintaining the 2nd rank for 10 years in both sexes, continuous increase in numbers, are alarming indicators. MOH should start an immediate massive national cancer control program including early detection, screening, and community health education programs.
FUNDING SOURCE: MOH

A-011 - Estimates Of The Incidence From Major Types Of Cancer In Peru, Based On The Records Of Both National Institutes For Neoplastic Diseases (INEN) And For Statistics And Informatics (INEI) Of Peru [2007-2013]

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Purpose
According to the Peruvian public health authorities, cancer is now the second leading cause of mortality in Peru. However, there is still a lack of tangible information that prevents an accurate description of the burden of cancer in the country. Our study is an attempt to fill this research gap and provides figures for cancer incidence and distribution in Peru.

Methods
We joined records from both National Institutes for Neoplastic Diseases (INEN) and for Statistics and Informatics (INEI) of Peru. These records included INEN cancer registries between 2007 and 2013 (n=68,168) and demographical data from INEI national censuses over the same period. We estimated the age- and gender-based distributions, as well as regional incidence for each category of cancer registered, as defined by the cancer dictionary of the GLOBOCAN database (C00-097, but C44).

Results
Top five most commonly diagnosed cancers were cervix uteri (C53) (16.1%), breast (C50) (12.2%), stomach (C16) (8.9%), leukemia (C91-95) (5.8%), and colorectum (C18-21) (5.4%) cancers. There was a general increasing trend in incidence for all types of cancer, except for Kaposi sarcoma (C46) and cancers of the trachea, bronchus, and lung (C33-34). However, this increase was not equivalent for all types of cancer and varied between regions; some remote regions of Peru being more impacted.

Conclusions
The burden of cancer in Peru appears to particularly afflict socially vulnerable populations, such as women and remote, deprived people. There is an urgent need for implementing a national cancer registry to confirm this plight. We are now conducting further geographical correlation studies to identify environmental determining factors for cancer amongst the Peruvian population.

Funding sources
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A-012 - Pancreatic Adenocarcinoma Scenario In Brazil: A Clinical-Epidemiological Study Of 4915 Patients

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PURPOSE: The aim of the study was to evaluate the variables associated with adequate response to treatment of pancreatic adenocarcinoma (PA) at the public health system in Brazil.

METHODS: Data from patients diagnosed as PA registered from 2000 to 2011 were obtained at Integrador system coordinated by Instituto Nacional de Cancer, and from Fundação Oncocentro de São Paulo. Patients without clinical stage information, and with previous cancer or oncological treatment were excluded. Clinical and demographics variables as well as treatment type information were collected. The categorical variables were compared using the chi-square test. Baseline characteristics were included in the univariate logistic regression analysis to identify the association between independent variables and response to treatment with p value <0.05 being considered statistically significant.

RESULTS: Among 4915 Brazilian patients, those with age <65yo (58.8%), male gender (53.1%), caucasian ethnic background (72.4%), living with a partner (67.5%), level of education >8ys (53.2%), no or former alcohol drinking (73.2%) or former tobacco smoking (57.0%), and clinical stage IV (66.6%) were predominant. They were diagnosed mainly from 2006 to 2011 (64.8%). There was statistical difference on adequate response according to treatment type (p<0.001). After stratifying by clinical stages, this difference was observed on III (p=0.022) and IV (p=0.047) stages. Adequate response was associated with being younger than 65yo (OR=1.24, 95% CI=1:06-1:45, p=0.008) or having more than 8ys of study (OR=1.36, 95% CI=1.13-1.64, p=0.001).

CONCLUSIONS: The two main sources of registry of Brazilian PA patients present certain discrepancy regarding epidemiological data (alcohol and tobacco smoking prevalence). However, they are useful to demonstrate certain variables impacting treatment response, with patients being generally diagnosed with advanced stage, and patients with <65yo and/or ≥8ys of study presenting a better chance to respond adequately to cancer treatment.

FUNDING SOURCE: The study was performed with no public or private funding.

A-013 - Regional Misclassification Of Cancer Incidence Registry In Iranian Provinces And Bayesian Correction

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Purpose: Most cancer patients throughout Iran seek diagnostic and medical treatments in neighboring facilitate provinces due to lack of proper facilities in their own residence and don't mention their permanent residence address. It makes misclassification error in cancer registry data. The aim of this study is to estimate the misclassified rate between neighboring provinces, using Bayesian method.
Methods: For this study gastric cancer data was extracted from Iranian annual of national cancer registration report in 2008. To correct the misclassification effect between each two neighboring provinces, a Bayesian approach was used with Poisson count regression. An informative beta prior distribution was assumed for the misclassified parameter and expected coverage of each province was used as prior for that parameter. Because the misclassified parameter is unknown, a latent variable approach was employed to simplify the full conditional models and estimate the posterior distribution using a Gibbs sampling algorithm. Analyses were carried out using R software version 3.2.0.
Results: After implementation of the Bayesian method, it was estimated that 43% of gastric cancer patients from North and South Khorasans were registered in Razavi Khorasan, 41% from Kohgilouye&boyerahmad in Fars and 8% in Isfahan, 36% from West Azerbaijan in East Azerbaijan, 43% from Golestan in Mazandaran, 46% from Ilam in Kordestan and 28% in Kermanshah, 63% from Hormozgan in Fars, 47% from Bushehr in Kerman, and finally 58% of cancerous from Sistan&balouchestan were registered in Yazd.
Conclusions: Policy makers that employ cancer registry data for programming should notice to regional misclassification, otherwise decisions for cancer control and prevention and allocating the facilities to different provinces will be erroneous. So it is needed to improve the registration system accuracy with employing more expert stuffs, refining foundations, and enhancing hardware and software resources.

A-014 - Global Projections Of Primary Liver Cancer To 2030

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Purpose: To predict the future incidence of primary liver cancer (PLC) for selected countries.
Methods: New cases of PLC (ICD-10 C22) diagnosed in 30 countries worldwide were available from cancer registries via CI5plus for the period 1993-2007. Observed trends were extrapolated from age-period-cohort models (NORDPRED) to estimate the future burden of PLC to 2030 by sex. Age-standardized incidence rates (ASR) per 100,000 person-years were predicted by country and sex.
Results: Among men and women, the vast majority of countries will see an increasing burden over the next 15 years. Among women, about half of the countries will see an increase in ASR. We estimate that, in 2030, there will be 175,077 new cases of PLC among men annually and 94,005 among women in the selected countries. This represents at least a twofold increase in the number of new cases in both sexes compared with 2005, a rise of 108% and 133%, respectively. Some of the most rapid ASR increases among men and women are observed in Brazil (6.5% per annum), USA blacks (3.1%), and Poland (3.4%). Rapid decreases in PLC among men and women are observed in Japan, Singapore, and Slovakia.
Conclusions: Despite heterogeneity of the predicted rates, the number of PLC cases is set to continue to increase in many countries over the next decades. Regional differences in the prevalence of hepatitis B and hepatitis C (HCV) virus infections, dietary aflatoxin exposure, obesity, and alcohol-related cirrhosis may explain some of the rate variations. Increasing rates in some countries may be partly the consequence of HCV acquired during the 1960-1970s. However, projections could be affected by treatment rates of HCV infection. Public health measures aimed at reducing HCV infection, and hence transmission, are likely to have contributed to the decrease in rates in others (e.g. Japan).
Funding: NHMRC fellowship* 1083090.

A-015 - A Twelve-Year Retrospective Study Of Liver Cancer At Calmette Hospital In Cambodia; Contribution Of Viral Hepatitis

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Purpose
Cambodia lacks a national cancer registry, consequently no reliable data are available for estimating the incidence and the mortality of patients with cancer in the country. Nevertheless, based on estimates, liver cancer is supposed to be the main cancer among males with the highest incidence and mortality rate. Our objective was to describe the clinico-epidemiological characteristics of Cambodian liver cancer patients attending one of the two public hospitals specialising in oncology in Phnom Penh.

Methods
A retrospective study was carried out at the Calmette hospital where 553 medical charts were reviewed, covering the period from January 2003 to May 2015. Socio-demographic data, tumour presentation, clinical manifestations, serological data, biochemical features and medical imaging were obtained from both oncology and hepato-gastroenterology departments.

Results
Hepatocellular carcinoma (HCC) was the predominant type of liver cancer (511 cases, 92.4%), while cholangiocarcinoma (CCA) represented only 7.6% (42 cases). Of the 511 HCC, chronic hepatitis B (HBV) and C (HCV) virus showed similar rates with 207 AgHBs+ and 201 anti-HCV+ cases, respectively. About two-thirds of HCC patients had a tumour larger than 50 mm, in most cases multifocal. Most HCC (84%) and CCA (73.8%) patients received palliative treatment only.

Conclusions
The present study reveals that HCC is the main form of liver cancer at the Calmette Hospital in Phnom Penh. Both HBV and HCV infection contribute to HCC, indicating that HCV-HCC patients should be closely monitored. The creation of cancer registries, the surveillance of populations at risk to develop HCC or CCA and the prevention of infectious agents should become a priority for health policy-makers.

Funding sources
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A-016 - Cancer Incidence In São Paulo, Brazil: Estimates For 17 Regions In 2010

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Purpose: This study aimed to estimate cancer incidence (standardized incidence rates = SIR) according to gender, age group and tumor type for 17 Regional Networks of Health Care (RNHC) in São Paulo state, Brazil, in 2010. Methods: We used as estimator the Incidence:Mortality ratio (I:M) adjusted for sex, five-year age group (0-80 years) and primary tumor site. The ratio numerator was composed by the aggregated number of new cases diagnosed in 2006-2010 in two active population-based cancer registries (PBCR), São Paulo and Jaú, covering 0.3% and 27.3% of the state population, respectively, while the denominator was the official number of cancer deaths in the same areas and period. The estimated number of incident cases resulted from the multiplication of I:M by the number of deaths registered in 2010 in the municipalities that compose the region. Results: We have estimated a total of 53,476 new cases of cancer for males and 55,073 cases for females (excluding non-melanoma skin cancers) in the state of São Paulo, corresponding to standardized rates (world population) of 261/100,000 and 217/100,000, respectively. Among males, RNHC-6 presented the highest standardized incidence rate of all cancers (285/100,000) and the RNHC-10, the lowest (207/100,000). Most frequent tumor sites in men were: prostate (SIR=75/100,000), colorectum/anus (SIR=27/100,000) and trachea/bronchus/lung (SIR=16/100,000). Among women, rates varied from 170/100,000 (RNHC-11) to 252.4/100,000 (RNHC-7); breast cancer was the most incident cancer site (SIR=60/100,000), followed by colorectum/anus (SIR=23/100,000) and cervix (SIR=10/100,000). Conclusion: Data from local PBCR can be used to obtain regional estimates. Our results showed different patterns of regional incidence with rates that often exceeded the values presented for the state. However, the estimated rates may be under- or overestimated reflecting the quality, completeness and the patterns observed in the most representative registry used in the analysis.

A-017 - The Contribution Of IARC In Strengthening Cancer Registry Informatics By Introducing CanReg Software Package To Sri Lanka Cancer Registry

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Purpose
Sri Lanka Cancer Registry (SLCR) plays a pivotal role in cancer control. The value of a cancer registry depends on the quality of its data. The CanReg software package developed by the International Agency for Research on Cancer (IARC) has immense influence on SLCR in producing quality cancer registry data.

Methods
The IARC experts had conducted 03 external reviews in 2005, 2008, and 2012 on SLCR and made important recommendations including introduction of CanReg software for cancer registration activities. Statistics show that the cancer incidence in Sri Lanka is on the rise. Cancer registry data sources are also increasing. Therefore reliable software for data entry, quality control, and consistency checks were deemed necessary. As a consequence CanReg4 was introduced to SLCR in 2008.

Results
Data entry had begun with the year 2006 data and included 14,320 records after consistency checking for duplicate records, multiple primaries and impossible or rare cases by using CanReg software. The migration from CanReg4 to CanReg5 was accomplished in 2010. The Patient, Treatment, Questionnaire and Sources sections of the data entry form of the application had to be customized to suit the SLCR needs before migration. It is hassle-free open source software with intuitive interface and multi user capabilities. The NCCP was able to increase its data sources for cancer registry from 06 in 2007 to 162 in 2015. The NCCP manipulates more than 106,858 records at present with this tool and was able to publish quality cancer incidence data for 2007, 2008 and 2009.

Conclusions
Cancer control planning without high quality cancer registry data from the cancer registry leads to misplaced emphasis and wasting of investment. The IARC has contributed immensely to yield quality cancer registry data by introducing CanReg software and strengthening of cancer registration informatics in Sri Lanka.

A-018 - Implement Cancer Registry Informatics In National Cancer Control Programme To Enhance Cancer Registry Data Accuracy, Completeness, And Timeliness As A Part Of Cancer Surveillance Informatics

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Purpose
Sri Lanka Cancer Registry (SLCR) plays a pivotal role in cancer control. Statistics show that cancer prevalence in Sri Lanka is on the rise. Since a considerable number of private health care institutions and government cancer treatment centres have started treatment of cancer patients, an efficient system for collecting, storing, processing, consistency checking for duplicate records and impossible or rare cases has become a necessity.

Method
The general objective of the project is to develop and implement a web-based application which supports capturing of cancer registry data. It will replace the current paper-based method. The basic software infrastructure is based on Free and Open Source Software (FOSS) like PHP, MySQL and Linux-based server. CanReg5 software will be integrated as a module for quality control, and consistency checks of the data.

Results
There are about 09 cancer treatment units, 09 Oncological surgery units, 67 Pathology laboratories and 25 Oral and maxillofacial units which are functioning under the Ministry of Health. Altogether there exist 110 units. They are all end users. Each end user is able to enter, edit or delete their records. Entered data will automatically be transferred to CanReg software for consistency check, eliminate duplicate records and impossible rare cases. Each unit also can analyze their own data only after data have been checked by CanReg5 software. Then refined data is sent back to the main table so that the end users are able to access quality data. The end users are then able to analyze their data, create pivot tables, charts, reports and are enable to export data in different formats.

Conclusion
The proposed system will ensure timely availability of information that is needed for better improvement in cancer surveillance. Integration of CanReg5 software will yield quality cancer registry data.

Funding Source: Government of Sri Lanka

A-019 - Adjustment For Misclassification Error In Iranís Cancer Mortality Registration, Using Bayesian Method

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Purpose: According to the Iranian death registry, about 15% to 20% of death statistics are recorded in misclassified categories such as septicemia, cancer without mention of details, and other ill-defined conditions. It calls misclassification error (disagreement between the observed and the true value), that makes the registered data inaccurate and often leads to major problems in epidemiological analysis with biased estimates of burden, and underestimating the health risks. The aim of this study is to use Bayesian method to estimate the rate of gastric cancer deaths that have registered as cancer (without label) in Iran registry system.
Methods: National death Statistic from 2006 to 2010 for gastric cancer [ICD-10; C16] which reported annually by the Ministry of Health and Medical Education included in this study. To correct the rate of gastric cancer mortality, a Bayesian approach was used with Poisson count regression and beta prior for male and female categories. Reported percent for misclassified cause of death were used as parameters of beta distribution.
Results: According to the Bayesian re-estimate, about 5 to 6 percent of deaths due to gastric cancer have registered as cancer without mentioning details. It makes an undercount of gastric cancer mortality in Iranian population.
Conclusions: Cancer registry data are important to monitor the effects of screening programs, earlier diagnosis and other prognostic factors. Although it seems that the misclassification rate in registry has been reduced, it is still exists as a major problem. Therefore, policy makers who determine research and treatment priorities on death rates should consider this underreported data in order to setup appropriate cancer prevention programs. To achieve this goal the accuracy of registration system should be increased specially in registering causes of deaths.

A-020 - Burden Of Gastrointestinal Cancers In Iran According To Cancer Death Statistics

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Purpose: Cancer is the third most common cause of death in Iran. Gastrointestinal cancer is the most important causes of mortality due to cancer. The cancer mortality data is important to monitor the effects of screening program, earlier diagnosis, demographic data and other prognostic factors. The aim of this study was to evaluate the mortality rates and trends from Gastrointestinal (GI) cancer in Iranian population from 1995 to 2003.
Methods: National death Statistic Reported by the Ministry of Health and Medical Education (MOH&ME) from 1995 to 2003, stratified by age group, sex, and cause of death is included in this analysis. Colorectal cancer (CRC) [ICD-9; 153-154], Gastric cancer (GC) [ICD-9; 151], Pancreas cancer (PC) [ICD-9; 25], Esophageal cancer (EC) [ICD-9; C15] and Hepatocellular carcinoma (HCC) [ICD-9; 20] were expressed as the annual mortality rates/100,000, general and/or per gender, and age group.
Results: The cause specific mortality rate of CRC slightly increased during the years under study and for GC and EC showed a sharp increasing. In contrast, the mortality rate of PC decreased slightly during the years under the study. The rate of HCC mortality moderately increased. All mortality rates were higher for male than female.
Conclusion: Our study indicated remarkable increasing trends in mortality of GI cancer in Iran specifically for CRC and GC. Developing for a GC and EC for both primary prevention and early detection programs and providing the facilities for CRC screening, would be the options to control the mortality and burden of GI cancers in the future.

A-021 - Hepatocellular Carcinoma In Asia, Prevention Strategy And Planning

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Purpose: To review all of epidemiological and etiological aspects of Hepatocellular carcinoma and examined the prevention of this disease in Asia.
METHODS: We conducted a systematic review according to the PRISMA guidelines. We were chosen articles that published previously, from PubMed (Medline), the Cochrane database and Scopus. The key words used in this research were as follows: Hepatocellular carcinoma in Asia and the way of prevention of this disease, with no language limitations.
RESULTS: More than 70% of all new cases of liver cancer were diagnosed in Asia, a region that 75% of all those chronically infected with hepatitis B virus in the world. Chronic hepatitis B virus (HBV) infection is the main cause of Hepatocellular carcinoma (HCC) in Asia. The prevalence of this cancer is high in Eastern and South-Eastern Asia, But Middle Eastern countries are characterized as moderate prevalence rate of HCC region and Central Asia and some part of Middle Eastern countries are known as low prevalence rate of HCC. In addition of HBV and HCV the other factors such as aflatoxin, alcohol, obesity, diabetes and non-alcohol fatty liver disease (NAFLD) might be responsible for a low prevalence of HCC in Asian countries. Currently available HCC therapies, chemotherapy, surgical are inefficient, mainly due to usually late diagnosis and high recurrence rates after surgical resection, and usually end with treatment failure. Liver transplantation also remains as a difficult strategy in patients with HCC. Thus prevention of HCC by treating and prevention HBV and HCV infection, the major causative agents of HCC.
CONCLUSION: The main challenge which still present in Asia, is the high prevalence of chronic hepatitis. So, prevention of HBV and HCV is the key strategy to reduce the incidence of HCC in Asia.

A-022 - Regional Disparities In Cancer Burden Measured From A Nationwide Cancer Registry In Japan

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Background: A national cancer registry allowing nationwide cancer registration will begin in 2016 based on the Cancer Registry Promotion Act. The Japan Cancer Surveillance Research Group measured crude national cancer incidences in Japan for the first time ahead of enactment of the Act, in order to clarify regional disparities.
Methods: Collected data for the year 2012 from all 47 prefectures were organized according to ICD-O-3 codes and logically checked for errors at the National Cancer Center. Data quality varied from registry to registry; DCO cases ranged from 2.9% to 28.5%, and M/I ratios ranged from 0.38 to 0.60. However, all registries met the criteria for inter-regional comparison.
Results: The total number of cancers in Japan in 2012 was 869,031 (all sites C00-97). Age-standardized rate (ASR, world population) was 267.2./100,000. The latest leading sites were stomach (ASR 55.7) for males and breast (ASR 64.8) for females, followed by lung, colon, prostate and liver for males, and uterine corpus, stomach, colon and lung for females. We observed clear regional disparities in incidences for some primary sites, such as stomach and liver, but not for others, such as colorectum. Disparities at these sites were associated with well-known risk factors, mainly differences in lifestyle factors. An analysis with mortality rates showed that gaps between incidence and mortality varied according to prefectures.
Discussion: The regional cancer registry was launched in all 47 prefectures, and data quality has improved rapidly as hospital-based cancer registration has become more widespread since 2006. The first challenge, to illustrate the nationwide cancer burden based on crude regional incidence in Japan, has now been successfully realized even before enactment of the Act.

A-023 - New Cancer Impact Data From North Africa

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Purpose In recent years, in North Africa Mediterranean countries (Morocco, Algeria, Tunisia, Libya and Egypt) the cancer registration coverage increased importantly, as a result of the establishment of new cancer registries (CRs) and the expansion of pre-existing ones.
This work aims to describe the current situation of cancer registration in the region, to gather and update available incidence data, and to make comparisons with European CRs.

Methods A web search for peer-review publications and reports, and direct contacts with CRs directors and researchers allowed to access the most updated data. Incidence rates were age-standardized on world population and compared with data from a pool of European CRs.

Results In 2015, 18 CRs were qualified as member of the International Association of Cancer Registries and other 2 actively published data on peer-review journals. The proportion of covered population varied from 8% for Algeria to 46% for Tunisia; the greatest improvement was observed in Egypt, with the 21% of the total population now covered and a National Cancer Registry Program able to provide national estimate for incidence rates. For the whole region the coverage reached the 14%.
Peculiarities in risk profiles showed a high risk of liver and bladder cancers in men in Libya and Egypt; low but increasing breast cancer rates in women; high levels of naso-pharynx carcinoma everywhere in the area, in both sexes.

Conclusions The cancer registration coverage increased in the whole area, despite of the socio-economic and political instability that affected some countries. The risk pattern is peculiar and coherent with what we know for other Islamic areas in Middle East; it is completely different from Europe, and, in particular from its Mediterranean part. Moreover, with low-moderate levels of infection related cancers, it is also completely different from Sub-Saharan Africa patterns.

Funding source
Funded by current institutional resources.

A-024 - Comparison Between Iran And France Regarding Breast Cancer: How Population Age Structure Changes Cancer Age Structure, Incidence And Cancer Control Plan

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As the most frequent women`s cancer, breast cancer is a health priority in developped countries since many years ago.National screening programme and better teratment has improved its prognosis. Because 25-28% of all female cancers is breast cancer, more than half of 1 700 000 global new cases are seen in developing countries where much lower incidence is compensated by higher population and higher mortality.
High price of technology depended screening, shortage of expert breast radiologist/interventionalist, low health budget and other health priorities are all against screening in these countries.
These barriers cannot be resolved quickly. Is there any way to bypass these limits toward international standars for breast cancer control in these countries? Still there is no answer for such an important health question.
In this study we try to compare breast cancer situation in Iran and France for similarities and differences that may help us to draw a correct cancer plan.
Material and Method:
Population and cancer age structure and cancer incidence were compared between Iran, Europe and France.
Then Iran age structure is transferred to France. Age specific cancer incidence of France (2012) is then applied to this new population age.
Results:
11% of Iranian population and 31% French are in screening age.Still 46% of cancers in Iran and 55% in France are in screening age. 89% of Iranaian population (86% less than 50) and 69% of french population are outside screening age with 54% of cancers in Iran and 45% in France.
By transfering Iran population (1.23 times to France) to France age specific incidence, the total number of cancer droops from 48763 to 26986.(55%)
Coclusion:
Cancer incidence depends on population age structure. Interestingly improved breast care is the key that can improve prognosis without screening as is seen in patients outside screening age in France.

A-025 - Trends In Incidence Of AIDS-Defining And Non-AIDS-Defining Cancers In Persons With AIDS: A Population-Based Study From São Paulo, Brazil

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Purpose: Several studies have shown increased risk for cancer among people with HIV/AIDS; however, risk has changed over time. Our study is analysing trends in AIDS-defining (ADC) and non-AIDS-defining cancers (NADC) among persons with AIDS in São Paulo, Brazil, between 1997 and 2012. **Methods:** We conducted a population-based registry linkage study. We linked the Population-based Cancer Registry of São Paulo (496,276 cancers) and the AIDS notification database (81,889 AIDS cases) to identify persons with AIDS who had cancer. To analyse cancer trends we estimated the annual percent change. **Results:** Among persons with AIDS 2,074 cancer cases were diagnosed (1,510; 72.8% in men), of which 51.0% (1,057) were NADC. In men, the most frequent were Kaposi sarcoma (KS; 469; 31.1%) and non-Hodgkin lymphoma (NHL; 304; 20.1%), followed by cancers of anus (63; 4.2%), of colon-rectum (59; 3.9%), and of lung (54; 3.6%). ADC, KS, NHL decreased -14.1%, -17.7% and -11.9%/year, respectively. NADC have increased (7.4%/year) since the mid 2000's driven by the upward trends of anal (24.6%/year) and lung cancers (15.9%/year). Among women, the most incident cancers were cervical cancer (CC; 114; 20.2%), NHL (96; 17.0%), breast cancer (72; 12.8%), KS (34; 6.0%) and colorectal cancer (19; 3.4%). Declining trends were found for ADC (-15.6%/year), KS (-26.7%/year), NHL (-15.8%/year), CC (-12.8%/year), NADC (-15.8%/year) and breast cancer (-10.1%/year), whereas, colorectal cancer remained stable. **Conclusions:** Trends in cancers among persons with AIDS in São Paulo, Brazil showed similar patterns to those found in developed countries. Although ADC have significantly decreased, NADC in men, including lung and anal cancer have shown an opposite trend. Therefore, cancer remains a concern in this population.
Funding source: Conselho Nacional de Desenvolvimento Científico e Tecnológico; the German Ministry for Economic Cooperation and Development through the German Academic Exchange Service and the Higher Education Excellence in Development Cooperation .

A-026 - Cancer Incidence Projections To 2035 In Northern Ireland

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Introduction
Monitoring trends in cancer incidence is essential for high quality cancer services. With incidence rates of many cancers increasing and the size of the elderly population expected to rise, projections of cancer incidence up to 2035 are presented to help guide future allocation of health service resources.

Methods
Age-specific rates for all cancers combined and 30 common cancers are determined for both sexes by year of diagnosis. The data is fitted separately for ages 0-49, 50-59, 60-69, 70-79 and 80+ using a generalised linear model with a power 5 link function. Five-year age group, five-year birth cohort and year of diagnosis are used as predictor variables. The resulting model is used to predict rates in future years, which are combined with population projections to provide estimates of the future number of cases.

Results
For all cancers (excluding non-melanoma skin) age-standardised rates are expected to fall by 1% by 2035 among males and rise among females by 13%. The number of cases is projected to increase by 25% among males and by 24% among females by 2020, while by 2035 increases of 65% for males and 63% for females are expected. Rates are projected to fall for male lung, bladder, brain, cervical, prostate, ovary and stomach cancers and leukaemia. Increases are expected for breast, colorectal, kidney, liver, oral, female lung, female pancreatic and uterine cancers, melanoma and non-Hodgkin's lymphoma. The number of cases is expected to increase for all cancer types except for cervical and stomach cancers.

Conclusion
This work monitors past changes to cancer cases and rates and predicts an increase of new cancer cases which will require preparation by service planners to meet the needs of future cancer patients. The potential exists to alter these projections through tobacco and alcohol control.

A-027 - Can We Apply Benfordís Law To Check Quality Of Cancer Incidence Data?

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Purpose
Benford's law states that the distribution of the occurrence of the first significant digit (FSD) of a number, in many large collections of numbers, is not uniform. The aim of this study was to evaluate whether population-based cancer incidence rates follow Benford's law and if this can be used in their data quality checking process.
Methods
Detailed databases from six population-based cancer registries (from Africa, North and South America, Asia, Europa and Oceania) were retrieved from the Cancer Incidence in 5 Continents-X website. These datasets consisted of 244 combinations of topography and morphological groups, 18 age groups and two sexes. The distribution of FSD was evaluated for the whole dataset, plus for some subgroups as cancer registries, cancer types and sexes.
Several statistics, including Pearson's coefficient of correlation, distance measures and specific tests, were applied to check for consistency between calculated FSD frequency distribution and the theoretical Benford's one.
Results
The distribution of FSD, calcutated for each combination, consistently showed mean values greater than the medians and were positively skewed. For the whole dataset (22,180 observations), and for single cancer registries (from 1,546 to 6,296 observations), the coefficient of correlation was high, ranging from 0.918 to 0.997. Also the distance measures were very low. Very similar results were obtained for major cancer sites, and sexes. The need for statistical tests, not influenced by sample size, was confirmed.
Conclusions
The data analyzed in this study had already been checked and approved for publication in Cancer Incidence in 5 Continents-X. Therefore, their quality was expected to be good. This study demonstrated that cancer incidence rates follow Benford's law. This suggests using the adherence to Benford's law of the FSD distribution of incidence rates as a quick tool in their quality evaluation, in order to identify possible deviations for further investigations.

A-028 - Trends Of Oral Cavity, Oropharyngeal, And Laryngeal Cancer Incidence In Scotland (1975 - 2012) ñ A Socioeconomic Perspective

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Aim: To examine incidence trends of oral cavity (OCC), oropharyngeal (OPC), and laryngeal cancer in Scotland between 1975 and 2012 by socioeconomic status.

Methods: Our study included all diagnosed cases of OCC (C00.3-C00.9, C02-C06 excluding C2.4), OPC (C01, C2.4, C09-C10, C14), and laryngeal cancer (C32) in the Scottish Cancer Registry (1975-2012). We collated cancer data and corresponding annual midterm population estimates by age, sex, geographic region, and area-based socioeconomic indices (Carstairs91 for 1975-2012 and Scottish Index of Multiple Deprivation SIMD09 for 2001-2012). Age-standardized incidence rates and adjusted Poisson regression rate-ratios (RR) compared subsites by age, sex, region, socioeconomic status, and year of diagnosis.

Results: The fully adjusted Poisson regression model for the whole period (1975-2012) showed that, relative to the least deprived, those living in the most socioeconomically deprived areas had the highest rate-ratios of OCC (RR 2.40; 95% CI 2.18-2.65), OPC (RR 2.49, 95% CI 2.18-2.86), and laryngeal cancer (RR 3.34, 95% CI 3.02-3.69), and an almost dose-like response was observed with increasing deprivation increasing cancer risk. In the most recent decade (2001-2012), incidence rates increased markedly for OPC, decreased for laryngeal cancer and were relatively stable for OCC. Over this period, socioeconomic inequality tended to increase for OPC (RR 3.33; 95% CI 2.72-4.07) and laryngeal cancer (RR 4.98; 95% CI 4.15-5.97) but remained relatively unchanged for OCC (RR 2.69; 95% CI 2.31-3.13). Males exhibited significantly higher rate-ratios across all subsites compared to females. The peak age of incidence of OPC was slightly lower (61-65 years) than the other subsites (71 -75 years).

Conclusion: Contrary to reports that OPC exhibits an inverse socioeconomic profile, our data shows that those from the most relative to the least socioeconomically deprived areas have consistently shown relatively higher rates of head and neck cancer across all subsites.

Funding Source: NHS Education for Scotland

A-029 - Ovarian Cancer Trends In São Paulo, Brazil: 1997-2011

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Ovarian cancer trends in São Paulo, Brazil: 1997-2011.
Purpose: The ovarian cancer (OC) behaves differently around the world, with the highest incidence rates occurring in populations of Central and Eastern Europe. The aim of the study was to describe OC patterns in the Municipality of São Paulo, Brazil, from 1997 to 2011.
Methods: Incident cases (C56, ICD-10) were provided by the São Paulo Population-based Cancer Registry. Deaths (C56, ICD-10) were obtained from the DATASUS online platform. Crude and Age-standardized (SEGI´s world population) for incidence and mortality rates per 100,000/women were calculated. Incidence tumors were classified as serous carcinoma, mucinous carcinoma, endometrioid carcinoma and adenocarcinoma. Age was grouped into the following age groups:< 35, 35-49, 50-59, 60-69, 70-79, and 80+. The coefficients were calculated by age and histological group. Trend analysis was conducted using the Joinpoint software, by estimating the Annual Percent Change (APC). Statistical analyses were considered as significant when p values < 0.05.
Results: 7,882 cases were diagnosed and 3,924 deaths were recorded from OC. Both incidence and mortality showed decreasing trends having APC -6.6% and -1.2%, respectively. The most significant declines in incidence and mortality were seen among women aged 50 and older. In the mortality trend is decreasing only from 50 to 79 years old and the other age groups remained stable. All histological groups had decreasing trends, except adenocarcinoma remained stable.
Conclusions: This study concluded that, overall, the trend of incidence and mortality in São Paulo is decreasing, and the trend of incidence had a greater decrease.
Funding source: Support Foundation of São Paulo Research

A-030 - Trends In Incidence And Mortality Of Colorectal Cancer In The Municipality Of São Paulo, São Paulo, Brazil, 1997-2012

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Purpose: Colorectal cancer (CRC) is one of the most incident worldwide. The risk for CRC development is influenced by genetic and environmental factors, such as tobacco smoking. We analyzed the trend of incidence and mortality from CRC by sex and age group, for the municipality of São Paulo from 1997 to 2012.
Methods: Ecological study using cancer and mortality records (C18-C20 codes of ICD-10). The incidence and mortality rates were calculated based on the population provided by IBGE and adjusted for the world population of SEGI, by sex and age group (40-49; 50-59; 60-69; ≥70 years). The annual percent change (APC) and Confidence Intervals 95% (95%CI) were estimated using the Joinpoint software.
Results: From 1997-2012, 47,297 incident cases (52.6% in women) and 19,854 deaths (53.4% in women) occurred. The average incidence rate was 22.5 per 100,000 women and 29.1 per 100,000 men; and mortality rate was 9.9 and 13.1 per 100,000 in women and men, respectively. In women, incidence is significantly decreasing (APC:-1.5%; 95%CI:-2.3;-0.7), but mortality remains stable. In men, incidence is also decreasing (APC:-1.3%; 95%CI:-2.1;-0.5), whereas, mortality is increasing (APC:0.7%; 95%CI:0.2;1.2). By age group, there was a decrease in incidence rates in women aged 60-69 years (APC:-2.5%) and ≥70 years (APC:-2.9%) and in men aged 60-69 years (APC:-2.5%) and ≥70 years (APC:-2.1%); in other age groups the incidence rates were stable. For mortality, there was, in women, reduction to 60-69 (APC:-1.7%) and increase to 40-49 years (APC:1.6%) and 50-59 years (APC:1.9%); in men, also increase, except in 60-69 year age group.
Conclusions: The CRC rates in São Paulo are intermediate when compared to other countries. Differences in CRC burden across age groups maybe associated with differences prevalence exposure to risk factors. Since mortality may reflect both the incidence and the difficulties of access to health services.
Funding source: CAPES

A-031 - Head And Neck Cancer Trends Using A Single Hospital-Based Cancer Registry, São Paulo, Brazil, 2008-2012

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Purpose: To describe epidemiological trends of patients with head and neck cancer, using a hospital-based cancer registry (HBCR).
Methods: This was a HBCR study carried out at a reference hospital for cancer treatment in Sao Paulo, Brazil, between 2008-2012. Records were retrieved and data about patients with head and neck cancer (oral cavity, oropharynx, hypopharynx, larynx, and not specified types), over 18 years, were included in the analysis. The calculation of relative risk (RR) was performed by Poisson regression with 95% confidence intervals. Analyses were performed using SPSS for Windows v.18.
Results: 1801 cases of head and neck cancer were diagnosed in the period, most of them were men (1,509 cases, 83.8%), mean age was 59 years (standerd deviation [SD] = 10.7 years). Among men, the most common tumors were located in the oropharynx (34.2%), followed by laryngeal tumors (9.5%). Among women, both the oropharynx and the larynx tumors had the same frequency (27.4%). More than 95% of the tumors were squamous cell carcinomas. A growing trend for all tumors frequencies was observed: oral cavity (RR = 1.18, 95% CI 1:09 to 1:27), oropharynx (RR = 1.23, 95% CI 1:16 to 1:31), hypopharynx (RR = 1.17, 95CI% 1:05 to 1:30) and larynx (RR = 1.20, 95% CI 1:12 to 1:27).
Conclusions: The analysis allowed us to observe a growing frequency trend in head and neck cancer at a reference center, over the last years. These findings should motivate further epidemiological investigations of differential associations of environmental factors, such as tobacco, alcohol and human papillomavirus infection.
Funding source: No funding.

A-032 - Trends In Incidence And Mortality Of Esophagus Cancer In The Municipality Of São Paulo, São Paulo, Brazil, 1997-2012

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Introduction: Esophageal cancer, although infrequent, it is an extremely lethal disease, which frequently affects men over 50s. This study aimed to verify the trends of incidence and mortality from esophageal cancer in São Paulo. **Methods:** The incident cases of esophageal cancer (C15, ICD-10) 1997-2012 were obtained from the population-based cancer registry of São Paulo. Deaths were obtained in DATASUS for the same period (1997-2012). The crude incidence and mortality rates were calculated based on population provided by the IBGE and adjusted considering the world population of Segi. The trend analyzes were performed for incidence and mortality by sex and age group (30-39, 40-49, 50-59, 60-69, 70 and over) using the *Joinpoint* software. The results were presented as annual percent change (APC). **Results:** Some 9219 cases were newly diagnosed (78.15% in men) and 6,513 deaths (81.04% men) occurred during the period. There was a significant decrease in incidence for males and females of -4.2% and -1.4%, respectively. This decreasing pattern was found for all age groups, except for the 30 to 39 age group, which was stable, for men and women, being more pronounced among men. For mortality, a similar pattern was found for both men and women: -1.5% and -3.1%, respectively. Among the youngest age groups (<60s), for females, the mortality rate has been stable, and a decrease in the age group 60-69 years (-3, 2%) and aged 70 or older (-1.4%). For males, the mortality rate has been stable for the age group 50-59 years and decreasing trends were found for the remaining age groups: 30-39 years (-9.3%), 40-49 years (-2.7%), 60-69 years (-2.2%) and 70 and over (-1.4%). **Conclusion:** The observed trends reflect changes in the behavior of the population regarding lifestyle, for example, tobacco consumption.

A-033 - Epidemiological Profile Of Cancer Patients Using A Hospital-Based Cancer Registry, São Paulo, Brazil, 2008-2012

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Purpose: To characterize the sociodemographic and clinical profile of cancer patients for the five main sites of malignant tumors, using a hospital-based cancer registry (HBCR).
Methods: The data set available at the HBCR of a regional cancer center in Brazil, containing information on patients registered during the period of January 2008 to December 2012, was applied. All cases above 18 years were included. Frequencies and percentages were calculated for each of the variables under consideration. All analyzes were performed using statistical package SPSS for Windows v.18.
Results: A total of 23,417 patients were reported. The mean age at diagnosis among males was 62.0 compared with 59.0 years for females. The most frequent malignancies in men were cancers of the prostate (33.0%), colon and rectum (9.3%), mouth and oropharynx (6.6%), and stomach (6.3%). For women, they were found to be cancers of the breast (24.7%), colon and rectum (12.8%), lung (8.5%), thyroid (6.7%) and stomach (5.4%). Approximately 72% of men with prostate tumors arrived at the institution in stage I or II. Some 48% of women, diagnosed with breast tumors, were classified in clinical stage I and II. It was observed a decrease in the number of prostate and breast cancer over the years. For other types of tumors, the frequencies were relatively stable, except for lung tumors in women, who had a rising trend.
Conclusions: HCBR can be considered as an effective way forward in getting a preview of cancer burden in the region. Proper surveillance and preventive programs need to be in place and healthcare policy should be adjusted to take into account the more pressing cancers in society.
Funding source: No funding.

A-034 - Comparison Between The Application Of Linkage Probabilistic Methods: Openreclink And R

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Purpose: The database relationship, also known as linkage, is frequently used in the studies of database management and its usage (duplicate identification cases, the completeness of the database, among others) has shown improvement in quality. However, there are several relationship techniques (probabilistic and deterministic), without a consensus, on what would be the best choice. The aim is to compare two linkage probabilistic methods, analyzing the time of each procedure, the number of true pairs found in each process and the ease of handling between the two procedures to be applied in a workplace, especially in cancer registries.
Methods: The information contained in the PROAIM database (Improvement Program for Mortality Information in São Paulo) and the RCBP-SP database (Population-Based Cancer Registry of São Paulo) related to ovarian cancer were used. The Openreclink and R computer programs were used for the linkage process.
Results: 2,944 true pairs in Openreclink were found in a timespan of 04h58min31s. On R, 1,719 true pairs were found in a timespan of 3h18min00s. The Openreclink program has a routine and a simpler understanding, which enhances and speeds its application in the work environment, such as the Population-Based Cancer Registry of São Paulo. However the R program, despite being more complex to understand (longer demand to understand the logic of the program and define the commands to be used), its steps are executed more quickly.
Conclusion: Although the R program is less time-consuming, the Openreclink program is more effective.
Funding Source: Support Foundation of São Paulo Research

A-035 - A Longitudinal Analysis Of Extramural Cancer Research Projects In LMICs Funded By The US National Cancer Institute (NCI)

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Purpose:
The NCI, along with other NIH Institutes and Centers, supports a large number of cancer research projects with international components. This analysis describes NCI-funded research projects conducted in low- and middle-income countries (LMICs) between NIH Fiscal Years (FY) 2008–2014. The purpose of this analysis is to identify future opportunities for prevention, early detection, and treatment research projects in LMICs that are aligned with the global occurrence and etiology of cancers.
Methods:
This analysis included NCI-supported extramural grants active between FY2008–FY2014. Each year a grant is active is counted as one grant-year. The grant data come from two internal NIH databases—IMPAC II and FACTS. Global cancer research grants were stratified by (1) WHO Region; (2) World Bank Lending Group; (3) Common Scientific Outline; and (4) anatomic tumor site. Organization names were standardized using GRID.
Results:
Between FY2008–FY2014, the NCI supported over 45,000 cancer research grant-years; approximately 8.8% (3,967) included foreign components and 1.5% (670) involved research in LMICs. The 670 active grants in LMICs yielded 1,230 research projects; the majority were within in the WHO Africa Region, 30.5%, (375) and the WHO Western Pacific Region, 28.8% (354). Analysis of the scientific content of these projects indicates that 11.4% focused on prevention research, 14.7% focused on early detection, and 21.3% focused on cancer treatment. The greatest number of LMIC research projects examine breast cancer, 9.6%, and lung cancer, 9.6%.
Conclusions:
Understanding the NCI's research portfolio in LMICs is vital for effective planning of research programs. Integrating this portfolio analysis with data on global cancer occurrence, etiology, risk factor prevalence, infection rates, and ecological exposures may guide the international research community as they develop programs to reduce the global burden of cancer.
Funding source:
This work has been generously supported by the NCI's Center for Global Health.

A-036 - Colorectal Cancer Trends In Young Adults In Great Britain, 1975-2012

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Purpose
Colorectal cancer is less common in younger age groups, although a recent US study showed that the incidence of colorectal cancer is increasing in adults aged 20 to 49 years old (1). By the end of the 1990s colorectal cancer incidence rates overall in Great Britain (GB) started to fall, but have since risen, particularly over the last decade (2). This may be associated with the introduction of the national bowel screening programme.

Methods
Trends in colorectal cancer (C18-20) incidence were analysed by age group to determine if there are differences to the overall trend or if similar trends were being seen as in the US. Annual European age standardised incidence rates (ASR) for GB were calculated. ASR trends between 1975 and 2012 were investigated using Joinpoint Regression Program for 20-34, 35-49, 50-74 and 75+ year olds. A log linear regression model was used to calculate the annual percentage change (APC) between data points and test for significant differences in linear trends.

Results
ASR increased significantly in 20-34 year olds since 1995 by 6% (5.4-7.1%) annually in GB. In those aged 35-49 years the APC was 1.2% (0.4-2%) since 2002.

Conclusion
There has been a significant increase in the incidence of colorectal cancer in younger adults aged 20-49 years in GB similar to the trend in US. It is predicted that as obesity in children increases colorectal cancer will continue to increase in younger adults. Awareness of the increasing burden in younger age groups is important to ensure early detection and the importance of prevention measures early in life.

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A-037 - Time Trends In Cancer Incidence And Mortality In A Mid-Sized Northeastern Brazilian City

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Purpose: The aim of the study is to describe time trends in cancer incidence and mortality in the population of Aracaju, Sergipe Brazil. These are important to assess the impact of control strategies, and provide tools to assess determinants of cancer risk at a population level.
Methods: We retrieved incidence data from the Population-Based Cancer Registry of Aracaju and mortality data from the official State Database for the period 1996-2011. We calculated incidence and mortality crude (CR) and age-standardized (ASR) rates (direct method, world population) for 23 cancer sites according to gender. Finally, we used these data to obtain time trends of top five, using the Joinpoint Regression Model.
Results: For the period studied, we observed 7061 incident cases in men and 7976 in women; 2988 deaths in men and 3200 in women. Top five most incident cancers in men were prostate, lung lip/oral cavity/pharynx, colorectal and stomach; and in women, breast, cervix, thyroid, colorectal and lung; top five most lethal were prostate, lung, stomach, lip/oral cavity/pharynx, and liver in men; and breast, lung, cervix, colorectal, and liver in women. Incidence trends showed a rising pattern in males until 2006, and then a downward trend. For females, the pattern was similar, except for a rising pattern again from 2009 on. Mortality trends showed a rising pattern only in males.
Conclusions: The features observed in the population studied have shown similarities with the ones observed in high-income areas, but conversely have shown, considering some cancer sites, such as cervix and oral cavity, the same pattern observed in low-income areas. Incidence, mortality rates, and trends for the most frequent cancers, might reflect different exposure levels to risk factors.
Funding source: the State of Sergipe Health Agency and Brazilian Health Ministry fund Aracaju Cancer Registry. No other source funded the present study.

A-038 - Comparison Between Estimated And Observed Colorectal Cancer Incidence For 2012

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BACKGROUND: The aim of this study is to examine differences in colorectal cancer incidence estimates of GLOBOCAN 2012 and observed colorectal cancer incidence rates in 19 selected countries. .

METHODS: Estimates of colorectal cancer incidence for 19 countries were gathered from GLOBOCAN 2012. Colorectal cancer incidence was retrieved from published data from 2008 to 2012. Observed colorectal cancer incidence rates were compared with colorectal cancer incidence estimates of GLOBOCAN 2012. Incidence rates were standardized using World standard population.

RESULTS: When observed colorectal cancer incidence rates of 2012 or nearest year to 2012 were compared with estimates of GLOBOCAN 2012, Slovenia, Australia, Japan, New Zealand, U.S.A showed 5% or higher incidence than estimates of GLOBOCAN 2012 in men. Especially, those of Australia, Japan, and New Zealand were 10% or higher than estimates of GLOBOCAN 2012. Korea, Denmark, Spain, Israel, Canada showed 5% or lower incidence than estimates of GLOBOCAN 2012 and among these countries, incidence rates of Korea and Israel were at 10% or lower than estimates of GLOBOCAN 2012. In women, New Zealand, Australia, Czech, Japan, U.S.A showed 5% or higher incidence than estimates of GLOBOCAN 2012 and among these countries, and incidence rates of New Zealand, Australia, Japan, U.S.A were 10% or higher than estimates of GLOBOCAN 2012. Korea, Denmark, Croatia, Israel, Italy, showed 5% or lower incidence than estimates of GLOBOCAN 2012 and among these countries, incidence rates of Korea and Israel were 10% or lower than estimates of GLOBOCAN 2012.

CONCLUSION: In this study, there was considerable difference in colorectal cancer incidence estimates of GLOBOCAN 2012 and observed colorectal cancer incidence rates. GLOBOCAN is important in setting global health priorities, but also consider limitation of the estimates.

FUNDING SOURCE: The National Research Foundation of Korea (2013R1A1A2A10008260)

A-039 - The Danish Prostate Cancer Database (DAPROCAdata)

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Purpose
The Danish Prostate Cancer Database (DAPROCAdata) is a nationwide clinical cancer database that has prospectively collected data on incident prostate cancer patients in Denmark since February 2010. The overall aim of DAPROCAdata is to improve the quality of prostate cancer care in Denmark by systematically collecting key clinical variables for the purposes of health care monitoring, quality improvement and research.

Methods
Study population: All Danish patients with histologically verified prostate cancer are included in DAPROCAdata.
Main variables: DAPROCAdata registers clinical data and selected characteristics for prostate cancer patients at diagnosis. Data are collected from linkage of nationwide health registries and supplemented with online registration of key clinical variables by treating physicians at urological and oncological departments. Main variables include Gleason scores, TNM cancer staging, PSA values, and therapeutic measures (active surveillance, surgery, radiotherapy, endocrine therapy, and chemotherapy).

Results
In total, 22,332 prostate cancer patients were registered in DAPROCAdata as of April 2015. A key feature of DAPROCAdata is the routine collection of patient-reported outcome measures (PROM), including data on quality-of-life (pain levels, physical activity, sexual function, depression, urine and fecal incontinence) and lifestyle factors (smoking, alcohol consumption, and body mass index). PROM data are derived from questionnaires distributed at diagnosis and at 1-year and 3-year follow-up. However, the PROM data is limited by low completeness (26% among newly diagnosed patients in 2014).

Conclusion
DAPROCAdata is a comprehensive, yet still young clinical database. Efforts to improve data collection, data validity and completeness are ongoing and of high priority.

Funding source
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A-040 - Comparing Risk For Cancer Among Persons With Aids And General Population: Results From São Paulo, Brazil

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Purpose: Several studies have shown increased risk for cancer among people with HIV/AIDS when compared to the general population. The aim of this study was to compare risk for cancer in persons with AIDS and the general population in São Paulo, Brazil, between 1997 and 2012.
Methods: We conducted a population-based registry linkage study. We linked the Population-based Cancer Registry of São Paulo (496,276 cancer cases) and the AIDS notification database (81,889 AIDS cases) to identify persons with AIDS who had cancer. To compare cancer risk, we calculated the standardized incidence ratio (SIR) and its 95% confidence intervals.
Results: Among persons with AIDS, 2,074 cancer cases were diagnosed (1,510; 72.8% in men). In men with AIDS the highest risks were found for anal cancer (SIR=33.0; 95%CI=24.9; 41.2), non-Hodgkin-lymphoma (NHL; SIR=13.4; 95%CI=11.9; 14.9), Hodgkin lymphoma (HL; SIR=5.8; 95%CI= 4.2; 7.5), eye cancer (SIR= 4.9; 95%CI=1.7; 8.1) and liver cancer (SIR=4.3; 95%CI= 2.3; 6.3). Cancers of the male genital organs (penis, prostate and testis) did not have increased risk. In women with AIDS, NHL (SIR=13.9; 95%CI= 11.1; 16.6), anal cancer (SIR=11.2; 95%CI= 4.3; 18.2), vulvar cancer (SIR=8.6; 95%CI=3.7; 13.5), cervical cancer (SIR=5.4; 95%CI= 4.4; 6.4) and oral cavity and oropharynx cancer (SIR= 2.8; 95%CI=1.1; 4.6) occurred in excess. Risk for ovarian and breast cancers did not differ from the general population, whereas, thyroid cancer occurred at lower rates in women with AIDS (SIR=0.5; 95%CI=0.3; 0.7).
Conclusions: Increased risk for cancer was not only restricted to AIDS-defining cancers. Other infection-related cancers such as HL, anal and liver cancer occurred at higher rates in the AIDS population.
Funding source: Conselho Nacional de Desenvolvimento Científico e Tecnológico and the German Ministry for Economic Cooperation and Development through the German Academic Exchange Service and the Higher Education Excellence in Development Cooperation.

A-041 - History Of The Recife, Brazil Cancer RegistryóPast, Present And Future

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PURPOSE - The population-based cancer registries are health information systems that permit collection, classification and analysis of diagnosed cancer cases. In Brazil there are 23 population-based cancer registries fed by a network of 282 cancer hospital Registers. METHODS - This paper describes the history and status of the Recife Cancer Registry, based on archival research, in order to understand its role in cancer control in Brazil.
RESULTS - The first population-based cancer registry was set up in Brazil in **1967** in Recife by Prof. Adonis Carvalho in the school of Medicine of the Federal University of Pernambuco in co-operation with the Bureau of Health of the State of Pernambuco, and the Ministry of Health .
In the period **1995-2002** the population-based cancer registry was managed by the Health Department of the State of Pernambuco. The following year was the municipalization of record where the Recife Health Department began to operate and manage the same.
From the year **2006** through Ordinance 2.607 28/12/2005, the Secretariat of Health Surveillance establishing with regular resources of the Surveillance Financial Ceiling Health financial incentive to fund the activities developed by populacional-based cancer registries. **Currently**, the population-based cancer registry Recife, collecting information of 27 general hospitals, one hospital cancer, 3 university hospitals, pathology laboratories and radio and chemotherapy services.
CONCLUSION - Federal University of Pernambuco had a historic role in creating the first registry Brazil. This Register is important because it allows a collective analysis of the epidemiological and other risk factors for cancer. However not all cancer hospitals participate in this program.
FUNDING SOURCE – FEDERAL UNIVERSITY OF PERNAMBUCO

Key Words—cancer register, epidemiology, health monitoring, health information systems.

A-042 - Incidence Of Childhood Cancer In Slovakia: Results For Period 2000-2012

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Purpose: The aim of the study was to describe cancer incidence in children (age-range 0-14 years) registered by National Slovak clinical cancer registry of children and adolescents for the period 2000-2012.
Methods: Patients were identified in three regional pediatric treatment centers (Bratislava, Banska Bystrica and Kosice), which use the same treatment strategies. The registry includes all tumors, irrespective of behavior, and includes skin tumors and histiocytosis X. During internship in IARC in 2014-2015, all cancer cases have been recoded from the original ICD-10 classification to the ICD-O-3 and ICCC-3 classifications, uploaded to tailored Can-Reg 5 software and analysed for incidence rates.
Results: In 2000-2012, 1,630 cases were registered in the registry. Among them, 95.6% were confirmed microscopically. The age-standardized (World standard) annual incidence rate (ASR) was 145.1 per million person-years. The most frequent were leukaemias (ASR=44.5), followed by CNS tumours (ASR=31.7) and lymphomas (ASR=15.4). The recorded data showed an average annual increase of 1.72% (p=0.01).
Conclusions: The observed incidence rates are comparable with those reported from National cancer registry of Slovakia (NOR) and also neighbouring countries. It is important to ensure long-term monitoring and put in place a mechanism of data exchange with the NOR, to improve data quality and completeness in both sources.
Funding source: National Scholarship Program of the Slovak Republic (NSP), IARC stipendium

A-043 - Trends In Cancer Incidence Among Adolescents And Young Adults (AYA) In São Paulo, Brazil, 1997-2010

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Purpose: This study aimed to analyze trends in cancer incidence among adolescents and young adults (AYA) (15-29 years) in São Paulo, Brazil, in the period from 1997 to 2010. Methods: This was an ecological time-series study, which used cases reported to the population-based Cancer Registry of São Paulo, Brazil, classified according to Birch & Alston classification. Age-standardized (world population) were reported for every 100,000 inhabitants, according to group and gender. Annual percentage changes (APC) were calculated using the Joinpoint method, with the calendar year as regressor variable. The null hypothesis that APC = 0 was rejected when $p<0.05$. Results: During the study period, 14,011 cases of cancer among AYA were registered in São Paulo. There was a non-significant decline in the incidence of all malignancies in men (APC=-1.04%, 95% CI -2.76;0.71%) and a significant increase in women (APC =2.55%, 95% CI 0.71;4.42%). Among males, there was a significant increase in the incidence of carcinomas (except skin) (APC=4.60%, 95% CI 1.95;7.33%) and a significant decline for leukemias (APC=-8.46%, 95% CI -11.36;-5.46%), CNS tumors (APC=-6.77%, 95% CI -10.05;-3.36%), and bone tumors (APC=-6.42%, 95% CI -10.16;-2.53%). Among females, there was a significant increase in the incidence of carcinomas (except skin) (APC=4.95%, 95% CI 2.27;7.70%) and unspecified malignant neoplasms (APC=8.32%, 95% CI 4.04;12.76%), and a significant decline in the incidence of CNS tumors (APC=-6.87%, 95% CI -10.76;-2.81%), bone tumors (APC=-7.30%, 95% CI -10.99;-3.45%) and soft tissue sarcomas (APC=-4.74%, 95% CI -8.00;-1.37%). No significant trends in incidence were observed for lymphomas and skin cancers. Conclusions: Distinct trends in cancer incidence among AYA were observed in São Paulo, Brazil, including increasing rates of carcinomas among women. These patterns and trends must be analyzed in order to tailor better strategies for cancer prevention and control in adolescents and young adults, more adequate their specific needs.

A-044 - IARC Regional Hub For Cancer Registration In Northern Africa, Central And Western Asia

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Purpose:
Izmir Cancer Registry, the first population-based cancer registry (CR) in Turkey, became the second IARC Regional Hub for Cancer Registration within the GICR (Global Initiative for Cancer Registry Development) program in October 2013. The Hub aims to build capacity for cancer registration in low- and middle-income countries within Northern Africa, Central and Western Asia.
Methods:
The Hub supports cancer registries in the region by being the first point of contact for the registry communities, providing localized technical and scientific support, delivering tailored training in population-based cancer registration, promoting the use of data, advocating for the cause of cancer registration and facilitating collaboration and networking between cancer registries. A Hub Advisory Committee, consisting of international and regional experts, has been established to develop the Hub activities.
Results:
Since 2013, sixteen training events at both basic and advanced levels, as well as two training visits to Izmir CR, have been organized in the Hub region and 237 cancer registry professionals trained. New training resources have been developed, including the first Russian language basic cancer registration course. A roster of regional experts has been created to assist in delivering Hub activities in training, site visits and directed country-level support. Eight site visits were carried out and recommendations provided to Algeria, Egypt, Georgia, Kyrgyzstan, Lebanon, Morocco, Uzbekistan, West Bank and Gaza Strip. Research collaborations have been initiated in the Eastern Mediterannean and Middle Eastern regions, and a series of site-specific articles on cancer in the Middle East submitted.
Conclusion:
Following successful implementation, the Izmir Hub is developing as a regional resource centre capable of providing targeted support for population-based cancer registries in the region. Further efforts are needed to empower regional cancer registry networks and integrate newly available data into cancer control programs.

A-045 - Changing Trends Of Incidence Of Lung Cancer In Southern Thailand

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Purpose: Lung cancer is one of the leading incident cancers in Thailand (#2 in males and # 4 in females). With the greatest religious diversity in the nation, the Southern region of Thailand presents a unique heterogeneity of behavioral and dietary patterns between Thai Buddhists and Muslims. Although the role of smoking has been well characterized, the incidence rate trends across Southern Thailand have not yet been examined by sex, religion and histology.

Methods: Lung cancer cases (n=3845) diagnosed from 1989-2013 were extracted from the Songkhla Cancer Registry. Age-standardized incidence rates (ASRs) were calculated by sex, religion and histology using software R. Incidence rates were standardized using the World Standard Population (WHO 2000-2025). Annual percent change (APC) were calculated to quantify the changes in incidence rates over time using Joinpoint regression analysis.

Results: Males have higher rates of lung cancer than females (ASRs: 21.1 and 7.3 per 100,000, respectively). Adenocarcinoma was the most common histology in both males and females (ASRs: 6.9 and 3.9 per 100,000, respectively). From 1989-2013, adenocarcinoma rates continued to increase for both males and females (APCs=4.7% and 5.7%, respectively), whereas squamous, large and small cell rates continued to decrease. In terms of religion, rates increased for Buddhist females (APC= 4.0%) and Muslim males (APC=5.4%), and both Buddhist males and females showed larger increases in incidence rates of adenocarcinoma than their Muslims counterparts.

Conclusions: In Southern Thailand, the continuing rise in lung adenocarcinoma in both genders especially in women who are non-smokers, suggest a need to better understand factors in addition to smoking, which may be contributing to this trend. Further investigation into the prevalence of risk factors by religion in Southern Thailand is needed to explain these trends.

Funding sources: Thai Studies Grant and Rackham Research Grant, University of Michigan

A-046 - Cancer Profile In The Eastern Mediterranean Region

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Purpose
Many countries in the Eastern Mediterranean region (EMR) are undergoing marked demographic and socioeconomic transitions that are increasing the annual cancer burden in each of the 22 countries. We sought to examine and illustrate similarities and differences in the national cancer incidence and mortality profiles as a support to regional cancer control planning in the EMR.

Methods
The incidence and mortality estimates by country, cancer type, sex, and age for 22 EMR countries were obtained from GLOBOCAN 2012. Numbers, rates (age-standardised per 100,000) alongside overall rankings of their magnitude are presented.

Results
The cancer incidence and mortality vary considerably between countries in the EMR. Incidence rates were highest in Lebanon (rates of 204 and 193 per 100,000 in males and females, respectively). Mortality from cancer was highest in Lebanon (119) and Egypt (121) among males and in Somalia (117) among females. The profile of common cancers differs substantially by sex. For females, breast cancer is the most common cancer in all 22 countries, followed by cervical cancer, which ranks high only in the lower-income countries in the region. For males, lung, prostate, and colorectal cancer in combination represent almost 30% of the cancer burden in countries that have attained very high levels of human development.

Conclusions
The most common cancers in the EMR – lung, and other smoking-related cancers, colorectal and female breast cancers are largely amenable to preventive strategies by primary and/or secondary prevention. There is therefore an urgent need for the implementation of effective interventions tackling smoking behaviour, encouraging physical activity and a healthier diet. The high mortality observed from breast and cervical cancer highlights the need to break the stigmas surrounding these cancers and improve awareness that will increase female participation in screening programmes in the region.

Funding source
WHO EMRO Action Plan

A-047 - Experience Of A Hospital Cancer Registry From A Microregion In A Developing Country

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Purpose: To describe the experience of a Hospital Cancer Registry (HCR) from Southern Brazil, over 10 years of translational discussion of the HCR data with clinical/scientific/administrative staffs and Municipal Health Departments, whose our institution is a reference center (22 cities). Methods: Overall cancer cases diagnosed/treated on our institution between 2005-2013 were identified from the institutional computerized system, registered annually by the HCR team and analyzed (SPSS program) annually and periodically. The findings were discussed with institutional staffs and Municipal Health Departments for planning actions based on these data. Regional projects are being prepared, also, based on critical data obtained through the HCR. Results: 7416 patients included. The findings, compared to national/international literature, were: high prevalence (23%) of cancer diagnosis under 50 years, of cancer family history (64.8%) and of smoking and drinking habits (46.7% and 28.4%, respectively); advanced clinical stage (ECIII) or metastatic (ECIV) in 16.9% and 23.3% of cases, being more prevalent in patients from the public health system (ECIII = IV = 19.7% and 28.9%) compared to private system (ECIII = 13.8% and IV = 16.0%); and for specific tumors - lung (ECIII = 12.6 and IV = 73.8%), head and neck (ECIII and IV = 14.7% = 63.2%) and colorectal (ECIII and IV = 33.1% = 27.7%). For tumors with a solid regional screening program, such breast cancer, the prevalence of ECIII-IV was lower (26%) with a reduction trend over the 10 years period. Five-years cancer survival for the most prevalent tumors were: 83.9% for breast, 70.0% for prostate, 25.0% for lung and 65.7% for colorectal cancers. Conclusions: These data indicate the public health importance of this type of approach using data from a regional HCR. The integration of HCR team and Municipal Health Departments is one of the cornerstone to regional cancer control.Funding source: Hospital Tacchini.

A-048 - Integrating Cancer And Other Disease Surveillance Systems: A Framework For Action

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Purpose:
Given the growing burden of noncommunicable diseases (NCDs) including cancer, it is critical to understand the differing characteristics of the major disease forms and their surveillance, particularly in economically transitioning countries where NCDs have equalled or surpassed communicable diseases (CDs) as major public health problems. We compare approaches to the global surveillance of cancer, relative to CDs as well as other NCDs, proposing a framework to support integrating cancer into national disease surveillance systems.
Methods:
A comparison of the major features of the surveillance of cancer *versus* CDs and NCDs was performed. We propose a basic framework for cancer and NCDs surveillance at the global level and provide schema to ensure key requirements for cancer incidence surveillance are met.
Results:
There are communalities in the surveillance of the major diseases; a general framework for cancer surveillance – applicable to all NCDs – shares population status attributes ('Healthy', 'New disease', 'Living with the disease' and 'Dying from the disease') as well as basic outcome measures (risk factor prevalence, incidence, prevalence, survival, mortality). There are also inherent differences however, in the appropriate surveillance strategies that should be applied. While risk factor surveys are used widely in the surveillance of the main NCDs, population-based cancer registries (PBCR) play a unique, fundamental role, in the surveillance of cancer incidence. Implementation of PBCR requires clear definitions in order to provide reliable data; these are examined in detail.
Conclusions:
Although the surveillance of NCDs necessitates an approach that utilises a common framework, the strategies for implementation must be tailored to support complete integration across disease domains. PBCR are the only means to obtain cancer incidence for cancer control at the population level.

A-049 - Epidemiological Profile Of Infant And Juvenile Cancer In The City Of Recife, Brazil 2002-2008

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Purpose: Cancer is the third cause of death and the fourth cause of hospital internments in Recife, State of Pernambuco, Brazil. Infant and Juvenile cancers represents two to three percent of all malignant tumors.
Method: This is a descriptive study based on data from the population-based cancer registry in the City of Recife. The Registry breaks down data about cancer into determined populations, with clinical and pathological characteristics statistically aggregated from various sources.
Results: Between 2002 and 2008 the Recife Registry captured 23.462 cancer cases, of which 527 (2.3%) occurred between infants and children 1-19 years of age. The majority of cases occurred between 15-19 years, (36.6%), and 0 to 4 years (26.9%); females showed the largest percentages of cases with 54.8%. Topographically, malignant tumors of the bone marrow and central nervous system are in first and second place respectively, with 41.1% and 28.2% of the cases. In third place is colon and uterine cancer with 19.0%.
Morphologically, leukemias are in first place with 23,1%. Residents of Sanitary Districts VI (20.7%) and II (17.6%) showed the most cases, these being neighborhoods of Varzea (5.3%) and Boa Viagem (4.4%), and Ibura (4.2%) being responsible for the majority of cases. Deaths occurred in greater proportion among adolescents 15-19 years of age (32.1%), children 0-4 years (29.9%).
Conclusion: Health professional surveillance and notification makes it possible to understand the epidemiological situation of infant and juvenile cancer, and permits targeting public policies of promotion, prevention, and integral attention to the patient in order to reduce morbidity and mortality.
FUNDING SOURCE – Ministry of Health of Brazil, Ministry of Education of Brazil (Programa de Educação Pelo Trabalho Para a Saúde – PET-SAÚDE)
Key Words: epidemiological profile, cancer, juvenile and infant cancers, health surveillance.

A-050 - IARC Regional Hub For Cancer Registration In Latin America

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Purpose:
The IARC Regional Hub for Latin America (LA Hub) was established within the GICR (Global Initiative for Cancer Registry Development) program in early 2014. The coordinating centre based within the National Cancer Institute (INC) of Argentina in Buenos Aires, incorporates additional expertise from other countries through designated Collaborating Centres. The LA Hub aims to build and improve capacity for cancer registration in Spanish and Portuguese speaking countries in the region.
Methods:
The LA Hub supports cancer registries in the region by providing tailored technical and scientific assistance, delivering training in population-based cancer registration, promoting the use of data, advocating for the cause of cancer registration and facilitating collaboration and networking between cancer registries. A Hub Advisory Committee with key regional partners and experts has been established to develop Hub activities.
Results:
Thirteen site visits were carried out in 2014-2015 with recommendations provided to Argentina, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay and Peru. Three intermediate level training courses have taken place, five CanReg5 webinars have been organized and regional transmission of registry training events has been facilitated. Criteria for for a mentorship program has been developed. INC has set up a virtual discussion forum using their website and a monthly update on GICR regional activities has been issued since March 2015. A series of articles on cancer and cancer registration in the region have been accepted for publication.
Conclusion:
Following successful implementation, the LA Hub is developing as resource centre capable of providing targeted support for population-based cancer registries in the region. Further efforts are needed to empower regional cancer registry networks and integrate newly available data into cancer control programs.

A-051 - Progress In The Fight Against Cancer: A Global Overview

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Purpose: Cancer has progressively become one of the leading causes of death worldwide. An assessment of the current state and progress in reducing the burden of cancer is therefore critical to guide the future global cancer control strategies.

Methods: We extracted population-based mortality data for all-cause, cardiovascular diseases and major cancer sites (lung, stomach, female breast, colorectal and prostate) between 1981 to 2010 from the WHO Mortality Database by sex, year and age in 61 countries with high or moderate quality data. Firstly, we used life-table methods to calculate the gain in life expectancy (GLE) due to elimination of a specific cancer death to evaluate the time-varying mortality burden. Secondly, we decomposed the change in Life expectancy between 1981 and 2010 and estimated each cancer site's contribution to it.

Results: During the past three decades, decline in cancer mortality contribute to life expectancy (LE) increase by 1.0 year in men and 0.6 year in women in high-resource countries, and 0.2 year for both sexes in low-resource countries. Among all cancer sites included, decrease in lung cancer mortality had the largest impact to the increase in male's LE in high-resource countries (up to 0.7 year in the Netherlands), yet its role was negligible in countries with lower resources and in women. Among women, declining breast cancer was responsible for the extension in life expectancy particularly among women in high-resource countries (up to 0.3 year in UK).

Conclusion: Our findings highlight that the marked variation in the progress in cancer control, leading to larger gap between highly and less developed country, but closing the sex gap. Global action should redirect some of the cancer control efforts to low-resource countries and support promotion of healthy lifestyles.

Funding Source: Section of Cancer Surveillance, International Agency for Research on Cancer

A-052 - International Burden Of Gallbladder Cancer

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Purpose: Gallbladder cancer is highly fatal and has a unique global distribution. Previous studies described variations in rates and temporal trends across countries; we have undertaken an updated analysis of current patterns and trends in gallbladder cancer mortality using the most recent available data.

Methods: The International Agency for Research on Cancer's GLOBOCAN 2012 was used to report country-specific estimates for 2012. We also present national age-standardized (world) mortality rates by sex up to 2014 and calculate the ratio of mortality rates in 2009-2013 relative to 1989-1993 by sex for countries with available data using the WHO Mortality Database.

Results: In 2012, the highest estimated mortality rates in the world were in South America and Asia, with rates as high as 10.3 deaths (per 100,000) among females in Chile. Rates among females were also high in Bolivia (10.1), Bangladesh (5.9), and Peru (5.0). The highest mortality rates among males were in Laos (6.3), South Korea (5.8), and Chile (5.0). Among high-risk populations with long-term mortality data, rates decreased in the past decades in both males and females. For example, mortality rates decreased by about 50% among females in Chile (15.5 in 1997 to 8.6 in 2013) and by 30% among males in South Korea (7.6 in 2001 to 5.1 in 2013). Between 1989-1993 and 2009-2013, rates decreased in both sexes for 27 of 33 countries considered in the analyses, with decreases of 30% to 60% in most lower-risk countries within Europe, Northern America, and Oceania.

Conclusions: Death rates are decreasing in most countries considered in this analysis. Further studies are needed to examine factors contributing to this pattern.

Funding source: American Cancer Society Intramural Research

A-053 - International Incidence Of Childhood Cancer

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PURPOSE
Cancers occur rarely in childhood. They are comprised of distinct histology types and raise a range of ethical, psychological, and societal concerns. The extent of cancer burden is unknown in many low-resource countries, as the data on childhood cancer incidence are not collected. IARC, jointly with the International Association of Cancer Registries (IACR), is coordinating a third study in the series, International Incidence of Childhood Cancer (IICC-3). The new publication will provide comparable data on childhood cancer occurrence worldwide.

METHODS
Cancer registries were identified through the IACR and other links. Of the total of 475 invited registries 410 had enrolled. Overall, 781 distinct datasets were processed and their quality was evaluated. The peer-review process was conducted by the IICC-3 Editors during three face-to-face meetings and over 50 teleconferences, according to standardised criteria. The quality of many datasets has improved considerably during this process. More than 350 datasets were qualified for inclusion.

RESULTS
The target period covered more than 20 years, starting with 1990, even though many registries included shorter periods. The reported rates in the age 0-14 years per million person-years varied widely across and within the continents. The lowest rates on average were reported from Africa (approximate range 50-100) and the highest from the North America (150-180). The incidence rates in the age group 15-19 were slightly higher. The incidence rates were higher than those reported in the previous edition of the series.

CONCLUSIONS
IICC-3 is a unique source of comparable data on childhood cancer and constitutes a good ground for assessment of cancer burden in children. The geographical differences suggest a variety of aetiological hypotheses. Sustained data availability over time and their quality is indispensable to devise cancer control mechanisms in this population.

FUNDING
IICC-3 is supported by IARC and the Union for International Cancer Control (UICC).

A-054 - Burden Of Cancer Associated With Type 2 Diabetes Mellitus In Japan, 2010-2030

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Diabetes mellitus constitutes a major disease burden globally, and the prevalence of diabetes continues to increase worldwide. We aimed to estimate the burden of cancer associated with type 2 diabetes mellitus in Japan between 2010 and 2030. In this study, we estimated the Population Attributable Fraction of cancer risk associated with type 2 diabetes in 2010 and 2030 using the prevalence estimates of type 2 diabetes in Japan from 1990 to 2030, summary hazard ratios of diabetes and cancer risk from a pooled analysis of eight large-scale Japanese cohort studies, observed incidence/mortality of cancer in 2010 and predicted incidence/mortality for 2030 derived from the age-period-cohort model. Our results showed that between 2010 and 2030, the total number of cancer incidence and mortality were predicted to increase by 38.9% and 10.5% in adults aged above 20 years, respectively. In the number of excess incident cancer cases associated with type 2 diabetes, an increase of 26.5% in men and 53.2% in women is expected between 2010 and 2030. The age-specific analysis showed that the population attributable fraction of cancer will increase in adults aged >60 years over time, but will not change in adults aged 20-59 years. In conclusion, this study suggests a modest but steady increase in cancers associated with type 2 diabetes.

A-055 - Tumor Burden In Bangladesh- A Pathology Based Tumor Registry Overview

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Introduction and Purpose: Cancer is a public health concern both in developed and developing countries. Appropriate prevention and surveillance of cancer deserves urgent attention since the disease is expected to be doubled in the next 20 to 25 years in most developing nations. Given the dearth of basic cancer-related data in the country and feasibility considerations, the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh in collaboration with The University of Chicago, USA has been continuing a pathology-based tumor registry in Bangladesh for the last 4 (from 2012 till date) years at Department of Pathology of BSMMU.
Methods: Basic epidemiological and socioeconomic data have been obtained through a questionnaire from all the patient (total 13040 patient, within 2012-2014) coming to the department lab for diagnostic purpose. Histo and/ or cytopathological data has been obtained from department database.
Result: Middle aged (30-50 years) people are more vulnerable (62%) than other extreme age group developing different tumor including cancer. Female (61.11%) are more prone to develop tumor than male (39.89%). Low socioecomic (86.73%) status and Poor education (< grade 5) level (69.48%) play key role of developing tumor in Bangladesh. In terms of occupation, Housewife (49%) is the most vulnerable group than all others. Skin tumor (55.6%) is the commonest benign tumor among male and Breast tumor (33.28%) in female. In case of malignancy, uterine malignancy (23.38%) atop in female and mouth and oral cavity cancer (11.7%) in male. Uterus (13.18%) is most commonest site of tumor, followed by breast (10.69%) in both sexes.
Conclusion: Although such effort is an underestimate of the true occurrence of the cancers in the population, these data are valuable for formulating any plan or program for epidemiology, prevention and treatment of cancers at the local/ national level.We don't have any dedicated fund.

A-056 - Cancer Incidence For 27 Sites In 2012 According To The Human Development Index

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Background
Social and economic factors are strongly associated with cancer incidence; however, these factors influence cancer patterns through different pathways (negative or positive relationships). We aimed to assess cancer incidence for 27 sites according to varying levels of human development.

Methods
Age-standardized incidence rates (ASRs) using GLOBOCAN 2012 were calculated for 27 cancer sites by four levels (low, medium, high, very high) of the Human Development Index (HDI) 2012. The HDI is a composite index of life expectancy, educational attainment, and gross national income.

Findings
As regions developed, decreases in the ASRs of infection-related (Kaposi sarcoma, stomach, liver, cervical) cancers were offset by increases in the ASRs of cancers related to industrialization. Infection-related cancers accounted for 35% of the total ASR for the cancers assessed in low HDI regions, whereas the corresponding percentage was 6% in very high HDI regions. Conversely, the proportion of the ASR attributable to breast, prostate, colorectum, and lung cancers rose from 40% in low HDI regions to 61% in very high HDI regions. When specific cancers were assessed, a stepwise negative relationship was observed for cervical cancers, where the ASR declined from 25 to 8 per 100,000 in low and very high HDI regions, respectively. Stepwise positive associations were found for lip/oral cavity, gallbladder, pancreas, melanoma, corpus uteri, ovary, kidney, testis, thyroid, brain/nervous system, leukemia, non-Hodgkin lymphoma, multiple myeloma, colorectum, lung, breast, and prostate cancers; most notable increases were for cancers of the lung (10-fold), prostate (6-fold), and colorectum (5-fold).

Interpretation
Our results suggest that societal and economical transitions are associated with a decline in infection-related cancers and an increase in cancers associated with industrialization; future cancer burdens for these cancers in countries transitioning from low and medium human development to higher levels can be decreased through effective primary prevention strategies and early detection.

A-057 - Examining Methods To Visualise The Cancer Population Using Cartograms: 20-Year Cancer Prevalence In The UK

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Purpose

An estimated 2.5 million people are living with cancer in the UK, predicted to increase to four million by 2030. The Macmillan-NCIN Cancer Prevalence project aims to provide the most granular understanding of the cancer population in the UK, with outputs produced at sub-national geographies.

A key challenge is how to visualise geographic variations in cancer prevalence, and how to best communicate which areas have the highest number of people living with cancer.

Methods

We use the National Cancer Data Repository (cancer registrations in the UK linked to mortality records) to identify people diagnosed with cancer between 1991 and 2010 and still alive on 31st December 2010.

The sub-national geography data is matched to spatial layers using ESRI ArcGIS software. GIS-based output is produced across different formats including: choropleth/thematic maps, and contiguous and non-contiguous cartograms. The results from each type of output are compared.

Results

There were 1.8 million people in the UK diagnosed between 1991 and 2010 who were matched to a sub-national geographical area.

Standard choropleth maps, which are often used within public health, result in small-scale variations being masked in small inner city areas such as London boroughs.

Initial cartogram output, based on a density-equalising method, distorts the overall shape of the UK but highlights geographies containing the highest number of people living with cancer by increasing their size, whilst maintaining geographical relationships.

We will explore further comparisons of different visualisations using different cartogram and mapping techniques.

Conclusions

Cartograms can help form a visual narrative to visualise geographical areas which contain the highest levels of cancer prevalence in absolute terms. This can demonstrate which areas are under the most increasing demand for health services, helping commissioners quickly understand and plan for better service delivery.

Funding Source

Macmillan Cancer Support

A-058 - Disparities In Cancer Incidence Between Indigenous And Non-Indigenous Adults In Canada: Results From Linkage Of The 1991 Census Mortality Cohort And The Canadian Cancer Registry

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Purpose: Canada has three constitutionally recognized Aboriginal groups: First Nations (FN), Inuit, and Métis, comprising 4.3% of the population. Ethnicity is not routinely collected in Canadian cancer registries so periodic studies using different methodologies are needed. This linkage provided an opportunity to examine cancer incidence in Canada's two largest indigenous groups, FN and Métis.
Methods: Respondents aged 25+ to the 1991 Long Form Census were matched with national cancer registry and mortality databases and followed from 1992-2009. Three cohorts were identified: FN (N~=62,000; 5,000 cancers), Métis (N~=11,000; 1,000 cancers) and non-Aboriginal (N~=2,653,000; 336,000 cancers). Incidence rates were estimated for common cancers, age-standardized to the World Standard population. Relative risk (RR) of cancer in FN or Métis was assessed compared to non-Aboriginal adults, adjusting for age, income and rurality.
Results: Compared to non-Aboriginal adults, FN had significantly lower incidence of prostate (RR=0.79, 95%CI=0.73-0.86), male lung (RR=0.79, 95%CI=0.72-0.87) and female breast cancers (RR=0.92, 95%CI=0.86-0.99), yet significantly higher incidence of colorectal (men:RR=1.15, 95%CI=1.04-1.26; women:RR=1.29, 95%CI=1.17-1.42), kidney (men:RR=1.65, 95%CI=1.41-1.93; women:RR=1.99, 95%CI=1.67-2.36), and cervical cancers RR=2.00, 95%CI=1.70-2.36). Métis had significantly higher incidence than non-Aboriginal adults for female breast (RR=1.18, 95%CI=1.02-1.37), lung (men:RR=1.22, 95%CI=1.03-1.43; women:RR=1.56, 95%CI=1.28-1.89), and cervical cancers (RR=1.84, 95%CI=1.23-2.76), and significantly lower incidence of female colorectal cancer (RR=0.69, 95%CI=0.50-0.95).
Conclusions: Indigenous people in Canada experience higher incidence of several cancers, supporting the need for: 1. additional research to understand why; 2. additional investment in prevention to reduce current and future burden in a wholistic and culturally appropriate manner; and 3. creation of databases for ongoing monitoring of cancer burden. Doing so will require application of novel methodologies and appropriate data sharing, collaboration and capacity-building arrangements with Indigenous organizations.
Funding source: Canadian Institutes of Health Research

A-059 - Cancer Registry: Information As A Tool For Disease Control In Colombia

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Objective: According to the national regulatory framework it was defined a registry of information that would meet the cancer situation from the needs of the health care system, the clinical interests and the decision makers.

Methods: A comprehensive literature review was performed to obtain documents to identify the relevant variables to determine monitoring indicators used by insurers and providers in the attention of patients with cancer. Variables were selected and defined by an agreement with clinical experts, thematic and methodological experts which were evaluated by the Ministry of Health in order to review and approve the structure to gather the information.

Results: a structure of 148 variables contained in a resolution (law) that requires all entities with populations under their charge to report annually to the High Cost Account all the patients with a diagnosis of cancer, clinical and demographic characteristics and the process of care, among others. In 2015 a total of 166,224 records for 165,125 patients living with a diagnosis of cancer were reported. Different indicators compared with some estimations for the country that allowed to identify existing gaps.

Conclusion: the implementation of a mandatory information registry as a public policy, can get real information for data analysis on the situation of the disease, standardized reporting methodology and encouraging the culture of information registration not only for quality analysis but to obtain indicators for decision making.

A-060 - Invasive Lobular Carcinoma Of The Breast: Experience For Centre Mohammed VI For The Treatment Of Cancers

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This is a retrospective study conducted over two years (January 2014-December 2015), including all cases of invasive lobular carcinoma of the breast supported at the centre Mohammed VI.
The purpose of our study was to describe the epidemiological, clinical, biological and therapeutic of this cancer.

Results
62 cases of invasive lobular carcinoma were recorded by central cancer registry, whose average age is 52.6 ± 11.8 years, ranging from 27 to 84 ans. 51.6% of patients were married, 19.4% used oral contraceptives and 27.4% were postmenopausal at diagnosis. The notion of family history of breast cancer was observed in 3.2% of cases. The left and right tumour laterality was respectively 48.4% and 46.8% of cases, 4.8% cases were bilateral.
The clinical TNM stage was T1 and T2 (35.5%), N0 (48.4%) N1 (30.0%) and metastasis was observed in 3.2% of cases. The SBR histologic grade II was the most common in 58.1% of cases. The most common stage at diagnosis was stage III (38.7%). Hormone receptor positivity was estrogens in 56.5% of cases, to progesterone in 54.8% of cases and the Her2 receptor over expression was observed in 10.0% of cases. The molecular phenotype of the tumours was more majority luminal A (50.0%), while the luminal B and Her2 that were respectively 4.8% and 1.6% of cases. Negative triple represented 8.1% of cases.
69.4% of patients received surgical treatment as adjuvant chemotherapy; radiotherapy and hormone therapy was administered to 51.6%, respectively, 35.5% and 16.1% of cases. 1.6% of cases had a recurrence.

The invasive lobular breast carcinoma is relatively rare in our centre. It is often diagnosed at an advanced stage and is conventionally recognized by its unfavourable prognosis. Therapeutic management varies depending on the condition of the patients, but surgery remains the primary treatment.

B-061 - Associations Of Red And Processed Meat With Survival After Colorectal Cancer And Differences According To Timing Of Dietary Assessment

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Purpose: Little is known about the prognostic impact of red and processed meat intake or about changes in consumption after a diagnosis of colorectal cancer (CRC). We investigated associations of baseline red and processed meat with survival outcomes and explored changes in intake among CRC survivors five years after diagnosis.
Methods: 3122 patients diagnosed with CRC between 2003-2010 were followed for a median time of 4.8 years (DACHS study). Patients provided information on diet and other factors in standardized questionnaires at baseline and at 5-year follow-up. Cox proportional hazards regression models were used to estimate HRs and 95% CIs.
Results: Among stage I-III CRC patients, baseline red and processed meat intake was not associated with overall (>1 time/day vs <1 time/day, HR 0.85; 95% CI, 0.67,1.09), CRC-specific (HR 0.83; 95% CI, 0.61,1.14), CVD-specific (HR 0.92, 95% CI, 0.51,1.68), non-CRC-specific (HR 0.88; 95% CI, 0.59,1.30) and recurrence free (HR 1.03; 95% CI, 0.80,1.33) survival; results among stage IV patients were comparable. An association with worse overall survival was found among patients with *KRAS*-mutated CRC (HR 1.99; 95% CI, 1.10, 3.56), but not with MSI or CIMP positivity. A much lower proportion of survivors reported daily consumption of red and processed meat at 5-year follow-up than at baseline (concordance rate 39%, kappa-value 0.10; 95% CI 0.07, 0.13).
Conclusions: Our findings suggest that baseline red and processed meat intake is not associated with poorer survival among patients with CRC. The potential interaction with *KRAS* mutation status warrants further evaluation. Major changes in consumption measured at the 5-year follow-up may have had an impact on our survival estimates.
Funding source: German Research Council (BR 1704/6-1, BR 1704/6-3, BR 1704/6-4, CH 117/1-1, HO 5117/2-1), German Federal Ministry of Education and Research (01KH0404, 01ER0814), the Interdisciplinary Research Program of the National Center for Tumor Diseases, Germany.

B-062 - Pre-Diagnostic Enterolactone Levels And Mortality Among Danish Men Diagnosed With Prostate Cancer

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Purpose: Prostate cancer is the most common cancer and the second most common cause of cancer-related death among Northern European men. Currently, there is a lack of knowledge about what men with prostate cancer can do to improve their prognosis. Lignans are phytoestrogens found as phenolic compounds in seeds, whole grains, nuts, and in some fruits and vegetables. In Denmark, whole-grain rye is the main source of lignans. Facilitated by the microbiota, plant lignans are converted to enterolignans (mainly enterolactone), and thereafter absorbed through the colonic barrier. Intervention trials have indicated that diets rich in whole-grain rye, and thereby lignans, may have beneficial effects on disease progression in prostate cancer patients. Therefore, the objective of this study was to investigate, in a prospective setting, the association between pre-diagnostic enterolactone levels and mortality among men diagnosed with prostate cancer.
Methods: The association between pre-diagnostic plasma enterolactone levels and all-cause mortality as well as prostate cancer-specific mortality was investigated in 1431 incident prostate cancer cases from the Danish “Diet, Cancer and Health” cohort study. These were followed from diagnosis until death (n=460, due to prostate cancer n=301), or end of follow-up (December 31, 2013). Enterolactone levels were analysed using a LC-MS/MS method, and information on vital status and cause of death was obtained through registries. Cox proportional hazards models with follow-up time as underlying time, stratified by 5-year intervals and adjusted for lifestyle factors, were used to estimate hazard ratios.
Results: High levels of enterolactone were associated with lower all-cause mortality, but the association was no longer statistical significant after adjusting for potential confounders. No association was found with prostate cancer-specific mortality.
Conclusions: High enterolactone concentrations were not associated with improved survival in a population of Danish men diagnosed with prostate cancer.
Funding source: Innovation Fund Denmark and Danish Cancer Society

B-063 - Pre-Diagnostic Enterolactone Concentrations And Survival After Breast Cancer

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Purpose: The high incidence of breast cancer in combination with a high relative survival, leads to a high prevalence of breast cancer in western countries and thereby a large interest in initiatives aimed at optimizing survivorship. Lignans are polyphenolic compounds found in seeds, whole grains, nuts, and in some fruits and vegetables. During digestion, lignans are converted to enterolignans (mainly enterolactone), which have estrogen-like activity. Biological evidence supports a role of enterolactone in breast cancer development and prognosis. The objective of the present study is therefore to investigate the association between enterolactone and breast cancer survival (all-cause and breast-cancer specific mortality).

Methods: We measured enterolactone using LC-MS/MS in pre-diagnostic plasma samples from 1511 incident breast cancer cases from the Danish part of the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. We followed the breast cancer cases from date of diagnosis until death, end of follow-up or last day of contact. During a median of 10 years, 433 of the women died (262 of breast cancer). We related pre-diagnostic enterolactone concentrations to all-cause and breast cancer-specific mortality using Cox Proportional Hazard Models with follow-up-time as underlying time scale. Analyses were adjusted for potential confounders. Analyses on recurrence as well as by clinical characteristics are ongoing.

Preliminary results: High pre-diagnostic enterolactone concentrations were related to improved survival. A doubling in the plasma enterolactone concentration was associated with a 7% lower both all-cause (HRdoubling,log2:0.93, 95%CI: 0.88–0.98) and breast cancer-specific mortality (HRdoubling,log2:0.93, 95%CI: 0.86–1.00).

Conclusions: High levels of enterolactone may be related to an improved survival among women diagnosed with breast cancer.

Funding Source: This work was funded by Innovation Fund Denmark (ELIN: 0603-00580B), and Danish Cancer Society

B-064 - Biomarkers Of Fatty Acids And Breast Cancer Risk, Overall And By Hormonal Receptor Status: Report From The European Prospective Investigation Into Cancer And Nutrition (EPIC) Study

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Purpose. Intakes of specific fatty acids have been postulated to impact breast cancer (BC) risk but epidemiological data based on biomarkers of exposure and metabolism are scarce. The objective of this study was to assess the association between biomarkers of fatty acids and BC risk in a large case-control study nested within the EPIC study.
Methods. Fatty acids were measured by gas chromatography in plasma phospholipids from 2,982 BC cases matched to 2,982 controls for center, age, menopausal status, exogenous hormone use, time of the day at blood collection, fasting status, and phase of the menstrual cycle. Conditional logistic regression models adjusted for date at blood collection, years of education, body mass index, height, menopausal hormone use at baseline, alcohol, age at first birth and parity combined, energy intake, and family history of BC were used to estimate odds ratios by quartiles of fatty acids. Subgroup analyses were performed by menopausal status and estrogen receptor (ER, 1,649 ER+, 398 ER-) and progesterone receptor (PR, 1,150 PR+, 579 PR-) expression in tumors.
Results. Overall, increased risk of BC was associated with increasing ratio of cis-monounsaturated fatty acids (MUFA) to saturated fatty acids (SFA) (odds ratio (OR)=1.28; 95% confidence interval (CI)=1.07-1.54; p for trend =0.002), as biomarkers of endogenous synthesis of MUFA. Stratification by menopausal status revealed no substantial difference. Increased risk of ER- BC was specifically and statistically significantly associated with increasing levels of industrial trans fatty acids (ITFA) (OR=2.01; 95% CI=1.03-3.90; p for trend=0.047), while no association remained with ER+ BC (OR=82; 95% CI=0.62-1.10; p for trend=0.102) (P-heterogeneity=0.015).
Conclusions. These findings suggest that increased endogenous synthesis of MUFA may increase BC risk, independently of menopausal or hormonal receptor status. Dietary ITFA may specifically increase ER- BC development.
Funding sources. Ligue Nationale contre le Cancer, Fondation de France, WCRF.

B-065 - Nutrient Intake Patterns And Their Association With Body Size In Black South African Females

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Purpose:
Black South African women are in a period of transition. Expanding urban areas contribute to lifestyle and diet changes that occur at different rates and with great inequalities. The influence of diet and body size on breast cancer in this population needs to be investigated. In addition, nutrient intake patterns have not yet been determined for the black female population of South Africa. The aim is to identify and describe main nutrient intake patterns and to investigate associations between nutrient intake patterns and lifestyle factors including body mass index in a sub-group (n=250) of the South African Breast Cancer (SABC) study.

Methods:
The SABC study is a population-based case-control study on breast cancer conducted in black South African women living in Soweto Johannesburg, a high-density urban population. Questionnaire data on lifestyle, reproductive factors, physical activity/inactivity, and diet are collected from all women. Anthropometry is measured for all women, who also undergo dual-energy X-ray absorptiometry and computed ultrasonography, to measure total-body visceral and subcutaneous fat. Nutrient intake patterns will be identified through a culture-specific quantified food-frequency questionnaire including 145 food items. Principal Component Analysis (PCA) will be applied to 25 nutrients and used to depict nutrient intake patterns.

Results:
To date, 118 cases and matched controls have been recruited in the study. The nutrient database is currently being implemented, and will be available in March. Results of preliminary statistical analyses to depict nutrient intake patterns, and their association with obesity and overweight in this population will be presented at the conference.

Conclusions:
This will be the first study describing main nutrient patterns in the South Africa population, and to investigate their associations with lifestyle factors.

B-066 - A Prospective Study Of Plasma 25-Hydroxyvitamin D Concentration And Prostate Cancer Risk

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Purpose:
Mechanistic hypotheses suggest that vitamin D may be involved in prostate carcinogenesis through various effects on differentiation, apoptosis, and cell proliferation. Plasma parathyroid hormone (PTH) concentration, closely related to vitamin D metabolism may also play a role in prostate carcinogenesis. However, epidemiological evidence is lacking for PTH and inconsistent for vitamin D. Our objectives were to prospectively investigate the association between vitamin D status, vitamin D-related gene polymorphisms, PTH and prostate cancer risk.

Methods:
A total of 129 cases diagnosed within the Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) cohort were included in a nested case–control study and matched to 167 controls (13 years of follow-up). 25-Hydroxyvitamin D (25(OH)D) and PTH concentrations were assessed from plasma samples obtained at baseline. SNPs of selected vitamin D-related genes (VDR BsmI, FokI and Cdx2, CYP24A1 rs4809958, GC rs4588 and rs7041, RXR rs7861779 and rs12004589, CaSR rs1801725 and rs4678174) were determined with TaqMan assay. Conditional logistic regression models were computed.

Results:
Higher 25(OH)D concentration was associated with decreased risk of prostate cancer (OR Q4 vs. Q1=0.30 (0.12-0.77); P-trend=0.007). PTH concentration was not associated with prostate cancer risk (P-trend=0.4) neither did the studied vitamin D-related gene polymorphisms.

Conclusions:
In this prospective study, prostate cancer risk was inversely associated with 25(OH)D concentration but not with PTH concentration. These results bring a new contribution to the understanding of the relationship between vitamin D and prostate cancer, which deserves further investigation.
Br J Nutr 2016, 115:305–314

Funding source:
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Cancéropôle Ile-de-France, Ile-de-France Region, PhD grant (Mélanie Deschasaux)

B-067 - Weight Status And Alcohol Intake Modify The Association Between Vitamin D And Breast Cancer Risk

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Purpose:
Mechanistic hypotheses suggest that vitamin D may contribute to the prevention of breast cancer. However, epidemiologic evidence is inconsistent, suggesting a potential effect modification by individual factors. Our objective was to investigate the prospective associations between the plasma 25-hydroxyvitamin D (25(OH)D) concentration, polymorphisms of genes encoding for the vitamin D receptor (VDR), and the vitamin D-binding protein (GC), and breast cancer risk, along with 2 potential modifiers: BMI and alcohol intake.

Methods:
A nested case-control study was set up in the Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) cohort (1994–2007), involving 233 women with breast cancer and 466 matched controls. The plasma total 25(OH)D concentration and gene polymorphisms were assessed on samples obtained at baseline. Conditional logistic regression models were computed.

Results:
A higher plasma 25(OH)D concentration was associated with a decreased risk of breast cancer for women with a BMIQ4vs.Q1=0.46 (0.23-0.89); P-trend=0.01, P-interaction=0.002), whereas it was associated with an increased risk in women with a BMI ≥median ($OR_{Q4vs.Q1}$=2.45 (1.13-5.28); P-trend=0.02, P-interaction=0.002). A plasma 25(OH)D concentration ≥10ng/mL was associated with a decreased risk of breast cancer for women with alcohol intakes ≥median ($OR_{\geq 10vs.<10ng/mL}$=0.50 (0.26-0.95); P=0.03, P-interaction=0.03). The genetic analyses were consistent with the results observed with plasma 25(OH)D.

Conclusions:
In this prospective study, plasma 25(OH)D was associated with a decreased breast cancer risk in lean women, whereas it was associated with an increased risk in women with a higher BMI. Plasma 25(OH)D was also associated with a decreased breast cancer risk in women with moderate-to-high alcohol consumption, whereas no association was observed among women with low alcohol intake. These effect modifications suggest explanations for discrepancies in results of previous studies.
J Nutr 2016

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B-068 - Prospective Associations Between Vitamin D Status, Vitamin DñRelated Gene Polymorphisms, And Risk Of Tobacco-Related Cancers

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Purpose:
Experimental evidence has suggested that vitamin D may be protective against tobacco-related cancers through the inhibition of the formation of tumors induced by tobacco carcinogens. To our knowledge, only one previous epidemiologic study investigated the association between vitamin D status and tobacco-related cancer risk, and no study has focused on vitamin D–related gene polymorphisms. Our objective was to prospectively study the association between plasma 25-hydroxyvitamin D [25(OH)D] concentrations, vitamin D–related gene polymorphisms (VDR, CYP24A1, GC, RXR, CaSR), and risk of tobacco-related cancers.

Methods:
A total of 209 tobacco-related cancers were diagnosed within the SU.VI.MAX (Supplémentation en vitamines et minéraux antioxydants) cohort (1994–2007) and were matched with 418 controls as part of a nested case-control study. Tobacco-related cancers (i.e., cancers for which tobacco is one of the risk factors) included several sites in the respiratory, digestive, reproductive, and urinary systems. Plasma total 25(OH)D concentration and selected gene polymorphisms were assessed on samples obtained at baseline. Conditional logistic regression models were computed.

Results:
A 25(OH)D concentration ≥30ng/mL was associated with reduced risk of tobacco-related cancers ($OR_{\geq 30 vs. <30\ ng/mL}$=0.59 (0.35-0.99); P=0.046). This association was observed in former and current smokers ($OR_{\geq 30 vs. <30\ ng/mL}$=0.43 (0.23-0.84); P=0.01) but not in never smokers (P=0.8). The vitamin D receptor (VDR) FokI AA genotype and retinoid X receptor (RXR) rs7861779 TT genotype were associated with increased risk of tobacco-related cancers.

Conclusions:
In this prospective study, high vitamin D status [25(OH)D concentration ≥30ng/mL] was associated with decreased risk of tobacco-related cancers, especially in smokers. These results, which are supported by mechanistic plausibility, suggest that vitamin D may contribute to the prevention of tobacco-induced cancers in smokers and deserve additional investigation.
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B-069 - Dietary Iron And Breast Cancer Risk ñ Modulation By An Antioxidant Supplementation In The SU.VI.MAX Randomized Controlled Trial

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Purpose:
Epidemiological evidence suggested that red and processed meat intake may be associated with increased breast cancer risk. Recent experimental studies showed that, among the pro-carcinogenic compounds found in red/processed meat, heme iron may be particularly involved in the initiation of carcinogenesis, through lipid peroxidation. Thus, it could be hypothesized that iron intake may all the more increase cancer risk as diet has a low antioxidant potential and a high lipid content. Our objectives were to prospectively investigate the association between dietary iron intake and breast cancer risk, and its potential modulation by antioxidant supplementation and lipid intake.

Methods:
The SU.VI.MAX study was a randomized, double-blind, placebo-controlled trial (1994-2002) in which participants received low-dose antioxidants or a placebo. This prospective study included 4646 women. 188 incident breast cancers were diagnosed (median follow-up=12.6y). Dietary iron intakes were assessed using repeated 24h dietary records. Associations were characterized by multivariate Cox proportional hazards models.

Results:
Dietary iron intake was associated with an increased breast cancer risk ($HR_{T3vs.T1}$=1.67 (1.02-2.71), P-trend=0.04). This association was more specifically observed in the placebo group of the SU.VI.MAX trial ($HR_{T3vs.T1}$=2.80 (1.42-5.54), P-trend=0.003), but not in the antioxidant-supplemented group (P-trend=0.7, P-interaction=0.1). Besides, in the placebo group, increased breast cancer risk associated with iron intake tended to be more specifically observed in women with higher lipid intake ($HR_{T3vs.T1}$=2.57 (0.86-7.69), P-trend=0.046).

Conclusions:
In this prospective study, dietary iron intake was associated with an increased breast cancer risk. This association was modified by an antioxidant supplementation and by lipid intake. Dietary iron intake was associated with breast cancer risk in the women not supplemented with antioxidants and in women with higher lipid intakes. These epidemiological findings support the experimental results suggesting that heme iron may increase breast cancer risk through lipid peroxidation.

Funding source:
Cancéropôle Ile-de-France, Ile-de-France Region, PhD grant (Mélanie Deschasaux)

B-070 - Prospective Association Between Cancer Risk And An Individual Dietary Index Based On The British Food Standards Agency Nutrient Profiling System

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Purpose:
The Food Standards Agency Nutrient Profiling System (FSA-NPS) constitutes the basis for the Five-Colour Nutrition Label suggested in France to be put on the front-of-pack of food products. At the individual level, a dietary index (FSA-NPS DI) has been derived and validated and corresponds to a weighted mean of all FSA-NPS scores of foods usually consumed by the individual, reflecting the nutritional quality of his/her diet. Our aim was to investigate the association between the FSA-NPS DI and cancer risk in a large cohort.

Methods: This prospective study included 6435 participants to the SUpplémentation en VItamines et Minéraux AntioXydants cohort (1994–2007) who completed at least six 24h dietary records during the first 2y of follow-up (median follow-up: 12.6y). FSA-NPS DI was computed for each subject (higher values representing lower nutritional quality of the diet). 453 incident cancers were diagnosed. Associations were characterized by multivariate Cox proportional hazards models.

Results:
The FSA-NPS DI was directly associated with overall cancer risk (HR1-point increment=1.08 (1.01-1.15), P-trend=0.02; $HR_{Q5vs.Q1}$=1.34 (1.00-1.81), P-trend=0.03). This association tended to be more specifically observed in subjects with moderate energy intake (≤median, $HR_{1\text{-point increment}}$=1.10 (1.01-1.20), P-trend=0.03). No association was observed in subjects with higher energy intake (P-trend=0.3). Results were not statistically significant for breast and prostate cancer risks.

Conclusions:
For the first time, this study investigated the prospective association between the FSA-NPS individual score and cancer risk. The results suggest that unhealthy food choices may be associated with a 34% increase in overall cancer risk, supporting the public health relevance of developing front-of-pack nutrition labels based on this score.
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National Institute for Prevention and Health Education (INPES)
French Ministry of Research and Higher Education, internship grant (Mathilde Donnenfeld)
Cancéropôle Ile-de-France, Ile-de-France Region, PhD grant (Mélanie Deschasaux)

B-071 - Prospective Association Between The Dietary Inflammatory Index And Cancer Risk And Mortality: Results From The SU.VI.MAX Cohort

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Purpose:
Chronic inflammation is one of the mechanisms involved in carcinogenesis. Diet is a major source of pro/anti-inflammatory compounds. The Dietary Inflammatory Index (DII) was designed to estimate its overall inflammatory potential. Our objective was to investigate the associations between DII and cancer risk (overall, breast and prostate) and mortality.

Methods:
The SU.VI.MAX study was a randomized, double-blind, placebo-controlled trial (1994-2002) in which participants received low-dose antioxidants or a placebo. This prospective study included 7997 participants (follow-up: 1994-2007). The DII was based on 36 food parameters and was calculated from repeated 24h dietary records. Higher scores reflected more pro-inflammatory diets. 559 cancers were diagnosed (median follow-up=12.6y), including 158 breast and 123 prostate cancers. 123 participants died from cancer. Associations were characterized by multivariable Cox proportional hazards models.

Results:
The DII was positively associated with prostate cancer risk ($HR_{Quartile4vsQ1}$=2.08 (1.06-4.09); P=0.005). Alcohol intake modified the association between DII and overall cancer risk (P-interaction=0.02). An increased risk was observed in low-to-moderate alcohol drinkers (HR_{Q4vsQ1}=1.75 (1.15-2.68); P-trend=0.02), whereas no association was detected in higher alcohol consumers (P-trend=0.8). This interaction also was observed for breast cancer (P-interaction=0.001). The DII was positively associated with cancer mortality in the placebo group of the SU.VI.MAX trial ($HR_{Tertile3vsT1}$=2.65 (1.18-5.98); P-trend=0.02) but not in the antioxidant-supplemented group (P-trend=0.3).

Conclusions:
Consistent with mechanistic data, these results showed that pro-inflammatory diets are associated with increased prostate cancer risk; increased overall and breast cancer risk among low-to-moderate drinkers; and increased cancer mortality in participants not supplemented with antioxidants, suggesting that antioxidants may counteract some of the deleterious effects of pro-inflammatory diets.

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US National Institute for Diabetes and Digestive and Kidney Diseases, grant R44DK103377 (NS, JRH, MDW)

B-072 - Prospective Association Between Dietary Folate Intake And Skin Cancer Risk: Results From The SU.VI.MAX Cohort

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Purpose:
The role of folate in skin carcinogenesis is unclear, with experimental data suggesting potentially protective but also deleterious effects. Our main objective was to investigate the prospective association between dietary folate intake and risks of skin cancer (overall), nonmelanoma skin cancer (NMSC), and basal cell carcinoma (BCC). As an exploratory analysis, we also investigated the prospective association between erythrocyte folate concentration and skin cancer risk.

Methods:
In this study, we included 5880 participants in the Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) cohort (follow-up: 1994–2007) who completed at least six 24-h dietary records during the first 2 y of the study. Associations between sex-specific tertiles of dietary and erythrocyte folate and skin cancer risk were assessed by using multivariate Cox proportional hazards models.

Results:
After a median follow-up of 12.6y, 144 incident skin cancers were diagnosed. Dietary folate intake was associated with increased risk of overall skin cancer ($HR_{T3vs.T1}$=1.79 (1.07-2.99); P-trend=0.03), NMSC ($HR_{T3vs.T1}$=1.85 (1.06-3.23); P-trend=0.03), and BCC ($HR_{T3vs.T1}$=1.78 (0.98-3.24); P-trend=0.05). This association was observed in women (corresponding P-trend=0.007, 0.009, and 0.009, respectively) but not in men. P-interaction values between tertiles of dietary folate intake and sex were 0.04, 0.02, and 0.02 for overall skin cancer, NMSC, and BCC, respectively. Erythrocyte folate concentration also was directly associated with increased risk of skin cancer (overall, NMSC and BCC).

Conclusions:
This prospective study suggests an association between dietary folate intake and erythrocyte folate concentration and increased risk of overall skin cancer, NMSC, and BCC. These results are in line with 2 previous large prospective studies on BCC and with mechanistic data suggesting a potentially deleterious effect of folate in carcinogenesis.
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Funding source:
French Ministry of Research and Higher Education, internship grant (Mathilde Donnenfeld)
Cancéropôle Ile-de-France, Ile-de-France Region, PhD grant (Mélanie Deschasaux)

B-073 - The Maternal Nutrition And Offspringís Epigenome (MANOE) Study: A Prospective, Monocentric, Observational Study

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Introduction: Epigenetic modifications, e.g. DNA methylation, have the ability to change the susceptibility to metabolic diseases like obesity. DNA methylation can change during a life course due to environmental exposures like diet.

Aim: To determine the effects of dietary intake of methyl-group donors (methionine, folate, betaine and choline) during pregnancy on the DNA methylation pattern of mother and child. In addition, the association between the DNA methylation pattern of the mother and child on body composition/weight gain of the infant during the first year will be studied.

Methods: We have recruited 175 and 105 expectant mothers and fathers respectively, who are followed up in UZ Leuven. A novel food-frequency questionnaire was developed and validated to categorize women in groups according to their methyl-group intake. Women are asked to fill out a 7-day estimated dietary record to have information about macro- and micronutrient intake. Body composition is followed up by means of the bio-electrical impedance method. Blood samples are collected at standard ultrasounds during pregnancy and after delivery until 1 year postpartum. After delivery, cord blood is taken and mouth epithelial cells are obtained from the infants (6 and 12 months). Samples are analyzed for global DNA (de)methylation by liquid chromatography–mass spectrometry and specific target genes involved in DNA (de)methylation and genes linked with obesity/adiposity/metabolisation by pyrosequencing.
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Results: Our results show that the intake of methyl-groups is stable, except for a decrease in folate and folic acid intake. Global DNA methylation analysis shows that maternal global DNA (hydroxy)methylation changes significantly over pregnancy, with a significant decrease at 12 weeks and 30 weeks of pregnancy, and at delivery.

Discussion: With this study we will gain insight on the effect of maternal nutrition on offspring DNA methylation and potentially identify DNA methylation biomarkers at birth that can mediate problems with metabolism/obesity.

B-074 - Sociodemographic And Economic Factors Are Essential Determinants Of Weight Gain Between Before And After Cancer Diagnosis: Results From The Prospective NutriNet-SantÈ Cohort

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Purpose: While many cancer patients are affected by weight loss, others tend to gain weight, which may impact prognosis and risk of recurrence and of second primary cancer. The aim of this prospective study was to investigate weight variation between before and after cancer diagnosis and socio-demographic, economic, lifestyle and clinical factors associated with moderate-to-severe weight gain.

Materials and methods: 1051 incident cases of first primary cancer were diagnosed in the NutriNet-Santé cohort between 2009 and 2015. Weight was prospectively collected every 6 months since subjects' inclusion (i.e. an average of 2y before diagnosis). Mean weights before and after cancer diagnosis were compared with paired Student's t-test. Factors associated with moderate-to-severe weight gain (≥5% of initial weight) were investigated by multivariable logistic regression.

Results: Weight loss was observed in men (-3.54kg in those who lost weight, p=0.0002) and in colorectal cancer patients (-3.94kg, p=0.0012). Weight gain was observed in breast and skin cancers (2.83kg, p=0.047, and 2.96kg, p=0.03 respectively). Women (OR=1.99[1.18-3.35]), younger patients (OR=1.78[1.05-3.03]), those with lower education (OR=2.17[1.07-4.37]), those with excess weight before diagnosis (OR=1.53[1.02-2.30]) and those who stopped smoking after diagnosis (OR=4.60[2.06-10.25]) were more likely to experience moderate-to-severe weight gain. In breast cancer patients, induced menopause was associated with weight gain (OR=4.12[1.76-9.67]), but no association was detected for tumor characteristics or treatments.

Conclusion: This large prospective cohort provided original results on weight variation between before and after cancer diagnosis, highlighting different weight trajectories. Socio-demographic and economic factors appeared to strongly influence the risk of weight gain, illustrating social inequalities in health

B-075 - Leisure-Time Physical Activity And Lung Cancer Risk: A Systematic Review And Meta-Analysis

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Purpose: To examine the association between recreational physical activity and lung cancer risk to update previous analyses and to examine population subgroups of interest defined by smoking status and histology we conducted a systematic review and meta-analysis.
Methods: We searched the PubMed and MEDLINE databases for studies up to May 2015. Individual study characteristics were abstracted including study design, number of cases, assessment of recreational physical activity and type and level of adjustment for confounding factors. Combined effect estimates were calculated for the overall associations and across subgroups of interest.
Results: We identified 28 studies that were eligible for inclusion in the meta-analysis. The overall analysis indicated an inverse association between recreational physical activity and lung cancer risk (Relative Risk (RR), 0.76; 95% Confidence Interval (CI), 0.69-0.85, p-value: <0.001). Similar inverse associations with risk were also noted for all evaluated histological subtypes, including adenocarcinoma (RR, 0.80; 95% CI, 0.72-0.88), squamous (RR, 0.80; 95% CI, 0.71-0.90) and small cell (RR, 0.79; 95% CI, 0.66-0.94). When we examined effects by smoking status, inverse associations between recreational physical activity and lung cancer risk were observed among former (RR, 0.77; 95% CI, 0.69-0.85) and current smokers (RR, 0.77; 95% CI, 0.72-0.83), but not among never smokers (RR, 0.96; 95% CI, 0.79-1.18).
Conclusions: Results from this meta-analysis suggest that regular recreational physical activity is associated with reduced risk of lung cancer. Only four studies examining never smokers were identified, suggesting the need for additional research in this population.
Funding Source: None to declare.

B-076 - Dietary Fiber And Whole Grain Intake In Relation To Breast Cancer Recurrence And Mortality

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Purpose: Breast cancer is among the most prevalent cancers among women worldwide. However, the importance of dietary and lifestyle factors for disease prognosis is still largely unknown, and the evidence upon which to base recommendations aimed at women living with breast cancer therefore slim. There are indications that whole grain foods or those rich in dietary fiber are associated with a lower mortality among women diagnosed with breast cancer, as was recently described in the WCRF Continuous Update Report. In the present study, we aim to examine how pre-diagnostic intake of whole grains and dietary fiber is associated with breast cancer recurrence and mortality in a prospective cohort. **Methods:** Incident breast cancer cases (n=2010) diagnosed among women participating in the Diet, Cancer and Health cohort (n=29,875), with complete information on the selected exposure variables, covariates, and outcome, were included in the study. A total of 422 have died, and of these, 290 with breast cancer as the main cause. The dietary variables of interest in this study are total dietary fiber and fiber from 4 sources: 1) vegetables, 2) fruits, 3) potatoes, and 4) cereals and cereal foods. For whole grains, two groupings are used: 1) total whole grain and 2) total whole grain products. The association between intake of whole grains and dietary fiber and all-cause or breast cancer-specific mortality will be investigated using Cox Proportional Hazards models. Follow-up time will be defined as time from date of breast cancer diagnosis until date of death or until last date of contact or end of follow-up for vital status. **Results and conclusion:** The study is currently underway, and the results are imminent; they will be finalized and ready for presentation at the conference.
Funding: The project is funded by the Danish Cancer Society.

B-077 - Energy Restriction At Young Age And Colorectal Cancer Risk: Involvement Of The Insulin-Like Growth Factor Pathway

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Purpose: We investigated joint associations of energy restriction (ER) at young age and variation in insulin-like growth factor-related (IGF-related) genes with CRC risk.
Methods: Participants in the Netherlands Cohort Study completed a questionnaire (n=120,852) and provided toenail clippings (~90,000) in 1986. Those living in Western cities during the Hunger Winter (1944–45) were exposed to ER at young age. After 16.3 years follow-up, toenail DNA of 3,768 subcohort members and 2,580 CRC cases (case-cohort) was genotyped for IGF pathway gene variants. Hazard ratios for CRC were estimated across combined categories of ER exposure and a genetic sum score of unfavorable alleles (based on 18 SNPs in 8 IGF-related genes) by Cox regression. ER exposed individuals in the lowest genetic sum score tertile were hypothesized to be at lowest risk and used as reference. ER and IGF1 19-CA repeat status combinations were also analyzed.
Results: A pattern of increasing CRC risks was observed across combined ER-genetic sum score categories in men but not women, although interactions were nonsignificant. Compared to the reference, men who lived in a Western city and were in the highest genetic sum score tertile had a hazard ratio for CRC of 1.23 [95% confidence intervals (CI): 0.74 to 2.04]; men who lived in a non-Western area and were in the lowest tertile had a hazard ratio of 1.51 (95% CI: 1.03 to 2.20); and men who lived in a non-Western area and were in the highest tertile had a hazard ratio of 2.04 (95% CI: 1.39 to 3.00). Irrespective of ER, women, but not men, carrying variant versus wild type repeat alleles were at a ~50% CRC risk reduction.
Conclusions: Data indicate potential IGF pathway involvement in ER-CRC associations.
Funding source: World Cancer Research Fund; Dutch Cancer Society; Biobanking and Biomolecular Research Infrastructure Netherlands; Health Foundation Limburg.

B-078 - Polyphenol Intake, Determined By Dietary Questionnaire And Plasma Biomarkers, And Risk Of Colorectal Cancer In The European Prospective Investigation Into Cancer And Nutrition (EPIC) Cohort Study

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Purpose. Epidemiological evidence on the association between polyphenol intake and colorectal cancer (CRC) risk is still inconsistent. Case-control studies suggest inverse associations, but these have not been confirmed in cohort studies so far. We aimed to investigate the association between polyphenol intake and CRC risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) study.
Methods. The study included 477,386 subjects aged 35-70 years from 10 European countries. Dietary questionnaires and plasma samples were collected at enrollment. Dietary polyphenol intakes were estimated using dietary questionnaires and the Phenol-Explorer database, including data on 502 individual polyphenols. Thirty-four polyphenols, representative of the main polyphenol classes, are being measured in plasma by tandem mass spectrometry currently.
Results. After a mean follow-up of 11 years, 4,701 validated incident CRC cases (2,979 colon and 1,722 rectal cancers) were identified and included in the analysis. A wide range of total polyphenol intake and a South-to-North geographical gradient (ranging from 584mg/d in Greek women to 1,786mg/d in Danish men) were observed. Phenolic acids (52.6%) and flavonoids (42.4%) were the main contributors to polyphenol intake. Coffee, tea and fruits were the major food sources of polyphenols. Using Cox regression, multivariable adjusted models showed a significantly inverse association between both stilbene (HRlog2 0.98, 95%CI:0.97-0.99) and tyrosol intakes (HRlog2 0.98, 95%CI:0.97-0.99) and CRC risk. Phenolic acid intake was associated with increased rectum tumor risk in women (HRlog2 1.11, 95%CI:1.02-1.21), but inversely associated with colon tumor risk in men (HRlog2 0.90, 95%CI:0.83-0.97). Multivariable logistic regressions will be conducted to investigate the relationships between plasma polyphenol concentrations and CRC risk in a nested case-control subset (700 cases and 700 controls).
Conclusions. This is the first study evaluating the association between the intake of all polyphenols, using questionnaires and biomarkers, and CRC risk.
Funding source. INCa grant 2011-105 and WCRF NL 2012/604

B-079 - Plasma B Vitamins, Alcohol Intake And Breast Cancer Risk Overall And By Hormone Receptor Status: Report From The EPIC Cohort

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Purpose. As important factors required for the generation of methyl groups, B vitamins may play a role in breast carcinogenesis (BC) through epigenetic changes. However, results from epidemiological studies have been inconsistent. A large nested case-control study within the EPIC study was conducted to evaluate the association between plasma concentrations of folate and vitamin B12 and BC.

Methods. A total of 2,491 BC cases were matched to 2,521 controls for study center, age, menopausal status, exogenous hormone use, time of the day at blood donation, fasting status, and phase of the menstrual cycle. Microbiological assays were used to determine plasma concentrations of folate and vitamin B12. Multivariable conditional logistic regression models were used to estimate odds ratios by quartiles of plasma B vitamins. Subgroup analyses were performed by menopausal status, hormone receptor status of breast tumors (ER, PR, and HER2), and levels of alcohol intake. The interaction between plasma folate and vitamin B12 on BC risk was also evaluated.

Results. No significant association emerged between plasma B vitamins and BC risk overall and by hormone receptor status. Stratification by menopausal status and alcohol intake unveiled a borderline increased risk associated with increasing levels of plasma vitamin B12 in women consuming high levels of alcohol (ORQ4-Q1=1.30; 95% CI=1.03-1.64; p for trend=0.051), but not in those drinking low amounts of alcohol (ORQ4-Q1=1.00; 95%CI=0.80-1.26; p-trend=0.928) (p-heterogeneity=0.14). Increased risk of BC was associated with increasing levels of plasma vitamin B12 in women with high concentrations of plasma folate (ORQ4-Q1=1.26; 95%CI=1.00–1.60; P-trend=0.014), while no association appeared in women with high levels of plasma folate (ORQ4-Q1=1.03; 95%CI=0.82–1.29; P-trend=0.806) (p-heterogeneity=0.059).

Conclusions. High levels of plasma vitamin B12, as biomarker of dietary intake, may increase the risk of BC in women with either high levels of alcohol intake or low levels of dietary/plasma folate.

B-080 - Are Complex Models In Nutritional Epidemiology Always Worth The Trouble?

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Purpose
It has been repeatedly emphasized that diet could account for up to 40% among preventable causes of cancer, although the consensus around this estimate is not unanimous. Despite several decades of research, comparatively few nutrition-related factors have been established as playing a causal role in human cancer.
Methods
The evaluation of role of diet on the occurrence of cancer has entailed a number of methodological challenges. First, extensive focus was given to procedures designed to perform correction of risk parameters for random and systematic measurement errors in individuals' dietary exposure estimates. Second, the evaluation of exposure/disease relationships in international multi-center study consortia motivated the need to exploit any level of etiological evidence, notably at the individual level (within-center) and at the aggregate level (between-center). Third, standard approaches have long focused on the relation between a limited list of foods or nutrients and the risk of cancer, which requires a relevant use of statistical assumptions when controlling for potential confounding by other dietary and lifestyle factors.
Results
Recognizing the multi-factorial nature of cancer and other chronic diseases, complementary holistic methodologies have been employed to address the notion of dietary patterns, a concept conceived to address the inherent inter-correlations between dietary variables. Strategies relying on *a priori* (evidence driven) or *a posteriori* (unsupervised or data driven) approaches have been proposed, thus contrasting analytical simplicity with computational sophistication. The merits and the pitfalls of each of the above points are illustrated and discussed.
Conclusions
In an effort to provide workable tools to understand the etiology and possibly prevent cancer and other chronic diseases, the day-to-day experience of nutritional epidemiologists is characterized by continuous concerns on the efficacy of cutting-edge statistical models to tackle biological complexity.

B-081 - Influence Of Obesity On Risk Of Second Cancers Among A Cohort Of U.S. Women With Breast Cancer

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Purpose: Increasing breast cancer incidence in the U.S., along with the aging population and improved survival, have resulted in a greater number of women at risk of developing a new malignancy. We investigated the association of elevated body mass index(BMI)—a surrogate marker of obesity—with risk of second primary cancers among breast cancer patients in a general community health plan.

Methods: Our retrospective cohort includes 7,541 women, ages 24-85 years, with a primary diagnosis of invasive breast cancer at Kaiser Permanente Northwest or Colorado between 1990 and 2008 and who survived for ≥one year. We assessed second cancer risk associated with BMI, calculated based on the patient's height and weight from electronic medical records. Relative risks(RRs) and 95% confidence intervals(CIs) were estimated using Poisson regression adjusting for study site, age and stage at diagnosis, ER status of initial tumor, time since initial breast cancer, diagnosis year, and breast cancer treatments (tamoxifen, aromatase inhibitors, chemotherapy with an alkylating agent, radiotherapy).

Results: Over a median(range) of 6.3(1.0-20.9) years of follow-up, 11.2% of breast cancer patients were diagnosed with a second primary cancer (including 248 contralateral breast, 83 colorectal, and 62 endometrial cancers). Obese women(BMI:30+ kg/m^2) experienced significantly increased risks of contralateral breast (RR=1.51, 95%CI:1.09-2.13) and endometrial (RR=2.56, 95%CI:1.27-5.59), but not colorectal (RR=1.04, 95%CI:0.58-1.89), second primary cancers as compared with normal weight women(BMI:18.5-<25 kg/m^2). For each 5 kg/m^2 increase in BMI, we observed significantly increased risks of contralateral breast (RR=1.18, 95%CI:1.07-1.29) and endometrial (RR=1.40, 95%CI:1.19-1.64) cancers, respectively.

Conclusions: Our results suggest that higher BMI, a modifiable risk factor, significantly increases risk of contralateral breast and endometrial cancers following a first breast cancer diagnosis. Reducing obesity may represent an effective strategy for second cancer risk reduction among breast cancer patients, but this hypothesis requires confirmation in clinical trials.

Funding source: NCI Intramural Research Program, NIH

B-082 - BMI Changes In The Follow-Up And The Risk Of Lung Cancer: A Prospective Study In China Kailuan Male Cohort

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Purpose: To investigate the association between BMI changes in the follow-up and male lung cancer incidence. Methods: A population-based cohort study was conducted in the whole male population, Kailuan Group, China during 2006 to 2011. By December 31, 2011, we followed 75151 men aged 18-108 years old. Cancer incidence information was obtained through follow-up and examination every two years and the records interview from the Financial Department of Kailuan Group, who was responsible for health reimbursement and death benefit of the group population. Incident cases occurred within 1 year after baseline interview was excluded. Body height and weight were measured by trained medical assistants. BMI changes in the follow-up were measured as the average annual proportional changes of BMI between the last follow-up and baseline interview, and were categorized into 5 groups: stable group (reference), minor loss or gain, and major loss and gain. Results Baseline BMI was inversely associated with lung cancer (highest tertile vs. lowest: HR=0.64, 95% CI: 0.44-0.94). While, the major loss and gain of BMI increased the risk of lung cancer (major loss vs. stable: HR=4.04, 95%CI: 2.15-7.59; major gain vs. the stable: HR=3.75, 95%CI: 1.99-7.07). Conclusions Major BMI changes in short term, both loss and gain, might indicate a potential role for body weight-related biological pathway in the development of male lung cancer.
Funding source: National Natural Science Fund of China (grant no. 81172757)

B-083 - Influence Of Diet, Physical Activity, Body Size On Breast Cancer In South Africa: A Study Of Women In Transition

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Purpose
There are suggestions of a different epidemiology of breast cancer (BC) in women of African ethnicity, a burden that appears in younger women with a higher proportion of ER- cases. Influences of diet, body fatness and physical activity on BC need to be investigated in African women in Africa because of the uniqueness of this population in rapid lifestyle transition, where BC has now become one of the most common incident cancers in women. Large differences between urban and rural populations in terms of dietary intake upon urbanisation, and lack of physical activity leading to obesity have been shown in South Africa, and prevalence of overweight and obesity is high. We have set up a population-based case-control study at the Baragwanath Hospital in Soweto, South Africa (The SABC study) to study BC etiology.
Methods
Questionnaire data on lifestyle, reproductive factors, physical activity/inactivity, and diet are collected from all women, as well as biological samples (serum, plasma, red blood cells, buffy coat and urine), which are stored at -80C. Anthropometry is measured for all women, who also undergo dual-energy X-ray absorptiometry and computed ultrasonography. Statistical differences between cases and controls for preliminary results were analysed by logistic regression models adjusting for potential confounding factors.
Results
To date, 118 cases and matched controls have been recruited in the study. 55% of the cases are classified as luminal A, and 15% as triple negative. Preliminary analyses showed no associations between obesity and pre-menopausal BC, while a strong inverse association was observed in post. High physical activity was protective against BC in all women.
Conclusions
Preliminary data indicate strong associations of lifestyle factors with BC risk in this population. The study will recruit a total of 500 cases and controls over the next 2 years.
Funding sources
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B-084 - Intake Of Vegetable And Fruit By Colors And Risk Of Colorectal Cancer

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Purpose
The colors of vegetable and fruit reflect their contents of unique phytochemicals and micronutrients which may contribute to health promotion. In this case-control study, we aimed to investigate the relationship between vegetable and fruit classified by color and colorectal cancer risk.
Methods
A case-control study was conducted with 923 colorectal cancer patients and 1846 controls recruited from the National Cancer Center in Korea. Information on dietary intake was collected using a food frequency questionnaire (FFQ) with 106 items. We classified vegetable and fruit into four groups by the color of their mainly edible part (eg, green, orange/yellow, red/purple and white). Vegetable and fruit intake level was classified by sex-specific tertile of control group. Residual method was used to adjust total energy intake. Binary and polytomous logistic regression models were used to estimate odds ratios and their 95% confidence intervals.
Results
High intake of total vegetable and fruit was strongly associated with a reduced risk of colorectal cancer in women (OR, 0.30; 95% CI 0.20-0.47 for highest vs. lowest tertile) and similar inverse association was observed for men (OR, 0.54; 95% CI 0.40-0.72). In color groups analysis, adjusted ORs (95% CI) comparing the highest vs. the lowest tertile of vegetable and fruit intake were: 0.47 (0.35-0.63) for green, and 0.50 (0.37-0.67) for white vegetable and fruit in men. An inverse association was also found in women for green (0.33 (0.21-0.51)), orange/yellow (0.65 (0.43-0.99)), red/purple (0.64 (0.43-0.96)) and white (0.29 (0.18-0.45)) vegetable and fruit.
Conclusion
We found a reduced risk of colorectal cancer among those with higher intake of vegetable and fruit of green or white as well as total intake amount in both men and women.
funding source
the National Research Foundation of Korea (2010–0010276 and 2013R1A1A2A10008260) and National Cancer Center Korea (0910220 and 1210141).

B-085 - Fruit And Vegetable Intake And Prostate Cancer Risk In The European Prospective Investigation Into Cancer And Nutrition (EPIC)

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Purpose: The aim of this study was to examine the prospective association of fruit and vegetable intake with the incidence of prostate cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC). We also examined the relationships of the major fruit and vegetables subtypes with prostate cancer incidence overall and by grade and stage of disease.
Methods: Lifestyle information for 142,254 men participating in EPIC from 19 centres in 8 European countries was collected at baseline. Validated dietary questionnaires were used to estimate fruit and vegetable intake, which was calibrated using 24-hr dietary recalls. Multivariable Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).
Results: After an average follow-up time of 14 years, 7,034 prostate cancer cases were identified. Compared with the lowest fifth, those in the highest fifth of total fruit intake had a significantly reduced prostate cancer risk (HR=0.88; 95% CI=0.81-0.96; P trend=0.005). Among fruit subtypes (citrus fruits, apples and pears, grapes, and bananas), only citrus fruits consumption was significantly associated with lower incidence of prostate cancer (HR in the highest versus lowest fifth=0.92; 95% CI=0.85-1.00; P trend=0.006). High vegetable consumption was not associated with lower incidence of prostate cancer (HR in the highest versus lowest fifth=1.00; 95% CI=0.91-1.10; P trend=0.53). None of the subtypes of vegetables (leafy vegetables, fruiting vegetables, root vegetables and brassicas) were associated with prostate cancer risk (P trend > 0.05). No evidence of heterogeneity between low- and high-grade or between localized and advanced-stage of the disease was observed.
Conclusions: Results from this large observational study suggest that a higher intake of fruit, especially citrus fruit, is associated with a small reduction in risk of prostate cancer.
Funding source: This work was funded by Cancer Research UK (C8221/A19170).

B-086 - Breast Cancer Risk Among Women With Type 2 Diabetes Differs By Ethnicity: The Multiethnic Cohort

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PURPOSE: Substantial research conducted primarily in white populations indicates a 20-30% elevated risk to develop breast cancer for T2D patients. This analysis investigated the association of T2D with breast cancer across five ethnic groups within the Multiethnic Cohort (MEC).

METHODS: In this cohort of 215,000 members aged 45-75 years at recruitment in 1993-1996, cancers were identified through tumor registries, deaths through vital records. T2D status was based on three questionnaires and three administrative data sources. Cox regression with age as the time metric was applied to estimate hazard ratios (HR) and 95% confidence intervals (CI). T2D status, i.e., a self-reported diagnosis confirmed by administrative data, was modeled as a time-varying exposure while adjusting for known confounders, including body mass index (BMI).

RESULTS: Among 100,855 (24,427 white, 20,025 African American, 7,596 Native Hawaiian, 26,396 Japanese American, 22,411 Latina) women, 6,557 breast cancer cases were identified after 14.8±4.1 years of follow-up. Of 17,991 self-reported T2D cases, 14,425 were confirmed by administrative data and 892 developed breast cancer. In models without BMI, T2D was significantly associated with T2D (HR=1.14; 95%CI 1.06-1.23), but including BMI lowered the estimate to 1.08 (95%CI 0.99-1.16). A strong association between BMI and breast cancer was observed in all ethnic groups except Latinas. The T2D-ethnicity interaction was borderline signficant (p=0.07); stratification by ethnicity showed elevated risks with and without adjustment for BMI among Latinas (HR=1.34; 95%CI 1.15-1.57 and HR=1.30; 95%CI 1.11-1.53) and African Americans (HR=1.18; 95%CI 1.02-1.37 and HR=1.30; 95%CI 1.11-1.53), but not in the other three ethnic groups.

CONCLUSIONS: As in previous reports, adjustment for BMI weakened the association of T2D with breast cancer and BMI was not a breast cancer predictor in Latinas. The signficant T2D association with breast cancer in Latinas and African Americans only is relevant for ethnic-specific prevention efforts.

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B-087 - General And Abdominal Obesity And Risk Of Cancer Development In Older Adults: A Study Of Cohorts In Europe

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Purpose: To investigate, in elderly European populations, the association of anthropometric indicators of general (body mass index, BMI) and central adiposity (waist circumference, WC; hip circumference, HC; and waist-to-hip ratio, WHR) with risk of cancer development, and potential effect modifications by sex, smoking and hormone replacement therapy (HRT).
Methods: We used data from 7 cohorts participating in the CHANCES consortium – a large collection of population-based cohort studies of older adults. Data were harmonized, analyzed separately using Cox proportional hazards models, and combined by random effects meta-analysis. Adjustment for the most important confounders common to all cohorts was performed.
Results: Overall, 43 419 men and women with a mean age of 62.5 y (range: 50-84 y) were included in this study, of whom 1 473 developed first incident cancers of the breast (postmenopausal), colorectum, pancreas, kidney, gallbladder, and endometrium, together labelled as 'obesity-related cancers' (median follow-up time: 12 years). Pooled analyses of adiposity indicators, per standard deviation (SD) increase, in relation to risk for obesity-related cancers yielded the following summary hazard ratios: 1.13 (95% CI: 1.02, 1.24) for BMI (SD=4.2 kg/m2), 1.12 (95% CI:1.01, 1.24) for WC (SD=12.1 cm), 1.10 (95% CI: 0.97, 1.22) for HC (SD=8.6 cm), and 1.11 (95% CI: 0.97, 1.24) for WHR (SD=0.1). For postmenopausal breast cancer, increased risks were confined to women who never used HRT (P-interaction<0.001), showing ~20% increases in risk per SD of BMI, WC, and HC; no association was observed with WHR.
Conclusions: General adiposity as measured by BMI and central adiposity as measured by WC show comparable positive associations with obesity-related cancers combined. Weaker results were observed for HC and WHR. Associations between anthropometric measures and postmenopausal breast cancer demonstrated effect modification by HRT use.
Funding source: FP7 framework programme of DG-RESEARCH in the European Commission (grant agreement no. HEALTH-F3-2010-242244).

B-088 - Healthy Lifestyle And Risk Of Cancer In The European Prospective Investigation Into Cancer And Nutrition Cohort Study

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Purpose: It has been estimated that at least a third of the most common cancers are related to lifestyle and as such are preventable. Key modifiable lifestyle factors have been individually associated with cancer risk; however, less is known about the combined effects of these factors.

Methods: This study generated a healthy lifestyle index score (HLIS) to investigate the joint effect of modifiable factors on the risk of (a) overall cancers; (b) alcohol-related cancers; (c) tobacco-related cancers; (d) obesity-related cancers, and (e) reproductive-related cancers. The study included 391,608 men and women from the multinational European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. The HLIS was constructed from five factors assessed at baseline (diet, physical activity, smoking, alcohol consumption, and anthropometry) by assigning scores of 0 to 4 to categories of each factor, for which higher values indicate healthier behaviours. Hazard ratios (HR) were estimated by Cox proportional regression and population attributable fractions (PAF) estimated from the adjusted models.

Results: There was a 5% lower risk (adjusted HR 0.952, 95% CI: 0.946, 0.958) of all cancers per point score of the index for men and 4% (adjusted HR 0.961, 95% CI: 0.956, 0.966) for women. The fourth versus the second category of the HLIS was associated with a 28% and 24% lower risk for men and women respectively across all cancers; 41% and 33% for alcohol-related; 49% and 46% for tobacco-related; 41% and 26% for obesity-related; and 21% for female reproductive cancers.

Conclusion: Findings suggest simple behaviour modifications could have a sizeable impact on cancer prevention, especially for men.

Funding sources: DGSANCO, European commission, Genesis Oncology Trust.

B-089 - Body Size And Breast Cancer Survival In The E3N Cohort Study

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Purpose
Obesity has been associated with poor breast cancer prognosis, but most studies focused on body mass index (BMI) and few considered different types of adiposity or changes in body size. Thus, we investigated associations between pre-diagnostic adiposity and breast cancer survival, considering BMI, waist and hip circumferences (WC and HC), waist-to-hip ratio (WHR), as well as associations between changes in body size before and around diagnosis, and breast cancer survival.

Methods
Analyses included ~3,000 women from the French E3N prospective cohort study diagnosed with primary invasive breast cancer between 1995 and 2008. We investigated overall, breast cancer-specific and disease-free survival, overall and according to stage, menopausal and hormonal status and year of diagnosis, using Cox proportional hazard models adjusted for tumor characteristics and lifestyle risk factors.

Results
When compared to women with a pre-diagnostic HC<95cm, those with a HC>100 cm were at increased risk of death from all causes (Hazard Ratio (HR)>100vs<95cm=1.46, 95% Confidence Interval (CI)=0.99-2.15,Ptrend=0.04) and from breast cancer (HR>100vs<95cm=1.63, CI=1.02-2.61, Ptrend=0.03), and of second invasive cancer event (HR>100vs<95cm=1.43, CI=1.10-1.84, Ptrend=0.006). Associations were stronger after adjustment for BMI. BMI, WC and WHR were not associated with survival after breast cancer. Analyses on changes in body size are ongoing and will be presented at the conference.
Conclusions
Our study underlines the interest of going beyond BMI when studying the association between adiposity and breast cancer survival. Further studies should be conducted to confirm our findings of an association between events after BC and hip circumference.

Funding source
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B-090 - Comparison Of Anthropometric Measurements Of Adiposity In Relation To Cancer Risk: A Systematic Review Of Prospective Studies

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Purpose:
In epidemiology, the relationship between increased adiposity and cancer risk has long been recognized. However, whether the association is the same for measures of abdominal or whole body adiposity is unclear. The aim of this systematic review is to compare cancer risk, associated with body mass index (BMI), an indicator of whole body adiposity, with indicators of abdominal adiposity in studies in which these indicators have been directly measured.
Methods:
We conducted a systematic search from 1974 (EMBASE) and 1988 (PubMed) to September 2015 with keywords related to adiposity and cancer. Included studies were limited to cohort studies reporting directly measured anthropometry and performing mutual adjustment.
Results:
Thirteen articles were identified, two on breast cancer, three on colorectal cancer, three on endometrial cancer, two on gastro-oesophageal cancer, two on renal cancer, one on ovarian cancer, one on bladder cancer, one on liver and biliary tract cancer and one on leukaemia. Evidence suggests that abdominal adiposity is a stronger predictor than whole body adiposity for gastro-oesophageal, leukaemia and liver and biliary tract cancer in men and women and for renal cancer in women. Abdominal adiposity was a stronger predictor for bladder and colorectal cancer in women, while only BMI was a predictor in men. In contrast, BMI appears to be a stronger predictor for ovarian cancer. For breast and endometrial cancer, both measures were predictors for cancer risk in postmenopausal women.
Conclusions:
Few studies used mutually adjusted and measured anthropometric indicators when studying adiposity–cancer associations. Further research investigating cancer risk and adiposity should include more accurate non-invasive indicators of body fat deposition and focus on the understudied cancer types.

Funding source:
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B-091 - Sarcopenia And Endometrial Cancer Prognosis

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Purposes: Sarcopenia has been recently recognized as an important risk factor for high mortality and surgical complications in cancer patients. Estimation of the cross-sectional muscle area measured by computed tomography scans provides a quick and easy way to identify patients at higher risks of worst outcomes. The association between sarcopenia and short term survival has never been demonstrated in endometrial cancer (EC) patients. The aim of the present study was to investigate the prevalence of sarcopenia and its impact on both short and long-term outcomes among patients undergoing oncological treatment for EC.
Methods: a database was created, comprising EC patients who underwent oncological treatment at Brazilian National Cancer Institute between 2008 and 2014 and had a CT scan available within 30 days before treatment. Clinicopathological features, surgical outcomes and one-year survival were retrospectively collected from medical records. The skeletal muscle index was measured on the CT scans was calculated to identify sarcopenia. Multivariate logistic regression were calculated to assess predictors of surgical complications. One-year survival were evaluated by Kaplan-Meier method and Cox Regression. Variables were considered statistical significant when $p<0.05$.
Results: 212 women with EC were included. Median age was 65 years-old, and 26.4% patients were diagnosed with sarcopenia. 47.2% of those who had sarcopenia were overweight according body mass index (> 25Kg/m2) and therefore classified as sarcopenic obesity. Sarcopenia and sarcopenic obesity were independent predictors of surgical complications. Sarcopenia was also associated with 30-day and one-year mortality. The average one-year survival of women with sarcopenia was 209.3 days (95% CI 168.757 to 249.861) versus 307.6 days for women without sarcopenia (IC 289.217 to 325.907). After ajustment, sarcopenia were an independent predictor of one-year survival in EC patients.
Conclusions: Sarcopenia is an independent prognosis factor in EC patients and should be assessed whenever possible to support early nutritional intervention.
Funding:FAPERJ

B-092 - Molecular Aspects Of Prostate Cancer: LDL And Cholesterol Metabolism

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Purpose: Epidemiological data suggest lifestyle factors are key in the development of aggressive prostate cancer (PCa). Low density lipoprotein (LDL) is a circulating blood lipid, modifiable through diet and drug intervention. A large body of literature supports an association between LDL and PCa, however, evidence is conflicting and causality has not been established.
Methods: Mendelian randomization techniques were used to investigate LDL as causal risk factor for PCa. Genetic risk scores representing a man's relative exposure to LDL were generated for 22,249 PCa cases and 22,133 controls from 22 studies within the international PRACTICAL consortium. Logistic regression was used to estimate the causal effect of LDL on PCa. In a subsidiary analysis, we examined the effect of a variant in HMGCR on PCa outcomes. The relationship between circulating LDL and PCa was further investigated in human prostate cell lines PNT2, LNCaP, DU145 and PC3. Cell proliferation was measured by tritiated thymidine incorporation. Protein expression of key effectors in cholesterol metabolism was assessed using western immunoblotting.
Results: A genetically instrumented standard deviation change in LDL was not associated with all-cause PCa (OR 1.24, 95% CI; 0.90, 1.69, p=0.18), however, weak evidence suggested a role for LDL in high vs low grade PCa (OR 1.50, 95% CI; 0.92, 2.46, p=0.11). The rs12916-T variant in HMGCR (which has been used previously to mimic statin intervention) was associated with a weak protective effect on PCa (OR 0.97, 95% CI; 0.94, 1.00, p=0.03). The proliferative response to LDL-cholesterol differed between prostate cell lines and protein analysis by western immunoblotting indicated that cancerous cell lines express higher levels of key effectors in cholesterol metabolism.
Conclusions: This work presents evidence at the epidemiological and cellular level that perturbed LDL metabolism influences prostate cancer.

B-093 - Sarcopenia Beyond Quantitative Assessment: The Quality Of Skeletal Muscle Mass Is Associated With Nutritional Status And One-Year Survival In Endometrial Cancer Patients

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Purposes: Myosteatosis, the excess deposition of triglycerides within skeletal muscle is associated with poor prognosis. Computed tomography (CT) scans are useful to quantify macroscopic accumulations of intermuscular fat. There is increasing evidence linking sarcopenia and cancer prognosis, despite no studies have evaluated, to date, the role of myosteatosis in cancer patients outcomes. The aim of the present study was to describe the relation with sarcopenia and myosteatosis with nutritional status and one-year survival in endometrial cancer (EC) patients.
Methods: a database was created, comprising EC patients who underwent oncological treatment at Brazilian National Cancer Institute between 2008-2014 and had a CT scan available within 30 days before treatment. Clinicopathological features and one-year survival were retrospectively collected from medical records. Skeletal muscle index (SMI) was calculated considering the range -29 to +150 HU measured on the CT scans, and reduced attenuation muscle in range -29 to +29 HU was classified as myosteatosis. By subtracting the myosteatosis area from total SMI, we created a new index designated "SMI free of myosteatosis" (SMIfree), as and indicator of high quality muscle area. Body mass index (BMI) were also assessed to classify nutritional status. One-year survival were evaluated by Kaplan-Meier method. Variables were considered statistical significant when $p<0.05$.
Results: 212 women with EC were included. Median age was 65 years-old. Median of SMIfree was significantly reduced in patients with sarcopenia. Obese women (BMI > 30Kg/ m²) had the higher amount of myosteatosis (51% >P50) and sarcopenic women had the lower amount of SMIfree (41.3% Conclusions: The quality of skeletal muscle mass is a promising predictor of prognosis in cancer patients, although more studies are needed to confirm this association.
Funding: FAPERJ

B-094 - A Longitudinal Examination Of The Interrelationships Between Multiple Health Behaviors In Cancer Patients

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Purpose

Cancer survivors are at a greater risk of developing secondary cancers and other chronic diseases. Health behaviors (HBs) are determinant protective factors of cancer recurrence and against other chronic illnesses. Understanding the possible interrelationships between HBs during and after cancer treatment is crucial to orient the development of more effective interventions to change HBs that are more effective.

The present study assessed the relationships between self-reported smoking, physical activity, alcohol intake and caffeine consumption among cancer patients with mixed cancer sites followed for 18 months. We explored the temporal associations of each HB with all three other HBs.

Methods

Patients completed an HB questionnaire at the perioperative period and then 2,6,10,14,18 months after. The interrelationships between HBs were examined using cross-lagged analyses conducted with structural equation modeling. The model was adjusted for age, sex, income, and cancer diagnosis, and for time-varying variables: weight, chemotherapy and radiotherapy.

Results

The study included 962 participants. The most frequent cancer sites were breast (49.4%), prostate (28.3%) and gynaecologic (10.8%). Although the model showed a good fit to the data, SRMR=0.050, RMSEA=0.060, and CFI=0.85, no significant cross-temporal paths emerged between HBs. However, higher levels of physical activity at 14 and 18 months were significantly predicted by a lower nicotine and alcohol consumption, and a greater caffeine intake at 14 and 18 months. For all four HBs, continuity paths generally indicated that one particular HB was significantly predicted by the same HB at the previous time point.

Conclusions

This study revealed that HBs assessed following cancer surgery are mostly independent. These findings suggest that interventions promoting HB changes during the cancer treatment trajectory could target several HBs simultaneously without any interference between them. They also suggest that physical activity is influenced by other HBs but only after when the cancer treatment is completed.

B-095 - Soft Drinks And Risk Of Obesity Related Cancers

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Purpose: To investigate the association between sugar-sweetened (SSD) or diet soft drinks (DSD, artificially sweetened) and obesity related cancers (ORC) in the Melbourne Collaborative Cohort Study (MCCS), in particular the role of body size.
Methods: The MCCS recruited 41,514 adults, aged 40 to 69 years in 1990-94 to identify risk factors for cancer. A Food Frequency Questionnaire specifically developed for the study was used to collect baseline data on the frequency of consumption of SSD and DSD over the previous 12 months. Data on incident ORC (oesophagus (adenocarcinoma), gastric cardia, pancreas, colon, rectum, post-menopausal breast (diagnosis > 55 years), endometrium, kidney, aggressive prostate (Gleason score>7) and ovarian) and mortality was obtained by data linkage to the end of 2012. Cox's proportional hazard models were fitted, with age as the time metric, to estimate hazards ratios and 95% confidence intervals in 38,621 people free of pre-baseline cancer.
Results: Increasing intake of SSD and DSD was associated with obesity. More than 5% of people with a history of diabetes, angina or heart attack (DM_CVD) consumed DSD > 2/day compared with just over 2% in those with no such history. In a model including 35,435 people with no DM_CVD, adjusting for sex, ethnicity, smoking, physical activity, alcohol consumption, Mediterranean Diet Score, socioeconomic status, and family history of cancer the HR and 95% CI for SSD >2/day versus <1/day was 1.06 (0.93, 1.21) and for DSD 1.27 (1.09, 1.48); for the 3,186 people with DM_CVD, the corresponding HRs were 1.52 (1.08, 2.13) and 1.46 (1.07, 1.98) respectively. Additional adjustment for BMI changed the HRs minimally.
Conclusions: In people with no DM_CVD, DSD were associated with an increased risk of ORC, while in those with DM_CVD, positive associations were seen for both DSD and SSD. These associations did not appear to be explained by obesity.

B-096 - Domain-Specific Physical Activity And Sedentary Behaviour In Relation To Colorectal Cancer Risk: A Systematic Review And Meta-Analysis

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Purpose: Physical activity reduces colorectal cancer risk; however, most studies addressing this research question have focused on physical activity performed within the occupation or recreation domains. The evidence in regards to other domains of physical activity and sedentary behaviour is limited and inconsistent. The purpose of this review was to examine associations of domain-specific physical activity and sedentary behaviour with colorectal cancer risk.
Methods: Medline, EMBASE and Web of Science were systematically searched from inception to December 2015 for cohort and case-control studies addressing this topic. Data from 17 cohort and 21 case-control studies were extracted, and pooled estimates were computed using random-effects meta-analysis. Meta-regression analyses were conducted to investigate whether the risk estimates differ by sex, cancer sub-site and study design.
Results: Comparing the highest versus lowest levels of domain-specific physical activity, the risk of colon cancer was 20% lower in individuals who were most active in the occupation (RR=0.80, 95%CI:0.67-0.96) and recreation (RR=0.80, 95%CI:0.72-0.89) domains, whereas weak or no associations were observed for rectal cancer (occupation RR=0.94, 95%CI:0.80-1.10; recreation RR=0.87, 95%CI:0.75-1.01). We noted non-significant colon cancer risk reductions for physical activity within the transport (RR=0.59, 95%CI:0.32-1.09) and household (RR=0.86, 95%CI:0.70-1.04) domains, but virtually null associations for rectal cancer (P>0.5). Sedentary behaviour was associated with increased colon cancer risk within the occupation domain (RR=1.44, 95%CI:1.29-1.62), but not with rectal cancer risk (RR=1.04, 95%CI:0.84-1.27). We noted significant heterogeneity across the studies, with differences in estimates mainly due to sex and cancer sub-site.
Conclusions: There is consistent evidence that physical activity in occupation and recreation domains reduces colon cancer risk; additional studies are required to improve precision in estimates for other domains. Reducing sedentary behaviour in the workplace may be an additional strategy to reduce colon cancer risk.

Funding source: Melbourne International Research Scholarship, awarded to Dr Mahmood.

B-097 - Modelling Substitution Of Sedentary Behavior With Standing Or Physical Activity To Study Associations With Quality Of Life In Colorectal Cancer Survivors

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Purpose: Previous research indicates that sedentary behavior (sitting/lying at low energy expenditure while awake) is unfavorably associated with health-related quality of life (HRQoL) of colorectal cancer (CRC) survivors. Using isotemporal substitution modelling, we studied how substituting sedentary behavior with standing or physical activity was associated with multiple HRQoL outcomes in 2-10 years post-diagnosis CRC survivors.

Methods: A cross-sectional study was conducted in stage I-III CRC survivors (n = 145) diagnosed between 2002-2010 at Maastricht University Medical Center+, the Netherlands. Participants wore the thigh-mounted MOX activity monitor 24 hours/day for seven consecutive days to assess time spent in sedentary behavior, standing, and physical activity during waking hours. Validated questionnaires were used to assess HRQoL outcomes, comprising global quality of life, physical, role, and social functioning, and disability (scales: 0-100), fatigue (20-140), depression, and anxiety (0-21). Isotemporal substitution modelling was applied to analyze associations with HRQoL of substituting 1 hour/day of sedentary time with equal time in standing or physical activity.

Results: On average, participants spent 10.2 hours/day sedentary (standard deviation, 1.7), 3.4 hours/day standing (1.3), and 1.7 hours/day in physical activity (0.8). In confounder-adjusted isotemporal models, a significantly higher physical functioning score was observed for substituting 1 hour/day of sedentary time with standing (unstandardized regression coefficient [β], 3.1; 95% confidence interval [CI]: 0.5,5.7) or with physical activity (5.6; 0.7,10.6). Additionally, substituting sedentary time with standing was associated with significantly lower levels of disability (β, -3.0; 95% CI: -4.9,-1.1) and fatigue (-4.0; -7.6,-0.3). No significant associations were observed with other HRQoL outcomes.

Conclusions: Our results suggest that substituting sedentary behavior with standing or physical activity may be beneficially associated with certain HRQoL outcomes in CRC survivors. Prospective studies are warranted to confirm whether actual substitution of sedentary behavior with these activities may improve HRQoL in CRC survivors.

Funding source: Dutch Cancer Society.

B-098 - Coffee Consumption And The Risk Of Malignant Melanoma In The Norwegian Women And Cancer (NOWAC) Study

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Background Numerous biologically active substances contained in coffee have been found to suppress carcinogenesis. Some new evidence has suggested a protective effect of coffee intake on risk of malignant melanoma. Coffee consumption habits among Norwegian women allow us to study the impact of heavy coffee intake on melanoma incidence.
Methods Information on total and filtered coffee consumption was available from self-administered questionnaires for 104 080 women at baseline in the Norwegian Women and Cancer Study. We also included update information on coffee consumption collected 6-8 years after the baseline data collection. Multiple imputation was performed as a method for dealing with missing data in the cohort. Multivariable Cox regression models were used to calculate hazard ratios (HR) for malignant melanoma.
Results During more than 1.7 million person-years, a total of 762 cases of malignant melanoma were identified. We found a statistically significant inverse association between low moderate (more than 1 and up to 3 cups/day) and high moderate (more than 3 and up 5 cups/day) filtered coffee consumption and the melanoma risk compared to light consumers (≤1 cup/day) (HR=0.81; 95% CI 0.66-0.99, HR=0.77; 95% CI 0.61-.98, respectively; ptrend=0.02). We did not find any statistically significant association between overall coffee intake and the risk of malignant melanoma in any of the consumption categories (>5 cups/day vs ≤1 cup/day HR=0.88; 95% CI 0.67-1.14, ptrend=0.20).
Conclusion The data from the NOWAC study indicate that the moderate intake of filtered coffee could reduce the risk of malignant melanoma.

B-099 - Diet, Cancer And Health ñ Next Generations. A Family-Based Population Study

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The Diet, Cancer and Health - Next Generations (DCH-NG) study is an extension of the existing Danish EPIC cohort. Biological children, their spouses and grandchildren of the original cohort members are invited. Using the unique personal identification number, 279,120 remnants of the original cohort members were identified. Of these, 189,833 fulfil the inclusion criteria: being alive, contactable and ≥18 years of age at time of invitation. Provided a participation of 25-30 %, about 50,000 participants are enrolled during 2015-2018. Participants are invited in family clusters, by postal letter, securing a familiar link.

Diet and lifestyle data, anthropometric and fitness measurements as well as DNA, serum, plasma, erythrocytes, spot urine, saliva and faeces samples are collected. For immediate use in research projects analysis of hemoglobin A1c, total, HDL and LDL cholesterol, triglycerides, high sensitive CRP and creatinine is performed. The physical examination includes measurements of waist and hip circumference, height, weight, body composition, blood pressure and pulse rate. In order to get a more objective measure of fitness an all-day activity tracker is implemented after baseline to be used by participants having a smartphone.

Participants sign up at the study homepage and get access to a personal web profile from where they book the physical examination and fill out web-based questionnaires. The original lifestyle and food frequency questionnaires have been further developed and modernised to make them as personalized and user-friendly as possible.

Two study centers are established in Copenhagen and Aarhus and in order to handle and integrate the large amount of data collected, a customized data-handling system has been developed. The DCH-NG cohort will constitute a unique resource for future trans-generational studies of the pathogenesis of multiple cancers and other non-communicable diseases.

B-100 - 3D Scanning For Obesity ñ First Results From The ADEPS Project

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Purpose
Obesity is associated with an increased amount of adipose tissue and linked to increased risks for certain types of cancer. Determination of body fat percentage (%BF) is not always possible due to limitations in available resources. Therefore, weight indexes like BMI offer a major advantage because they are quick and inexpensive to use. Although the BMI is extensively used, it is unable to differentiate adipose tissue from lean body mass. Therefore, the principal aim of the ADEPS project is to examine the extent to which %BF can be predicted using anthropometric measurements and to develop predictive equations useful as field method to asses %BF in clinical practice and research.
Methods
A dataset of anthropometric measurements obtained by 3D body scanning (n=1200, males & females, 18-65 years) was available within the research unit. From these data, samples of candidate anthropometrical measurements for total body volume prediction were selected. Regression analysis on sequentially selected datasets yielded anthropometric predictors useful to create a predictive model for densitometry-based %BF estimation. This model was then validated by comparison with %BF obtained from air-displacement plethysmography in a validation sample (n=200).

Results
Correlations of anthropometrics with total body volume (L) of body scans were evaluated. The strongest model in females included waist girth, body height, thigh girth and wrist girth (r^2 = 0,96, RMSE = 1,46). In males the model included waist girth, body height, thigh girth and upper arm girth (r^2 = 0,98, RMSE = 1,58). The recruitment of participants for validation is ongoing.

Conclusions
Our analyses show that more than 96% of variation in body volume can be predicted using the selected anthropometric measurements. From this volume, %BF can be calculated using known densities for fat and fat-free mass. Accuracy of these %BF predictions will be presented during the conference.

Funding
University College Ghent

B-101 - Physical Activity Domains And Risk Of Gastric Adenocarcinoma In The MCC-Spain Study

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Purpose: Evidence for a protective role of physical activity against development of stomach cancer is yet inconclusive. We studied the association of domain-specific physical activity and the risk of gastric adenocarcinoma (GAC), by site and histological type, in the MCC-Spain case-control study.
Methods: 428 histologically confirmed GAC cases including gastro-esophageal region (67% men) and 3225 controls were included. Cases were recruited in hospitals from 9 different Spanish regions, and age- and sex-matched population controls were randomly selected within the respective hospitals' catchment areas. A physical activity questionnaire was used to gather information on the type, frequency and duration of household and recreational activities, allowing estimation of physical activity volume (in MET-h/week). Participants also self-reported the intensity of working physical activity (from sedentary to very active) and their daily sitting time. Questionnaire data on diet, lifestyle and clinical factors (including *Helicobacter pylori* serology) were available. Adjusted odds ratios (OR) of GAC were estimated for domains of physical activity, stratifying by sex, site (cardia vs. non-cardia), and Lauren classification (intestinal vs. diffuse).
Results: Recreational physical activity was associated with lower overall GAC risk (OR=0.65, 95% CI: 0.50, 0.85 –highest recreational activity vs. none), particularly at moderate levels of intensity such as walking (OR=0.60, 95% CI: 0.45, 0.78). Household physical activity showed the strongest association among men (OR=0.41, 95% CI: 0.29, 0.60 –highest vs. none). Associations were stronger for non-cardia tumours, whereas no significant results were found in women. Sedentary time was not related to GAC risk (p-trend=0.438), but the potential protective effects of recreational physical activity were restricted to non-sedentary participants.
Conclusions: Both recreational and household physical activity were independently related to lower GAC risk. Gastric cancer prevention strategies should concomitantly promote adherence to recommended physical activity levels and avoidance of sedentary behaviours.
Funding source: Institute of Health Carlos III (PI11/01403).

B-102 - Antioxidant Content Of Four Leafy Vegetables From Montenegro

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It has been suggested that daily intakeof leafy vegetables have a positive effect in preventions of chronic human disease such as cancer,due to the presence of antioxidants. Antioxidant compounds,phenolic compounds, flavonoids and some minerals (Cu, Fe, Zn and Mn) have been reported as chemicals that contribute to the antioxidant potential. The aim of this paper was to determine the antioxidant potential of selected leafy vegetables from Montenegro (swiss chard, spinach, collard green and parsley), measuring total phenol and flavonoid content as well as mineral (Fe, Zn, Cu and Mn).
The leaves of selected vegetables wereair-dry at room temperature and grounded to fine powder. Dried samples were extracted with boiling water and every sample was analyzed for total phenol and flavonoid content by the Folin-Ciocalteau and colorimetric aluminium chloride methods respectively using spectrophotometric technique.Total concentration of Cu, Zn, Fe and Mn was prepared using microwave digestion (ETHOS1) with HNO3 and H2O2 and measured by ICP-OES instrument.
Total phenolic content of extracts ranged from 227,2mg of galic acid equivalent (GAE) /g of dry sample (parsley) to 432,7mg (GAE)/g of dry sample (spinach). Flavonoid content is highly positively correlated with phenolic content(R2=0,998448) and consequently the highest value was in spinach 135 mg of quercetin equivalent/g of dry samples and the lowest in parsley 43,52mg of QE/g of dry samples. All analyzed minerals showed the highest value in spinach (Zn=104,7mg/kg of dry samples, Cu=137mg/kg, Mn= 130,7mg/kg and Fe=154,2mg/kg) and the lowest in parsley (Zn=28,55mg/kg of dry samples, Cu=15,97mg/kg, Mn= 49,75mg/kg and Fe=74,5mg/kg).
The tested vegetablesshowedthe high phenolic, flavonoid and mineral content and should be included in daily consumption for diseases prevention.
This work has been supported by the Ministry of Science of Montenegro and the HERIC project through the BIO-ICT Centre of Excellence (Contract No. 01-1001).

B-103 - Adherence To The Mediterranean Diet And Cancer Risk In EPIC

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Purpose: To summarize the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study results on the association between adherence to the Mediterranean diet (MD) and risk of specific cancers, including gastric adenocarcinoma (GC), breast cancer (BC), pancreatic cancer (PC), colorectal cancer (CRC), bladder cancer (BLC) and overall cancer.
Methods: EPIC includes approximately half a million subjects, aged 35-70 years, from 10 European countries. During recruitment (between 1992-2000) dietary and lifestyle information was collected. Adherence to the MD was estimated using Mediterranean diet scores (MDS) considering the combined intake of key MD components. The associations between the MDS and incidence of each cancer site were assessed through separate Cox regression models, controlling for cancer specific confounders.
Results: The mean follow-up period ranged from 8-11 years and the number of incident cases identified by cancer site was: 449 GC cases, 10,225 BC cases, 865 PC cases, 4,355 CRC cases, 1,425 BLC cases and 30,731 cancer cases overall. High compared to low MD adherence was associated with a significant reduced risk of GC (Hazard Ratio (HR) 0.67; 95% Confidence Interval (CI) 0.47, 0.94), CRC (HR 0.89; 95% CI 0.80, 0.99), BC overall (HR 0.94; 95% CI 0.88, 1.00) and particularly in hormone receptor negative BC tumours (HR 0.80; 95% CI 0.65, 0.99) and overall cancer risk (HR 0.93; 95%CI 0.90, 0.96). In contrast, no significant association was found for BLC (HR 0.84; 96%CI 0.69, 1.03) or PC (HR 0.99; 95%CI 0.77, 1.26).
Conclusions: These results support the important role of following a MD pattern on reducing risk of certain cancers, such as GC, BC and CRC, as well as overall cancer. These findings underscore the potential scope for cancer prevention through dietary modification such as following key attributes of the traditional MD.
Funding sources: AGAUR: Exp.2014.SGR.726, RETICC: RD12/0036/0018

B-104 - Prevention Of Breast Cancer Recurrence Through Weight Control, Diet, And Physical Activity Intervention (PREDICOP): Design Of An Ongoing Study

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Advances in screening and treatment have resulted in an increasing number of breast cancer (BC) survivors. However, because the 5-year recurrence risk still ranges between 10 and 20%, there is a need to investigate modifiable factors that could impact long-term prognosis. Current evidence suggests that adiposity and physical inactivity could be determinants of prognosis. Nevertheless, to date the only two published studies on lifestyle intervention and BC recurrence only used a dietary intervention and provided controversial results.
The main purpose of the study is to investigate the effect of a diet and exercise intervention on BC recurrence.
The PREDICOP study is a multicentric randomized trial carried out in Spain that aims to include 2108 women, aged 18 to 75, having recently completed standard treatment for a non-metastatic invasive BC. Participants randomised to the control group will receive usual care and those in the intervention group will additionally receive a one-year lifestyle program. This program will include one supervised nutrition class and two supervised exercise sessions of moderate-to-high intensity per week during the first six months and monthly reminding sessions thereafter. All participants will subsequently be followed-up for four years. Data will be analysed on an intention-to-treat basis using time-to-event analysis.
Before setting-up the PREDICOP study, a one-arm trial was implemented to assess participation and compliance of overweight/obese BC survivors to a 12-week lifestyle intervention involving diet and exercise and demonstrate the capacity of the intervention to induce weight loss. This study showed a high compliance (> 80% of scheduled sessions attended), a significant 7% weight reduction and improvements in perceived quality of life.
If this lifestyle intervention results in a reduction in BC recurrence or an improvement in overall health and quality of life among BC survivors, it will help develop new clinical guidelines for BC patients.

RETICC:RD12/0036/0018, AGAUR:2014SGR726, FIS:PI12/00335

B-105 - Effects Of Physical Exercise During Adjuvant Breast Cancer Treatment On Physical And Psychosocial Dimensions Of Cancer-Related Fatigue: A Meta-Analysis

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Background - Cancer-related fatigue has a multidimensional nature and complaints typically increase during adjuvant treatment for breast cancer. Physical exercise might prevent or reduce cancer-related fatigue. So far, no meta-analysis has investigated the effects of physical exercise on different dimensions of fatigue.
Purpose - To investigate the effects of physical exercise during adjuvant breast cancer treatment on physical and psychosocial dimensions of fatigue.
Methods - We performed a systematic literature search in PubMed, Embase and the Cochrane Library in June 2015. Randomised controlled trials reporting the effects of physical exercise during adjuvant breast cancer treatment on different dimensions of fatigue were included.
Results - Pooled effects of 6 exercise programmes (including 784 patients) showed significant beneficial exercise effects on general fatigue (ES: -0.22, 95%CI -0.38; -0.05) and physical fatigue (ES: -0.35, 95%CI -0.49; -0.21). Effects on fatigue subscales 'reduced activity' (ES: -0.22, 95%CI -0.38; -0.05) and 'reduced motivation' (ES: -0.18, 95%CI -0.35; -0.01)' were also in favour of physical exercise. No effects were found on cognitive and affective fatigue. Including only the supervised exercise programmes (n=4 studies), slightly larger pooled effect estimates were found on general fatigue (ES: -0.25, 95%CI -0.47; -0.04) and physical fatigue (-0.39, 95%CI -0.56; -0.23).
Conclusions - In conclusion, physical exercise during adjuvant breast cancer treatment has beneficial effects on general fatigue, physical fatigue, 'reduced activity' and 'reduced motivation', but did not show effects on cognitive and affective fatigue. Largest effect sizes are found for physical fatigue, suggesting that this is the fatigue dimension most sensitive to physical exercise.
Funding source - The contribution of JK van Vulpen was supported by the World Cancer Research Fund The Netherlands (WCRF NL, project number 2013/997).

B-106 - Use Of Belts And Tight Clothing And Gastric Cancer: Is Mechanical Carcinogenesis Confirmed?

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Purpose. The hypothesis that mechanical carcinogenesis due to the abdominal pressure, for example from the use of belts, has been examined in two epidemiological studies with conflicting evidence. We examined the relationship between use of belts, tight clothes or girdles (a belt or sash worn around the waist) and gastric cancer in a population-based case- control study in Spain (MCC-Spain study) conducted between 2008-2013.
Methods. 459 histologically confirmed gastric cancer cases and 3438 population controls were included from different regions of Spain. Exposure was assessed by face-to-face interview administered by trained personnel. Odds ratio (OR) and 95% confidence intervals (CI) were calculated, adjusting for potential confounding factors for all gastric cancer cases and by anatomical sub-site.
Results. We observed an increase in gastric cancer risk for the average lifetime regular users of girdles (OR= 3.3; 95% CI 2.0-5.2) and an increase in cardia gastric cancer risk for the average lifetime regular users of tight pants or skirts (OR=2.2; 95% CI 1.1-4.4). Obese regular users of girdles had an 8-fold risk of gastric cancer. Users of girdles had a higher BMI, were less educated, and smoked and drank less alcohol than non-users. We did not find any association with use of belts.
Conclusion. This study confirms the hypothesis that mechanical abdominal pressure is related to gastric cancer risk, particularly in obese subjects. A proposed mechanism for this association is that the use of tight clothing may increase the gastro-esophageal reflux, although in our study the increased risk was observed in both cardia and non-cardia tumours.
Funding source. The study was partially funded by the by the Instituto de Salud Carlos III-FEDER (PI08/1770).

B-107 - Physical Fitness In The Danish Cohort ëDiet, Cancer And Health ñ Next Generationsí ñ A Validation Study

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Purpose
Physical fitness comprises several components, of which, cardiorespiratory fitness (VO_{2max} (ml O_2/kg/min)) is of particularly interest due to its strong inverse association with risk of chronic diseases, including cardiovascular disease, diabetes and cancer. Less complicated methods than standard test of cardiorespiratory fitness including submaximal exercise testing and non-exercise questionnaire based methods are mostly used in epidemiological research.
The aim was to evaluate the validity of a submaximal fitness test The Danish Step Test (TDST) and a simple self-reported question (SSRQ) as methods for estimating physical fitness. This was done by comparing these two methods with a VO_{2max}test, which is considered the gold standard.

Methods
125 participants aged 19-67 years were recruited from the cohort. Participants completed a VO_{2max}test, TDST and answered the SSRQ rating their physical fitness level. Pearson product-moment-correlation-coefficients were calculated to assess the relationship between the VO_{2max}test and TDST. The VO_{2max}test, TDST and the SSRQ were grouped into five categories. The degree of misclassification across categories between TDST and the SSRQ, respectively, in relation to the VO_{2max}test were investigated.

Results
Moderate correlations between the VO_{2max} test and TDST were found (men: $r=0.555$, $n=60$, $p<0.05$, women: $r=0.658$, $n=65$, $p<0.05$).
When comparing the categories of physical fitness from TDST with the VO_{2max}test, on average only 6% of the women were classified outside the same (±1) category. However, for men there was a higher degree of misclassification with 38% outside the same (±1) category, where TDST especially seemed to underestimate physical fitness. When comparing the categories from the SSRQ with the results from the VO_{2max}test, only 9% of the women were misclassified. Among men, only 13% fell outside the same (±1) category.

Conclusions
The SSRQ was found to be a superior method to TDST when estimating physical fitness in a less cost prohibitive and more practical way than the VO_{2max}method.

B-108 - Selenium Pathway Genotypes Are Associated With Colorectal Cancer Risk And Modified By Selenium Status

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Purpose: Suboptimal intakes of the micronutrient selenium (Se) and selenoprotein genetic variation may contribute to colorectal cancer (CRC). We recently reported the association of higher Se status with lower CRC risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort (Hughes et al. 2015; PMID 25042282). In this study, we examine the association of Se pathway genotypes with CRC risk, including the interaction of SNP-Se status in disease risk modification.
Methods: Tagging SNPs (N=1050) in the Se pathway (153 selected genes comprising 159 variants in 24 of 25 selenoprotein genes plus 891 variants in 129 genes in pathways sensitive to Se intake) were successfully assayed by Illumina *Goldengate*^{TM} genotyping in DNA samples from 1478 CRC case-control pairs matched within EPIC (a further 99 SNPs with at least 20% missing data were excluded from analysis). Multivariate logistic regression was used to assess the influence of Se pathway genetic variation on CRC risk. In pathway analyses, genes were sorted into at least one known functional pathway and gene and pathway p-values were computed using the PIGE package Adaptive Rank Truncated test.
Results: Genetic variations in 20 of 41 selenoprotein and Se biosynthesis genes, plus variations in several other Se pathway genes, are associated with CRC risk (not adjusted for multiple testing). Additionally, genetic variation can interact with Se status (as assessed by our existing data on serum Se and Selenoprotein P) to decrease or increase CRC risk. Pathway analyses suggest that gene only and gene-Se interactions in selenoprotein, anti-oxidant and apoptosis pathways may alter CRC susceptibility risk.
Conclusions: Individuals of particular risk Se pathway genotypes and / or those with suboptimal Se status may especially benefit from an increased dietary Se intake for CRC prevention.

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B-109 - Obesity And Risk Of Postmenopausal Breast Cancer By Subtype ñ Meta-Analysis Of Prospective Studies

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Purpose
To systematically review the findings from prospective studies on the association of obesity with risk of breast cancer, overall and by hormone receptor subtypes, in postmenopausal women.

Methods
Relevant publications from prospective studies on obesity, as measured by body mass index (BMI), and breast cancer risk were searched in PubMed up to May 2015, as part of the WCRF Continuous Update Project. Random-effects dose-response meta-analyses were conducted to calculate the summary relative risks (RRs) for each 5 kg/m^2 increase in BMI and postmenopausal breast cancer and its subtypes.

Results
Fifty-six studies (80 404 cases) could be included in the meta-analysis. The summary RR per 5 kg/m^2 was 1.12 (95% confidence interval (CI)=1.09–1.15) for postmenopausal breast cancer, which confirmed the positive association that is well-established in the past reviews.
There was evidence of high heterogeneity between studies (I^2=75%, P<0.001). Further analyses showed that the significant increased risk was only observed in menopausal hormone therapy (MHT) never users (RR=1.16, 95% CI=1.10–1.23) (15 studies) and not ever users (RR=1.01, 95% CI=0.96–1.06) (13 studies), and in women with oestrogen receptor (ER) positive (RR=1.17, 95% CI=1.09–1.25) (14 studies), progesterone receptor (PR) positive (RR=1.47, 95% CI=1.36–1.60) (5 studies), and joint ER+PR+ breast cancers only (RR=1.29, 95% CI=1.19–1.40) (9 studies); which could partly explain the different associations between the studies, although high heterogeneity remained in most of the subgroups.

Conclusions
Our results show an increase in risk of obesity with hormone sensitive breast cancer in postmenopausal women and support the purposed hormonal pathway that underlies the relationship. Further studies should limit the analysis to MHT never users to avoid the masking of the association by hormone use.

Funding source
This study was funded by the World Cancer Research Fund (WCRF) International (Grant number: 2007/SP01).

B-110 - Circulating C-Reactive Protein And Breast Cancer Risk ñ Meta-Analysis Of Prospective Studies

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Purpose
To explore the magnitude and the shape of the association between circulating C-reactive protein (CRP), a low-grade inflammation biomarker, and breast cancer risk in women through systematic literature review and meta-analysis.

Methods
Relevant publications from prospective studies on the association were identified in PubMed and Web of Science up to February 2015. Random-effects linear dose-response meta-analyses were conducted to calculate the summary relative risks (RRs) for breast cancer, overall and in postmenopausal women, and second order fractional polynomial models were used to examine any potential non-linear relationship.

Results
Overall twelve studies on any breast cancer (3 522 cases), and nine studies on postmenopausal breast cancer (2 516 cases) could be included in the meta-analyses. For each doubling of CRP concentration, the summary RRs were 1.07 (95% confidence interval (CI)=1.02–1.12; I^2=47%, P heterogeneity=0.04) and 1.06 (95% CI=1.01–1.11; I^2=32%, P heterogeneity=0.17), respectively. Positive associations remained in the studies that examined reverse causation by excluding the cases diagnosed in the early years of follow-up. Subgroup analyses showed similar summary RRs in the studies adjusted or not adjusted for body mass index, but the associations attenuated in the studies adjusted for other lifestyle factors (smoking, physical activity, and alcohol use).
Although the test for departure from linearity was statistically significant (P non-linearity=0.01 overall and <0.001 in postmenopausal women), the associations appeared linear over most of the range of CRP concentrations. For postmenopausal women, the increase in risk was sharper and tailed off after 4 mg/L, possibly because of limited data points after this value.

Conclusions
Low-grade inflammation may be associated with breast cancer risk. More studies are needed to clarify the confounding factors in the association.

Funding source
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B-111 - Selenium Status And Risk Of Prostate Cancer In A Danish Population

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Purpose: Low selenium status may be associated with higher risk of notably advanced prostate cancer. In a population with a relatively low selenium intake, we investigated the association between pre-diagnostic selenium status, and 1) risk of total, advanced and high-grade prostate cancer, and 2) all-cause and prostate cancer-specific mortality among men with prostate cancer.
Methods: Among 27,179 men included in the Danish "Diet, Cancer and Health" cohort, we identified 784 incident prostate cancer cases through 2007. Each case was risk set matched to one control. Two-thirds (525) of the cases had advanced disease at the time of diagnosis and among these 170 had high-grade disease; 305 cases died (212 from prostate cancer) during follow-up through 2012. Plasma selenium was assessed by inductively coupled plasma-mass spectrometry (ICP-MS), and plasma selenoprotein P using high performance liquid chromatography coupled to ICP-MS. Conditional logistic regression and cox proportional hazard models were used for the statistical analyses.
Results: Plasma selenium was not associated with total or advanced prostate cancer, but higher selenium levels were associated with lower risk of high-grade disease (HR (95% CI): 0.77 (0.64, 0.94), P = 0.009). In survival analyses, higher plasma selenium was associated with lower all-cause (HR (95% CI): 0.92 (0.85, 1.00), P = 0.04), but not prostate cancer-specific mortality. Higher levels of selenoprotein P were associated with lower risk of high-grade disease (95% CI): 0.85 (0.74, 0.97), P = 0.01), but not with risk of or mortality from advanced prostate cancer.
Conclusion: Levels of plasma selenium and selenoprotein P were not associated with risk of total and advanced prostate cancer, but higher levels of these two biomarkers were associated with lower risk of high-grade disease.
Funding sources: Bjarne Saxhof Foundation, Danish Cancer Society, Wereld Kanker Onderzoek Fonds (WCRF NL; grant 2015/1412) as part of the WCRF International grant program.

B-112 - Nutrient Dietary Patterns And Colorectal Cancer Risk In The EPIC Cohort Study

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PURPOSE: We investigated the association between nutrient patterns (NP) and colorectal cancer (CRC) risk in adults participating in the European Prospective Investigation into Cancer and nutrition (EPIC) study.
METHODS: Amongst 477,312 EPIC subjects, intakes of 23 nutrients were estimated from validated dietary questionnaires. Four NP, obtained across all centers were identified using principal component analysis, explaining 67% of the total variance of nutrient intakes. Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed using Cox proportional hazards models to quantify associations of 1 standard deviation (SD) increments in NP scores and overall CRC risk and by anatomical subsites. Adjustments were made for relevant confounders.
RESULTS: During an average of 11 years of follow-up, 4,517 first incident cases of colorectal cancer were documented. A NP characterized mainly by vitamins and minerals was inversely associated with CRC risk (HR=0.94, 95% CI 0.92, 0.98) as was a NP characterized by total protein, riboflavin, phosphorus, and calcium (HR=0.96, 95% CI 0.93, 0.99). A NP characterized by nutrients from plant food sources was not associated with CRC risk overall but the findings by anatomical sub-site did suggest an inverse association with cancer of the distal colon (HR=0.93, 95% CI 0.86, 1.00). Finally, a NP characterized mainly by dietary vitamin D was not associated with CRC risk.
CONCLUSIONS: A NP characterized by a high variety of vitamins and minerals, and one driven by total protein, riboflavin, phosphorus, and calcium, were both associated with a modest but statistically significant decreased risk of CRC. This is the first study investigating associations between NP and CRC risk in a large prospective international cohort and adds to the understanding of the role of dietary factors in CRC development.Funding source: the EPIC Study was funded by the EC and this work by the French Institution ‘Fondation de France’ (2010-2011)

B-113 - 3D Scanning Of Foods For Density Calculation

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Purpose
Foods, diets and nutritional status are important determinants of non-communicable diseases like cancer. Therefore, nutritional surveillance is important to monitor population intakes. During conversion of reported foods to consumed foods, coefficients for conversion are essential for proper intake estimation. When converting food volumes to weights, densities of foods are required. Density determination of foods typically associated with bulk density are challenging because the way they appear as consumed is difficult to maintain during volume measurement (for instance, salads and crisps or fries). Therefore, a method is developed to measure their volume using 3D scanning.

Methods
Foods are placed in or on a reference plate with known dimensions and volume. A 3D handheld scanner is moved around the food while real-time surface alignment gives a good understanding of what has been scanned so far and what still needs scanning. As many scans as needed to capture the whole object can be made. During image processing scans are first aligned to get the full model. Next, all scans are fused together to get a single triangulated mesh of one 3D model. The model can then be imported into imaging software to determine the volume of the food. Together with the weight, this allows for calculation of density.

Results
The method is still under development and first results for salads will be presented during the conference. Also, results on accuracy and precision of the 3D scans will be presented. Previous evidence already showed the potential of 3D scanning in many different fields.

Conclusions
3D scanning of foods is a potential solution for density measurements of foods with bulk density which are difficult to measure correctly using traditional underwater weighing methods.

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Fund for Applied Research of University College Ghent

B-114 - Diet, Body Size, Physical Activity And Risk Of Prostate Cancer: An Umbrella Review Of The Evidence

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Purpose: The literature evidence on the relationship of diet, body size, physical activity and risk of prostate cancer was summarised by the World Cancer Research Fund (WCRF) Continuous Update Project (CUP). We conducted an umbrella review using data from the CUP to further evaluate the robustness of the evidence.

Methods: The robustness of the evidence was evaluated using several criteria addressing evidence strength and validity, such as the statistical significance of the random effects summary estimate and of the largest study in a meta-analysis, the number of prostate cancer cases, between-study heterogeneity, 95% prediction intervals, small-study effects bias, excess significance bias and sensitivity analyses with credibility ceilings.

Results: A total of 248 meta-analyses were extracted from the CUP, which studied associations of 23 foods, 31 nutrients, 8 indices of body size and 3 indices of physical activity with risk of total prostate cancer development, mortality or cancer development by stage and grade. Of the 176 meta-analyses that used a continuous scale to measure the various exposures, no association presented strong evidence by satisfying all the aforementioned criteria. Only the association of height with total prostate cancer incidence and/or mortality presented highly suggestive evidence with a 4% higher risk per 5cm greater height (95% CI, 1.03-1.05). Seven associations of five exposures, including body mass index (BMI), weight, height, dietary calcium and spirits intake, were supported by suggestive evidence. The strongest association of those was for BMI and prostate cancer mortality, where an 11% higher risk per 5 kg/m2 greater BMI was observed (95% CIs, 1.06-1.17). The grading of the evidence was similar in the 72 meta-analyses with a categorical exposure assessment.

Conclusions: The association of diet, body size and physical activity with prostate cancer risk has been extensively studied, but no association was graded with strong evidence.

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B-115 - Circadian Control Of Daily Eating Patterns And Cancer: The MCC-Spain Study

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Purpose: In 2007 the IARC classified shift work involving circadian disruption as probably carcinogenic to humans. Perturbed circadian system in modern life involves erratic eating patterns. Mistimed eating patterns are associated with several health endpoints in experimental studies. Studies on nutrition and cancer focus on "what" and "how much" we eat rather than on "when" we eat. We assessed whether timing of eating patterns is associated with breast and prostate cancer risk.
Methods. We conducted a population-based case control study on multiple cancers in several regions in Spain. After excluding subjects who had ever worked night shift and those with incomplete information on circadian patterns, we examined data from 569 confirmed cases of prostate cancer and 795 population controls, and 1021 confirmed cases of breast cancer and 1160 population controls.
Results. Risk for both prostate and breast cancer decreased with increasing time between supper (main evening meal) and sleeping. Compared to subjects sleeping immediately after supper, those sleeping 2 hours after supper had an adjusted OR for prostate cancer of 0.73 (95%CI 0.54-0.98) with a statistically significant dose-response with time elapsed. The corresponding OR for breast cancer was 0.80 (0.62-1.01). Risk stratification by diurnal preference (an attribute reflecting personal preference for activities in the morning or evening), indicated a stronger protection for early morning types. The protection of prolonged time between supper and sleeping was strongest among subjects adhering to the WCRF/AICR recommendations (score above 4).
Conclusions. This is the first study in humans showing that timing of eating patterns is associated with cancer risk. Misclassification of exposure is inevitable when evaluating timings retrospectively and this may have diluted observed effects. However the hypothesis we tested is supported by experimental evidence and stresses the importance of evaluating circadian disruption in studies on diet and cancer.
Funding: Instituto Salud CarlosIII PI11/1889.

B-116 - Relating Urinary Polyphenol Metabolite Profiles To Specific Polyphenol-Rich Foods In The European Prospective Investigation Into Cancer And Nutrition (EPIC) Study

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Purpose: Metabolomics offers great potential to improve the accuracy of dietary intake measurements in nutritional epidemiology. This study aimed to develop an analytical framework to use profiles of urinary polyphenols to predict intake of polyphenol-rich foods, applying a multivariate statistical technique, reduced rank regression (RRR), in the EPIC cross-sectional study.
Methods: This study included 475 subjects aged 35-70 years randomly selected from 4 European countries. Dietary data were collected using 24-hour dietary recall (24-HDR) and dietary questionnaires (DQ). Thirty-four urinary polyphenols were measured by UPLC-ESI-MS-MS in 24-hour urines, collected the same day of the 24-HDR interview. RRR analyses identified linear combination of polyphenols to maximize the explained variability of specific foods and food groups. To evaluate the performance of RRR models, cross-validation analyses were conducted by splitting the data into a training and a test set, and computing correlation coefficients and area under curve (AUC) statistics to discriminate between consumers and non-consumers.
Results: The RRR scores of polyphenol profiles were correlated with intakes of red wine (24HDR $r_{adjusted}$=0.67, DQ $r_{adjusted}$=0.22), citrus fruit (24HDR $r_{adjusted}$ =0.62, DQ $r_{adjusted}$=0.21) and coffee (24HDR $r_{adjusted}$=0.61, DQ $r_{adjusted}$=0.54). Highest predicting performance was observed for coffee (ROC AUC=91.4%), red wine (87.6%) and citrus fruits (85.0%) from 24-HDR. Correlation coefficients and ROC AUC values were consistently higher for 24-HDR than for DQ. The RRR models in the test set also well predicted intakes of coffee (AUC=85.0%), red wine (79.9%), and citrus fruits (76.6%) from 24-HDR.
Conclusion: RRR lent itself as a useful tool to identify linear combinations of polyphenols that can predict intake of specific food groups, especially from 24-HDR. Compared to single food/metabolite comparisons, multivariate analyses provide better predictive performance, and a promising strategy to integrate available metabolomic and dietary information.
Funding source: EU-financed FP7 project (NutriTech grant no.289511), NA funded by EDISS, Université de Lyon.

B-117 - A Prediction Model For The Absolute Risk Of Death From Cancer And Other Causes

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Background: There are numerous modifiable risk factors for premature death, with tobacco smoking, overweight and obesity, high alcohol consumption, poor diet, and physical inactivity being among the most important. Whilst the importance of these factors is widely known in the general public, the joint magnitude of their influence on the absolute risk of death is less well appreciated. We sought to build a model to calculate the absolute risk of death as a function of these modifiable factors.

Methods: We analysed data from the European Prospective Investigation into Cancer and Nutrition study, which is a prospective cohort of over 500,000 European adults. We restricted our analysis to the approximately 330,000 participants with complete covariate data follow-up information. Absolute risk of death was estimated using flexible parametric survival models including sex, smoking status, BMI, a composite indicator of quality of diet, alcohol intake, and physical activity.

Results: Among the available cohort of 330,000 participants, there were approximately 25,000 deaths that occurred during follow-up. A model including all covariates could discriminate well between those individuals at high and low risk of death within 5 years (c-statistic 0.769; 95% confidence interval [0.763, 0.775]). This represented a modest improvement over a model including only age and sex (c-statistic 0.747; 95% confidence interval [0.741, 0.7553]). We will present risk profiles according to various patterns of risk factors, and show how these factors influence the absolute risk of death from cancer and other causes for individuals of various ages.

Summary: Whilst age and sex alone can discriminate well between those at high and low risk of death, the absolute risk of death varies strongly with several modifiable risk factors, most notably tobacco smoking. This model could be used as an aid to public heath communication, or to motivate the maintenance of healthy habits.

B-118 - The Oxidative Balance Score And Risk Of Colorectal Cancer Development In European Populations

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Purpose: Oxidative stress and antioxidant status have been implicated in the etiology of several major chronic diseases, including various cancers such as colorectal cancer (CRC). Recently, a comprehensive score called the Oxidative Balance Score (OBS) has been developed combining dietary and/or biomarker measures of oxidative damage and antioxidant defence. Our objective was to assess the association of the OBS with CRC development using data from a large prospective cohort study.

Methods: OBS, comprised of 13 *a priori* selected pro- and anti-oxidant exposures (Dietary Factors: polyunsaturated fatty acids; Biomarkers: vitamin C, lycopene, α-/ β-carotene, lutein, β-crypoxanthin, zeaxanthin, retinol, α-tocopherol; Lifestyle Factors: alcohol consumption, smoking status, and body weight/waist circumference) was calculated using data from a CRC case-control study nested within the EPIC cohort. Conditional logistic regression was used to estimate multivariable-adjusted odds ratios (OR) and 95% confidence intervals (95%CI) for risk of CRC (and its anatomical sub-site) in relation to OBS. Effect modification by various factors relevant to CRC was also assessed. A total of 1,264 complete case-control pairs of first incident CRC cases (colon n=805; rectal n=459) and their matched controls were included in the analysis.

Results: Higher OBS, which represents predominance of anti-oxidants over pro-oxidants, was not associated with CRC risk (OR=0.90; 95%CI, 0.63-1.29, highest vs. lowest quartile). Analyses by CRC sub-sites showed a statistically significant association for colon (OR=0.58; 95%CI, 0.35-0.93), but not rectal cancer (OR=1.38; 95%CI, 0.78-2.43).

Conclusions: In this large prospective cohort of European populations, OBS did not show an association with risk of CRC development overall, but findings by anatomical sub-site suggest an inverse association for colon but not rectal cancer.

B-119 - Systematic Evaluation Of Korean Food Composition Databases Against International Standards ñ A Prerequisite Towards Development Of A Standardized Korean Nutrient Database For Use In International Settings

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Purpose: In the context of global nutritional surveillance, standardized nutrient databases (NDBs) are a prerequisite to derive reliable and comparable nutrient intake data across countries for prevention and control of non-communicable diseases. Recently, the first Asian version of an international standardized dietary assessment tool (GloboDiet Korean version) has been developed under the IARC-WHO Global Nutritional Surveillance initiative framework. For validation and further implementation of the GloboDiet Korean version, a standardized Korean NDB is required. Therefore, this review aimed to systematically evaluate available existing Korean NDBs and food composition databases (FCDBs) against the international standards with the ultimate objective to compile a standardized Korean NDB for use in nutritional surveillance and research in international settings.
Methods: Twenty-three food components in existing Korean NDBs/FCDBs were prioritized for validation and implementation purposes. In terms of modes of expression, units, definitions and analytical methods with the international standards provided by Food and Agriculture Organization/International Network of Food Data Systems (FAO/INFOODS), they were then compared. These food components were divided into 'comparable', 'convertible' or 'not-comparable' groups based on the evaluation.
Results: More than two-thirds of components were 'comparable' with the international standards. The carbohydrate and energy values were classified as 'convertible' and the rest of the components as 'not-comparable' due to lack of documentation, inappropriate methods, and/or missing values in the Korean databases. Data from dietary supplement databases are not documented so they were categorised as 'non-comparable'.
Conclusion: This review completes the first step towards standardization of the Korean NDBs for use in nutritional surveillance and researches in international settings. Furthermore, this study served as a pilot initiative to develop Standard Operating Procedures (SOPs) to ease standardization of NDBs in countries participating to the IARC-WHO global nutritional surveillance.
Funding source: Korean National Research Foundation (NRF2013R1A6A3A03060992), DEX-IARC resource, and National Cancer Center of Korea (NCC1231100)

B-120 - Vitamin D Supplements May Reduce MHT-Associated Breast Cancer Risk: Evidence From The E3N Cohort

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Purpose: The high prevalence of vitamin D inadequacy in Europe and in North America has raised concern about potential adverse health effects of vitamin D deficiency. Experimental studies support protective effects of vitamin D on breast cancer, but epidemiological data remain inconclusive. Recent in vitro studies suggested potential interactions between vitamin D and estrogens. Our objective was to investigate the relationship between vitamin D supplementation and breast cancer risk, considering the recency of vitamin D supplementation and a potential interaction with menopausal hormone therapy (MHT) use.

Methods: Between 1995 and 2008, 2482 invasive breast cancers were diagnosed among 57,403 postmenopausal women from the French E3N cohort. Vitamin D supplementation was prospectively assessed from biennially self-administered questionnaires sent in 1995, 2000, 2002, and 2005. Multivariable HRs for primary invasive breast cancer and 95% CIs were estimated with Cox models.

Results: Current but not past vitamin D supplementation was associated with decreased postmenopausal breast cancer risk, compared with never use, (HR: 0.82, $CI_{95\%}$: [0.69, 0.97] for current use, and HR: 1.08, $CI_{95\%}$: [0.91, 1.30] for past use, $P_{homogeneity}$ = 0.02), especially for ER+ tumours (HR: 0.73, $CI_{95\%}$: [0.59, 0.91]). The association with current vitamin D supplementation was modified by MHT use ($P_{homogeneity}$ = 0.02): the decreased risk was restricted to MHT ever users: HR: 0.74, $CI_{95\%}$: [0.60, 0.90], while HR: 1.13, $CI_{95\%}$: [0.89, 1.56] among never users.

Conclusions: In our study, vitamin D supplementation was associated with decreased postmenopausal breast cancer risk in MHT users only. These findings should be confirmed before considering vitamin D supplementation to partly balance the MHT-associated increased breast cancer risk.

Funding source: French Ministry of Research, Fondation de France, Mutuelle générale de l'éducation nationale, European Community, Ligue Nationale Contre le Cancer, Gustave Roussy, and Institut national de la santé et de la recherche médicale.

B-121 - A Prospective Cohort Study Of Risk Factors For Prostate Cancer In 230,000 Men From UK Biobank

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Purpose
Prostate cancer is the commonest cancer among men in the UK, yet there are no known modifiable risk factors to inform prevention. With the aim of advancing the understanding of the aetiology of prostate cancer, in 2013 we initiated the UK Biobank Prostate Cancer Epidemiology Consortium to exploit the maturing UK Biobank resource with its uniquely detailed exposure phenotyping.

Methods
Between 2006-2010 the UK Biobank study recruited 500 000 participants aged 40-69 from across Britain. We examined the baseline characteristics of the 230,000 men in UK Biobank in relation to risk of prostate cancer using Cox regression, stratified by age at entry and region, with adjustment for potential confounders, and using attained age as the underlying time variable.

Results
After an average of 2.9 years of follow-up, by 31st December 2011 there were 1888 incident cases of prostate cancer. Preliminary analyses show that risk of being diagnosed with prostate cancer was elevated for men with known risk factors including family history of prostate cancer (HR 1.99, 95% CI 1.73 to 2.29 for men with any versus no first degree family history) and black ethnicity (HR 3.45, 95% CI 2.47 to 4.82 for black versus white ethnicity). Further endpoint data will be available in January 2016 and results from the extended analyses for a wide range of putative risk factors will be presented.

Conclusions
By 2017 there will be 5000 incident cases of prostate cancer in UK Biobank. Future analyses will examine risk factors for distinct prostate tumour subtypes, with a particular focus on high risk disease (including advanced stage and high grade tumours) and on the exposures infrequently characterised in large prospective cohort studies, including medical history, early development, sexual history, sophisticated measures of body composition, metabolic profile and biomarkers of infection.

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Cancer Research UK

B-122 - Iron Biomarkers, Hepcidin And Gastric Cancer Risk: The EPIC-Eurgast Study

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Introduction: Iron, an essential element for human life but also toxic when in excess has a very well-regulated metabolism. Although evidence suggests that dietary iron is associated with gastric cancer, results from studies measuring iron biomarkers is rather insufficient to lead to any conclusions. Recently, hepcidin has been discovered as a key regulator of iron homeostasis.
Aim: To investigate the relationship between body iron biomarkers, serum hepcidin levels and gastric cancer risk.
Method / Design: We conducted a nested case-control study in the multi-centric European Prospective Investigation into Cancer and Nutrition (EPIC) study. The study included 456 primary incident gastric adenocarcinoma cases and 900 matched controls that occurred during an average of 11 years of follow-up. We measured pre-diagnostic serum iron, ferritin, transferrin, and C-reactive protein, and hepcidin levels and further estimated total iron-binding capacity (TIBC) and transferrin saturation (TS). Odds ratios (OR) and 95% confidence intervals (CI) for the risk of gastric cancer by iron metrics were estimated from multivariate conditional logistic regression models
Results: After adjusting for relevant confounders, we observed a statistically significant inverse association between gastric cancer and ferritin and TS indices (ORlog2=0.80, 95% CI=0.72-0.88; and OR10%increment=0.87, 95% CI=0.78-0.97, respectively). Hepcidin levels was also inversely related to gastric cancer (OR for Q4 vs Q1 0.41, 95% CI=0.28-0.61; p for trend<0.0001).No statistical differences were found by gastric cancer localization (cardia and non-cardia) or histological (diffuse or intestinal) type. TIBC increased risk of overall gastric cancer (OR50µg/dl=1.13, 95%CI=1.02-1.2) and also with non-cardia gastric cancer and intestinal type. Additional analysis suggests that time since diagnosis of gastric cancer and pepsinogen levels could modify these findings.
Conclusions: Our results showed a decreased risk of gastric cancer related to body iron status. Further investigation is needed to clarify the role of iron in gastric carcinogenesis.

B-123 - Evaluation Of Multi-Morbidity In The European Investigation Into Cancer And Nutrition (EPIC) Study

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Purpose
Recent trends in population ageing triggered increasing research to evaluate the occurrence and determinants of multi-morbidity. In this study the association between major modifiable lifestyle factors and the risk of multi-morbidity, defined here as the development of at least two conditions among cancer, coronary heart disease (CHD) or type II diabetes (T2D), was evaluated. Etiological relationships between morbid conditions were also investigated.
Methods
Incident events of CHD and T2D were assessed in the EPIC-CVD and EPIC-InterAct studies respectively, and were linked to incident cancers in the EPIC study over the period 1991-2007. The association between multi-morbidity risk and modifiable lifestyles factors was assessed using multinomial logistic models. The association between previous morbid conditions and the risk of developing a second disease was modelled using time-dependent covariates in Cox models.
Results
During a median follow-up of 7.4 years, 42,371 cancer, 13,604 T2D and 10,463 CHD events occurred. A total of 60,190 and 3,467 study participants developed, respectively, one and two morbid events. When compared with normal BMI(18.5 Conclusions
Modifiable risk factors are strongly associated to the risk of multi-morbidity, thus suggesting a great potential for disease prevention policies. This study confirmed that developing T2D and CHD increases the risk of subsequent cancer development.
Funding source
DGS–multymorbidity GR-IARC-2013-11-05-01

B-124 - Socioeconomic Inequalities, Dietary Patterns And Adherence To Dietary Guidelines: Evidence From The E3N-EPIC Cohort Study

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Purpose
It is crucial to understand the socioeconomic brakes and leverages of adopting a healthy diet, diet being of the main modifiable factors that public health can act on to reduce the burden of non-communicable diseases such as cancer.

Methods
We used data from 58,193 participants of the large French E3N-EPIC cohort study. As the socioeconomic factors are highly correlated, we derived socioeconomic patterns thanks to a latent class analysis and we studied the relationships between these profiles, French dietary guidelines and dietary patterns.

Results
Respect to dietary guidelines, we found the alcohol intake was inversely associated with a deprivation index ($p<0.001$) and the number of siblings was positively associated with the consumption of vegetables ($p<0.001$). Regarding our analysis on patterns, women in the “Highly Educated” pattern who had a high education level and highly educated partners, were found to be more frequently in the “Western” dietary pattern ($p<0.01$). Women in the “Rural” pattern, who had a high deprivation index and a lower education level, were more frequently in the “Processed Food” pattern ($p<0.001$).

Conclusions
Thanks to an innovative modeling, we disentangled the relationships between the socioeconomic environment and dietary habits. We have also shown that it is compulsory to study the influence of the socioeconomic environment thanks to the conjunction of several factors, when available, rather than a single factor such as the level of education. Public health and nutritional prevention strategies for cancer should be universal, but modulated according to the socioeconomic position.

Funding source:
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B-125 - A Bayesian Hierarchical Model For Dietary Exposure And Biomarker Measurements

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Purpose
In nutritional epidemiology, self-reported assessments of dietary exposure are prone to random and systematic measurement errors. As a result, estimates of the association between dietary factors and risk of disease can be biased. To partially account for exposure misclassification, it has been suggested to complement self-reported dietary assessments with objective measurements, such as dietary biomarkers. A holistic approach which uses all available information is still missing. In this work, dietary and biomarker measurements were integrated in a Bayesian model, which was used in two nested case-control studies within EPIC.

Methods
A Bayesian latent factor hierarchical model with three structural components was developed: 1) an exposure model, to define the distribution of unknown true exposure (the latent factors), 2) a measurement model, to disclose the relationship between observed measurements (dietary questionnaires, 24-hour recalls and biomarkers) and the true exposures, 3) a disease model, to estimate the relationship between dietary exposures and disease status. Hierarchical models are used to build complex models through the specification of simpler conditional independence relationships, for which each variable in the model is conditionally related to only a few other variables. The marginal posterior distribution of model parameters is obtained from the joint posterior distribution, using Markov Chain Monte Carlo (MCMC) sampling techniques. Analyses were carried out using JAGS.

Results
The work focused on two applications. Firstly, the association between dietary fat and risk of breast cancer was complemented by gas-chromatography plasma phospholipids from 2,982 breast cancer cases matched to 2,982 controls. Secondly, the relationship between B-vitamins with kidney cancer risk was estimated by integrating dietary and blood level measurements.

Conclusions
Bayesian models make it possible to integrate complex problems into modular components with simpler structure, allowing the complex nature of dietary measurements to be accounted for.

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B-126 - Weight, Body Composition And Biological Changes After A 6-Month Adapted Physical Activity Program During Adjuvant Treatment For Localized Breast Cancer: A Randomized Controlled Trial

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Purpose: After a breast cancer (BC) diagnosis, weight gain and loss of physical fitness are negative prognostic factors. In contrast, healthy diet and regular physical activity (PA) might prevent comorbidity and mortality. The randomized controlled trial PASAPAS (www.clinicaltrials.gov, no.NCT01331772) was designed to evaluate the feasibility of a 6-month adapted PA program concomitant to adjuvant chemotherapy in early-stage BC patients.
Methods: 61 patients were recruited between 2011 and 2013 and randomly allocated between an intervention and a control arm (2:1 ratio). All participants benefited from dietetic counseling. The intervention arm was offered a 6-month aerobic exercise program of two to three weekly group sessions. Blood draw, anthropometrics, body composition and PA questionnaires were obtained at baseline and 6 months. Effects of exercise were investigated using correlation analyses.
Results: 60 (98%) of the patients completed the study and one patient retrieved from the trial after randomization. At baseline, the intervention (n=41) and control (n=19) arms were similar in all aspects. In the intervention group, median adherence to the program was 85% of the sessions. Mains reasons for non-compliance were logistic and second or reconstructive surgery. After 6 months, there were no differences in anthropometrics, body composition and PA level between arms. However, most (>70%) women maintained or decreased their weight, waist circumference or fat mass, and maintained or increased their lean mass. The amount of moderate-to-vigorous (>4 METs) PA was inversely correlated with weight (p=.04) and body fat (p=.01) variations. Sedentary behavior was positively correlated with fasting glycemia (p=.04) and total cholesterol (p=.03) variations.
Conclusions: This study showed that implementing a 6-month exercise program is feasible during adjuvant chemotherapy for BC in a French population. It will serve as foundation for future randomized controlled trials of efficacy.
Funding sources: INCa, Ligue contre le cancer; Fondation de France, CLARA, French Ministry of Research

B-127 - The Impact Of Body Mass Index On Endometrioid Endometrial Carcinoma Prognosis

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Purposes: Endometrial cancer is the fifth most commonly diagnosed cancer among women worldwide and is classified into two subtypes of tumors with different clinicopathological features and prognosis. Endometriod endometrial carcinoma (EEC) is the most frequent subtype, is often diagnosed in early stages and present a favorable prognosis. Obesity is considered a major risk factor for EEC carcinogenesis. Several studies have described association between obesity and EEC incidence, but with no survival analysis. A recent systematic review showed controversial results concerning the role of obesity on prognosis. Therefore, the aim of this study was to analyze the impact of body mass index (BMI) in disease-free survival (DFS) and overall survival (OS) in women diagnosed with EEC.
Methods: a database of EEC cases was created, comprising patients who underwent surgical treatment at Brazilian National Cancer Institute between January, 2000 and December, 2011. Clinicopathological features were collected from medical records for exploratory analysis of the variables distribution. Nutritional status were separated on euthrofic, overweight and three obesity grades, according to BMI criteria. Univariate and multivariate DFS and OS were calculated by Kaplan-Meier method and Cox Regression, respectively. Variables were considered statistical significant when $p<0.05$.

Results: 849 women with EEC were included. Mean age was 63.58 years-old. Mean BMI was 31.83 at time of diagnosis and 83.2% patients were obese or had overweight. Patients were followed for an average of 34.97 months. There were 111 recurrences (13.1%) with mean DFS of 51.90 months and 140 deaths (16.5%) were registered (mean OS of 52.25 months). There was no difference on DFS and OS curves related to BMI classification. Regarding OS, there was no statistically significant difference related to BMI at time of diagnosis of EEC.

Conclusion: Overweight and obesity had no impact on EEC prognosis on the assessed cohort.
Funding: CNPq, FAPERJ, CAPES, MS.

B-128 - Diabetes Mellitus And Head And Neck Cancer

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Purpose: Diabetes mellitus (DM) is directly associated with some cancers. However, studies on the association between DM and head and neck cancer (HNC) have rendered controversial results. Assessing DM and cancer, emphasis should be given to metformin, a medication used for DM type 2, which is shown to be inversely associated with some cancers. The objective of this study was to evaluate the association between DM and HNC, as well as the impact of metformin use on the risk of HNC.
Methods: This case-control study included 1021 HNC cases with squamous cell carcinoma, histologically confirmed, admitted in five large hospitals in the state of São Paulo, from 2011 to 2014. A total of 1063 controls were selected in the same hospitals and were frequency-matched to cases by sex and age (in 5-year groups). In order to assess the risk of CCP associated with DM, odds ratios (OR) and 95% confidence intervals (CI 95%) were estimated using unconditional logistic regression.
Results: Diabetic participants had an inverse risk of HNC (OR=0.68; 95% CI: 0.49-0.95), and this inverse association was more intense among diabetic metformin users (OR=0.54; 95% CI: 0.29-0.99). Diabetic metformin users that were current smokers (OR=0.13; 95% CI: 0.04-0.44) or had an alcohol consumption of >40 g/day (OR=0.31; 95% CI: 0.11-0.88) had lower risk of HNC than non-diabetic participants.
Conclusion: DM patients have um inverse risk of HNC and the use of metformin may at least partially explain this association.
Funding source: This work was supported by the São Paulo Research Foundation (FAPESP, grant 2010/51168-0, 2013/20548-0, 2013/21702-3, 2014/18893-4).

B-129 - Food And Nutrient Intake And Risk Of Gastric Cancer In Iran

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Gastric cancer (GC) is the second cause of cancer death worldwide. GC is the most common cancer among Iranian men. Unfortunately, there is no consensus about GC screening and the patients are usually diagnosed in advance stage and experience poor prognosis. Although dietary factors are considered as a main risk factor for gastric cancer, most of the results are based on studies in high income countries. We conducted a case-control study an examined food and nutrient intakes as a risk factor for gastric cancer in the Cancer Institute of Iran. We recruited 226 GC patients (58 women and 178 men) and, 245 controls (93 women and 152 men) who were matched for age, gender, and area of residence. A questionnaire has been completed by face to face interview and food intake was assessed by a phone interview, based on diet history questionnaire. Associations between nutrient and food intake and risk of cancer were estimated by logistic regression. We found that using trans-fatty acids (OR=1.5) and milk (OR=1.3) intakes were positively associated with the risk of gastric cancer. In contrast, we found inverse association between GC and consumption of riboflavin (OR=0.08), thiamin (OR=0.23) and zinc (OR=0.3). In conclusion, dietary factors play important role in the risk of GC in Iran. Primary prevention and healthy lifestyle and dietary habit would decrease the incidence of GC.

B-130 - Compilation And Evaluation Of A European Nutrient Database Extension Of Methyl-Group Donors

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Purpose:
Within the EPIC Nutrient Database project (ENDB), a reference European nutrient database was created. Values for methyl-group donors like choline, betaine and methionine were still lacking as these values were not available in national food composition tables. In this study, the ENDB has been extended with the methyl-group donors folate, choline, betaine and methionine.
Methods:
The ENDB food list was linked to 4 food composition databases that include nutritive values for folate, choline, betaine and methionine. In order of priority: the US National Nutrient Database for Standard References, the Canadian Nutrient File, the Danish Nutrient Database and the German Nutrient Database. Each ENDB food item was linked to a similar item in one of the 4 databases, respecting the order of priority. If no perfect match could be found, an appropriate recipe was searched for The matched folate values were compared with reference ENDB folate values to evaluate the validity of the methyl-group donor matching. Analysis were carried out with the Statistical Package for the Social Sciences (SPSS).
Results:
Not all four methyl-group donors could be found for every food item, 1.1% missing values remained for folate, 21% for choline, 22.7% for methionine and 69.3% for betaine. Some of these missing values might be logic zeros. Strong correlations (r=0.79) were found with the standardized international folate values that are considered as reference values. Correlations were even stronger when considering the frequency of consumption of the different food items (r=0.87).
Conclusions:
Only limited food composition data was available for betaine. Strong correlations between the matched folate values and reference folate values confirm the validity of the nutrient matching. The increase in correlations when considering consumption frequencies indicates that less well matched foods are those that are less consumed.

Funding source:
MDB, HVP & VV were funded by the ERASMUS PROGRAMME.

B-131 - Mediterranean Diet And Colorectal Cancer: A Mediation Analysis In The EPIC Italy Cohort

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Purpose
Several clinical and biological mechanisms have been hypothesized to explain the protective effect of Mediterranean diet (MD) on colorectal cancer (CRC).
In the Italian section of the EPIC study, we examined the role of abdominal adiposity (measured by waist-to-hip ratio - WHR) and chronic inflammation (measured by the inflammatory marker plasminogen activator inhibitor-1 - PAI-1) as potential mediators of the relationship between MD and CRC.
Methods
We used the Italian Mediterranean Index (IMI, a score from 0 to 11 based on the consumption of various Mediterranean foods) as a summary measure of adherence to MD. Using a Cox proportional hazard model, we calculated the total effect of IMI (categorized into 4 categories - 0-1, 2-3, 4-5 and 6-11), WHR and PAI-1 on the risk of CRC.
We then estimated the indirect (mediated) and direct (unmediated) effects of IMI on the risk of CRC adapting to survival outcomes the weighting approach for multiple mediators. The mediation analysis was conducted by considering first only WHR and then introducing PAI-1. The confounders considered were age, smoking status, sex, centre, physical activity and education.
Results
Increasing adherence to MD was associated with a significantly decreasing risk of CRC and there was a positive relationship between WHR, PAI-1 and CRC. In the cohort, the total effect of IMI on CRC was mainly explained by the pure direct effect (HR 0.47, 95% CI: 0.35-0.57 for the highest category of IMI compared to the lowest one), while the natural indirect effect (i.e. mediated by WHR) was minimal (HR: 1.00, 95% CI: 0.91-1.08). In the case-cohort, the introduction of the second mediator PAI-1 did not improve the mediated effect estimate .
Conclusions
The protective effect of MD on the development of CRC is minimally mediated by abdominal adiposity and chronic inflammation.

B-132 - The Preventability Of Cancer Due To Overweight And Obesity ñ Assessing The Global Prevention Potential

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Purpose: In 2012, nearly half a million cancer cases have been attributed to overweight and obesity. Yet, it is unclear how many of these cases could have realistically been avoided by public health efforts. In this study, we aim to assess and quantify the global prevention potential of cancer related to high body mass index (BMI).

Methods: Estimates of mean BMI in adults by age, sex, and country and relative risks obtained from published meta-analyses were used to calculate preventable fractions. The number and proportion of cancer cases that could have been avoided through realistic reductions in mean BMI was compared across five different prevention scenarios. This was done using more plausible counterfactual BMI distributions that have been achieved in the past, have been observed within the same world region or could be reached using public health interventions.

Results: Depending on the scenario, between 23% and 53% out of 481,000 estimated cancer cases attributable to overweight and obesity could have been avoided through prevention (17-56% in males, 26-54% in females), ranging up to 72% in cases occurring below age 50. Overall, the global prevention potential was greatest if countries adopted the lowest (healthy) mean BMI as observed in a neighbouring country of the same world region. Global prevention efforts to reduce mean BMI by one unit could decrease the cancer burden attributable to excess weight by 39%, translating into about 180,000 fewer cases in 2012. Different potential impacts were observed across the world regions, reflecting the different stages of the obesity epidemic.

Conclusions: The majority of the global cancer burden attributable to overweight and obesity is realistically avoidable through prevention efforts. Yet it seems that region-specific approaches are required to halt the obesity epidemic and its impact on cancer.

Funding Source: World Cancer Research Fund International (grant number SG 2012/619).

B-133 - Inventory Of Existing Surveillance Systems In Europe ñ Dietary Assessment Methodologies For Dietary Monitoring: A DEDIPAC Study

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Purpose: To gather information on dietary assessment methodology currently used for dietary monitoring in Europe.
Methods: The information was collected within the framework of the Determinants of Diet and Physical Activity (DEDIPAC) Knowledge Hub (KH) as part of an inventory of existing surveillance systems in Europe targeting different populations and health outcomes. An ad hoc inventory questionnaire was developed and disseminated among the representatives of the eleven DEDIPAC countries. Eligible surveillance systems were required to meet specific inclusion criteria.
Results: Fifty-one surveillance systems met the inclusion criteria: six international surveys and forty-five national initiatives. Dietary intake was assessed in the six pan-European surveillance systems and in 37 national surveillance systems. Food frequency questionnaires (FFQs, 29 studies) followed by 24-hour dietary recalls (24-HDRs, 11 studies) were most used. FFQs were mainly self-administrated and paper-based whereas 24-HDRs were computer-based interviews, i.e. face-to-face- or telephone-based. Many studies assessed the whole diet or collected information on many food items to evaluate the overall diet of the individuals. The number of food items included in the questionnaires varied from between 1 to 210. Few tools were validated and tested for reliability.
Conclusions: Many on-going surveillance systems assessed dietary intake. The methodologies applied varied across surveys with FFQs and 24-HDRs as the most popular tools. A need was observed for standardization of dietary methodologies applied to ensure the comparability of dietary data across Europe. Emphasis should be given to the implementation of a validated and standardized dietary methodology for dietary surveillance across Europe. The inventory helped to identify gaps and needs in terms of dietary monitoring and will contribute to the roadmap for an integrated pan-European surveillance system.
Funding sources: International Agency for Research on Cancer, Joint Programming Initiative ‘Healthy Diet for a Healthy Life.

B-134 - Body Composition Indicators Are Positively Associated With Underreporting Of Energy Intake In European Adolescents: Results From The HELENA Study

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Purpose: Misreporting of food intake, including underreporting, is a major concern when addressing diet-disease associations and remains a key limitation of self-reported dietary intake. Although information is still scarce among adolescents, existing literature suggests a positive association between underreporting and body mass index (BMI); however, there is no evidence about the association with body composition indicators. Therefore, we aimed to investigate the association between underreporting and body mass compartments in European adolescents.
Methods: Two self-administered computerized 24-hour dietary recalls were obtained from 1,493 adolescents aged 12.5-17.5 across eight European countries (Austria, Belgium, France, Germany, Greece, Italy, Spain and Sweden). Objective measures of height, weight, waist circumference and tricipital and subscapular skinfold thicknesses were obtained. The percentage of fat mass (%FM) and total FM (kg) and fat free mass (FFM, kg) were calculated by applying skinfold-thickness equations from Slaughter et al. Bioelectrical impedance was used to obtain indices of FM and FFM. Adapted Goldberg cut-offs were applied to identify underreporters using individual objective measures of physical activity. Associations between underreporting and body composition indicators were investigated by multilevel logistic regression analyses after adjustment for confounders.
Results: The risk of underreporting significantly increased with predicted %FM (OR=1.07, 95%CI=1.03-1.11) and with predicted total FM (kg) (OR=1.13, 95%CI=1.08-1.18) and FFM (kg) (OR=1.12, 95%CI=1.08-1.18). Identical results were observed for FM (kg) and FFM (kg) measured with bioelectrical impedance. Waist circumference was positively associated with underreporting (OR=1.12, 95%CI=1.07-1.17).
Conclusions: Underreporting seems to be influenced by adolescents' abdominal fat and total body mass, regardless of the compartment evaluated, i.e. FM or FFM. However, adolescents reporting low energy intake may reflect attempts to lose weight corresponding to real undereating rather than underreporting. Identification of factors influencing underreporting in young populations is crucial to interpret potentially biased findings.
Funding sources: European Community Sixth RTD Framework Programme (FOODCT-2005-007034).

C-135 - Oxidative Burden Of Fine Particulate Air Pollution And Risk Of Cause-Specific Mortality In The Canadian Census Health And Environment Cohort (CanCHEC)

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Purpose: Fine particulate air pollution (PM2.5) is known to contribute to cardiorespiratory mortality but it is not clear how PM2.5 oxidative burden (i.e. the ability of particulate air pollution to cause oxidative stress) may influence long-term mortality risk.

Methods: We examined the relationship between PM2.5 oxidative burden and cause-specific mortality in Ontario, Canada. Integrated PM2.5 samples were collected from 30 provincial monitoring sites between 2012-2013 and oxidative potential (% depletion/µg) was measured as the ability of filter extracts to deplete antioxidants (glutathione and ascorbate) in a synthetic respiratory tract lining fluid. PM2.5-oxidative burden measurements were assigned to cohort members by multiplying PM2.5 exposures by regional estimates of oxidative potential. In total, this study included 193,300 people who completed the Canadian long-form census in 1991 and who lived within 5 km of a site where oxidative potential was measured. Deaths occurring between 1991 and 2009 were identified through record linkages and Cox proportional hazard models were used to estimate hazard ratios (and 95% confidence intervals) for interquartile changes in exposure adjusted for individual-level covariates.

Results: Glutathione-related oxidative burden was associated with cause-specific mortality. For lung cancer specifically, this metric was associated with a 12% (95% CI: 5.0-19) increased risk of mortality whereas a 5.0% (95% CI: 0.1, 10) increase was observed for PM2.5. Indirect adjustment for smoking and obesity decreased the lung cancer hazard ratio for glutathione-related oxidative burden but it remained significantly elevated (HR=1.073, 95% CI: 1.005, 1.146). Ascorbate-related oxidative burden was not associated with mortality.

Conclusions: Our findings suggest that glutathione-related oxidative burden may be more strongly associated with lung cancer mortality than PM2.5 mass concentrations.

C-136 - Association Between Oral Leukoplakia And Risk Of Upper Gastrointestinal Cancers Deaths: Follow-Up Study In The Linxian General Population Trial

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Purpose
Oral leukoplakia is a precancerous disorder which is common among residents in Linxian. Few studies have investigated the association between oral leukoplakia and risk of upper gastrointestinal cancers deaths. In this study, we further investigated the association between oral leukoplakia and upper gastrointestinal cancers deaths in the Linxian General Population Trial Cohort.

Methods
A prospective cohort study was performed in the Linxian General Population Trial. Participants with oral leukoplakia were treated as an exposed group, the others were selected as a control group. All subjects were followed monthly. Hazards ratios (HRs) and 95% confidence interval (*CIs*) were evaluated using proportional hazards models and proportional subdistribution hazard models, respectively.

Results
Through May 31, 2012, there were 29 476 subjects of follow-up over a median of 27 years of observation. A total of 17 473 deaths were identified, including 2 345 esophageal squamous cell carcinoma (ESCC) deaths, 1 139 gastric cardia carcinoma (GCC) deaths, and 506 gastric non-cardia carcinoma (GNCC) deaths. Significant increased risk in ESCC mortality among exposed group versus control group was observed (9.66% vs. 7.39%). Furthermore, subjects with oral leukoplakia had a 22% higher risk of ESCC (HR: 1.22, 95%CI: 1.10 – 1.34) after adjusted covariates, especially among subjects ≤ 52 years of age at the baseline (HR: 1.32, 95%*CI*: 1.13 – 1.54). No significant associations were observed for GCC and GNCC deaths.

Conclusions
Oral leukoplakia can increase risk of ESCC death, especially in younger population. These association appear biologically plausible, and the mechanism should be investigated in further studies.

Finding source
This work was supported by National Cancer Institute contacts [N01-SC-91030 and N01-RC-47701 to the Cancer Institute, Chinese Academy of Medical Sciences]; the international Research Program of the Division of Cancer Epidemiology and Genetics, National Cancer Institutes of Health; the Cancer Institute, Chinese Academy of Medical Sciences.

C-137 - Clinicopathologic Aspects, Socioeconomic Status, Life Style And Dietary Factors Associated With Specific Mutations In Colorectal Cancer In Northwest Of Iran

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Purposes
Although there are some known factors that can have an etiological role in colorectal cancer (CRC), however few studies have addressed how and to what extent these factors affect the genetics and the disease processes. This study aimed to investigate any relationships between clinicopathologic, lifestyle, dietary, and socioeconomic factors and the risks of specific mutations in CRCs.

Methods
Patients with definitive diagnosis of colorectal cancer (n=100) were included. To perform molecular tests, fresh tissue samples from the colon and rectal areas of subjects were obtained by biopsy during colonoscopy. The presence and type of the mutations for KRAS (exon 2) and BRAF (exon 15) were determined by Sanger sequencing method. Logistic regressions were performed for computing un-adjusted and adjusted Odds Ratios (OR) with a 95% Confidence Interval (CI).

Results
Men had 1.37 times higher likelihood of KRAS mutation, and rectal tumors had 1.53 times higher odds of mutation. Metastatic CRCs showed 2.95 times higher likelihood of KRAS mutations and patients with a positive family history of cancer had 4.42 times higher likelihood of mutation. High socioeconomic status had significantly associated with higher likelihood of KRAS gene mutation. Findings suggest significant association of alcohol consumption and carbohydrate intake with higher likelihood of mutation. Patients with less working times and more common sedentary life style were more likely to have mutant KRAS gene. Association with BRAF mutations was not feasible due to absence of BRAF mutations in the samples.

Conclusion
Improving control and prevention of the risk factors, which affect the incidence of mutations associated with genetic and environmental variables, can help in enhancing the prognosis of colorectal cancer (CRC) in affected patients and in designing family-based prevention programs.

Funding sources
Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Key Words
Colorectal Cancer; KRAS; BRAF; Mutation; Regression

C-138 - Long Term-Exposure To Fine Particulate Matter Air Pollution And The Incidence Of Breast Cancer: Findings From The Canadian National Breast Screening Study

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Long-term exposure to fine-particulate matter air pollution (PM2.5) is classified as a human carcinogen based largely on findings from epidemiological studies of lung cancer. A few studies suggest that exposure to air pollution may increase the risk of breast cancer, but to our knowledge, only one of these has been longitudinal and it was limited to a 6 year follow-up interval and did not specifically examine PM2.5. Our aim was to characterize associations between residential exposure to PM2.5 and the incidence of breast cancer in a prospective cohort of 89,248 women who first enrolled in the Canadian National Breast Screening Study between 1980 and 1985. Incident cases of cancer were determined through probabilistic record linkage to national registry data through the end of 2005. Individual-level estimates of long-term exposure to PM2.5 were derived from satellite observations. In total, 6,549 incident cases of breast cancer were identified during the two decade long follow-up interval. The hazard ratios (HR) and their 95% confidence intervals (CI), computed from these models were adjusted for several individual risk factors, including reproductive history, as well as neighborhood-level characteristics. Stratified analyses were undertaken to determine whether the associations differed by menopausal status. The average residential concentration of PM2.5 was 9.50 µg/m3 (standard deviation=3.44). In fully adjusted models, a 10-µg/m3 increase in PM2.5 exposure was positively associated with an elevated risk of incident premenopausal breast cancer (HR, 1.34; 95% CI, 1.05 – 1.71), but not those diagnosed in postmenopausal women (HR=0.99, 95% CI=0.91-1.07). The findings from this study provide additional support for the hypothesis that exposure to very low-levels of ambient PM2.5 increase the risk of breast cancer in premenopausal women.

C-139 - Piping Hot Milky Tea In The Tanzanian Oesophageal Cancer Hotspot: A Cross-Sectional Study

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OBJECTIVE. Esophageal cancer is a devastating disease with poor prognosis. In East Africa, it ranks amongst the top 4 most common cancers and its histology is mainly oesophageal squamous cell cancer (ESCC). Causal factors in this area are not well identified. As hot beverage drinking has been strongly linked with ESCC in the high risk area of Iran, we measured population-level hot beverage drinking habits in the oesophageal cancer hotspot of North Tanzania.
METHODS. We conducted a cross-sectional study of established and putative ESCC risk factors in 188 participants from the general-population in Kilimanjaro, North Tanzania. Temperature of and time taken to drink tea were measured. A questionnaire on regular tea habits was also administered. We examined these measurements in relation to external international means and to tea type ("milky tea"= up to 50% milk and water boiled together; "black tea"=no milk at all) and socio-demographic factors.
RESULTS. In tea preparation, 62% of participants added milk before boiling. Participants started drinking tea at a mean of 70.6°C (standard deviation 3.9), which was higher than in all previous studies worldwide ($p \leq 0.01$), in particular it was much higher than in Golestan, Iran. The strongest determinant of tea drinking temperature was the type of tea. Milky tea (milk and water boiled together) was drunk 3.2°C (95% confidence interval: 2.1, 4.3) hotter than black tea. Men drank their tea hotter and faster than women. The prevalence of reported tongue burning was high and agreed with measured tea temperatures.
CONCLUSION. Repeated thermal injury to the esophageal mucosa may be implicated in carcinogenesis, by damagining the mucosa repair mechanism. Akin to the deeper dermatological scald burns caused by hot milk than by hot water, piping hot milky tea drinking may be a significant risk factor for EC in this area.

C-140 - Hepatitis C Virus And Cancer: A Summary Review Of Epidemiologic And Meta-Analytical Studies And Portfolio Analyses Of Funded Grants

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Background: The global burden of infection with Hepatitis C virus (HCV) is substantial (~130-150 million people experiencing chronic HCV infection). HCV infection is one of the leading causes of liver cancer (2nd cause of cancer-related deaths worldwide), and emerging evidence suggests an etiologic role in the development of other cancer sites. To obtain a global view of the research landscape and the state of the science on the epidemiology of HCV and cancer risk, we assessed the robustness of the evidence using meta-analyses (2006-2014), summarized emerging evidence (2010-2015), and analyzed current funding from the U.S. National Cancer Institute (NCI).

Methods: We identified relevant publications (original articles and meta-analyses) and funded grants using PubMed and the National Institutes of Health's Information for Management, Planning, Analysis, and Coordination database, respectively. For meta-analyses, we assessed qualitatively the strength of evidence based on a priori criteria and calculated the population attributable fraction (PAF) of individual cancer caused by HCV.

Results: The meta-analytic evidence for HCV infection is 'strong' for hepatocellular cancer (HCC), 'moderate' for pancreatic cancer, and 'low' for cholangiocarcinoma; the associated PAF's are 20-23%, 1%, and 5-6%, respectively. For HCC, there is evidence of additive effect modification with hepatitis B virus (HBV), and genotype 1b appears to be the HCV mutation reportedly associated with risk. Evidence suggests an interplay between HCV infection and co-morbid conditions (e.g., diabetes/obesity), associations with non-liver cancers (e.g., non-Hodgkin lymphoma and renal), and racial/ethnic differences. The current NCI's funding portfolio for the epidemiology of HCV-associated cancers is sparse with no HCV-focused grants.

Conclusions: There is robust evidence linking HCV infection with HCC, with the strongest risks associated with HCV genotype 1b and co-infection with HBV. Summary of literature review, coupled with a dearth of funding on HCV-focused grants, suggests that the etiology of HCV in cancer warrants further investigation.

C-141 - Acid Suppressing Therapies And Subsite-Specific Risk Of Stomach Cancer

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Purpose: Acid suppressive drugs are top prescribed medications worldwide. Previous studies have addressed associations of the two major classes, histamine type-2 receptor antagonists (H_2RA) and proton-pump inhibitors (PPI), with risk of overall stomach cancer, with conflicting results. The main effects of these exposures are difficult to ascertain due to marked confounding by indication. As an alternative approach, this study investigated associations in the first decade of use of these drugs with incidence of stomach cancer by anatomic sub-site. We hypothesized that proximal extension of *Helicobacter pylori* infection resulting from acid suppression would disproportionately increase cancer risk at proximal non-cardia sub-sites.
Methods: 1.1 million individuals from the Danish Prescription Drug Registry exposed to any acid suppressing drugs between 1995 and 2011 (median 11.4 vs. 4.5 years for H_2RAs and PPIs, respectively), matched by age, sex and municipality with up to 10 unexposed control persons using the Danish Civil Registration System. We used Cox proportional hazards modelling to calculate stomach cancer Hazard Ratios (HRs) and 95% confidence interval (CI).
Results: Sub-site-specific HRs for any exposure to H_2RAs and PPIs were 3.7 (95% CI: 2.85-4.86) and 4.17 (95% CI: 3.50-4.98) for fundus/corpus as compared to 6.78 (95% CI: 5.23-8.80) and 6.26 (95% CI: 5.14-7.64) for antrum/pylorus, respectively. Restricted to individuals who filled five or more prescriptions, corresponding HRs were 4.06 (95% CI: 2.28-7.22) and 6.36 (95% CI: 4.93-8.20) for fundus/corpus vs. 8.01 (95% CI: 4.94-13.0) and 10.3 (95% CI: 7.68-13.7) for antrum/pylorus.
Conclusion: Moderate duration exposure to acid-suppressive drugs did not favour proximal localization of stomach cancer. These findings do not resolve a potential contribution to gastric carcinogenesis overall.
Funding source: The Intramural Research Program of the National Cancer Institute, National Institutes of Health, USA and the OAK foundation, supported this work.

C-142 - Dietary Protein Restriction Of Pregnant Mouse And Susceptibility To The Development Of Chemically-Induced Esophageal And Liver Cancer

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Purpose: The developmental origins of health and disease (DOHaD) hypothesis suggests an association between mammalian prenatal environmental exposure, including maternal diet, and subsequent risk of developing non communicable chronic disease, such as metabolic syndrome and obesity in adulthood. However, the relation between this hypothesis and cancer is still sparse in the literature. Thus, the aim of this study is to investigate the effect of low protein maternal diet on the susceptibility of developing chemically-induced esophageal and liver cancer in mouse offspring. **Methods**: Dams were fed a control protein diet (CPD - 17% protein) or a restricted protein diet (RPD - 8% protein) throughout pregnancy. All pups received standard diet after weaning. Both offsprings, from CPD and RPD dams, were divided in groups that received the carcinogen N-nitrosodiethylamine (NDEA, 40 ppm) in the drinking water or pure water. After different periods of time, the animals were euthanized and the esophagus and liver were collected for histopathological analyses by hematoxilin-eosin examination. **Results**: Esophagus and livers from all animals that didn't receive the carcinogen presented normal morphology. Animals treated with NDEA for 2 months showed a mild inflammation in the esophagus, independently of maternal diet or gender. In the liver, tubule-glandular lesions were observed in all females, while only 20% of the males showed a similar profile. After 4 months of treatment, 40% of the males presented tumors in the esophagus, independently of the maternal diet, and 20% of the females only from RPD dams showed similar lesions. On the other hand, livers from all animals showed atypical morphological alterations. **Conclusions**: Low protein diet during pregnancy doesn't seem to affect the susceptibility of developing esophageal and liver tumors induced by NDEA in the adult offspring. **Funding source**: Ministério da Saúde, FAPERJ and CNPq.

C-143 - Formaldehyde Concentration Contained In The Paints For Auto-Vehicle

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This study was conducted to evaluate the formaldehyde concentrations in paints for auto-vehicle. A total of 21 paints for auto-vehicle, including nine oil-based paints and 12 water-based paints, were collected from 2 manufacturers in South Korea. Oil-based paints and water-based paints were diluted with toluene and de-ionized water, respectively. The DNPH derivative in the 2, 4-DNPH cartridge adsorbed diluted solution of paint was analyzed using high performance liquid chromatography. Airborne concentrations from paints were measured in two conditions of temperatures, 20 ℃ and 50 ℃, similar to painting booth and exit of dry oven in auto-vehicle manufacturing company. Emission ratio (ER) was calculated as a ratio between the airborne mass (mg) of formaldehyde and the mass (g) of paint used in experiment. A total number of 12 paints (an oil-based paint, 11 water-based paints) among 21 paints contained formaldehyde from 0.3% (wt/wt) to 1.25%. However, no paints provided the information of formaldehyde as an ingredient in material safety data sheet (MSDS). One oil-based paint with 0.3% of formaldehyde contained melamine-formaldehyde resin. The average formaldehyde contents of 0.74% in water-based paints showed significantly higher than 0.3% of oil-based paint ($p<0.05$). Airborne concentrations of formaldehyde ranged from 0.22 ppm to 6.72 ppm. For experiment condition, the average formaldehyde concentration, 2.76 ppm, measured in 50 ℃ showed significantly higher than 0.43 ppm of 20 ℃ ($p<0.05$). ER of formaldehyde ranged from 0.04 mg/g to 1.07 mg/g and the average value of 0.53 mg/g in 20 ℃ showed significantly higher than 0.093 mg/g of 50 ℃ ($p<0.05$). Based on the results of this study, we confirmed that paints for auto-vehicle contained formaldehyde over 0.1%, the listing criteria for carcinogen on the MSDS. In particular, the painters using water-based paints for auto-vehicle could be potentially exposed to formaldehyde at the painting booth.

C-144 - The Environmental And Lifestyle Exposure Assessment (ELEA) Tool For Cancer Epidemiology Research In Low Resource Settings

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PURPOSE: From 2008 to 2030 cancer incidence is predicted to increase by 61% globally but the importance of modifiable risk factors remains undescribed in much of the world's population. Reducing modifiable risk factors could lower cancer incidence by 30-50%. However, their prevalence is largely theorised in low resource settings due to the absence of data. We aim to develop an easy-to-use and systematic process for collecting information on the prevalence of key cancer risk factors, the Environmental and Lifestyle Exposure Assessment (ELEA) project which includes a brief standardised questionnaire (ELEA tool) and protocols for its use (ELEA protocols).

METHODS: A review has been conducted to identify the key risk factors in low resource settings. The tool is being developed by searching existing literature for risk factors measurements that are potentially modifiable or important confounders, are most likely to have the greatest impact on the cancer burden, and have valid and reliable survey items tested in different populations with high response rates. In parallel, the protocols are being devised.

RESULTS: The ELEA tool is being developed using a combination of existing survey measurements items for review by content experts, which will use the Delphi method to reach a consensus. The ELEA protocols cover interviewer selection, interviewer training, participant recruitment, questionnaire administration and data analysis.

CONCLUSIONS: Current tools for cancer epidemiology lack universal applicability. By developing a concise, standard data collection tool, and taking advantage of web based flexible technology, ELEA will develop a strong collaborative research platform for comparative measurement of cancer risk factors, and by doing so, increase research capacity and address a gap in knowledge where it is implemented.

FUNDING SOURCE: EF's work is being undertaken during the tenure of an IARC-Australia Postdoctoral Fellowship from the International Agency for Research on Cancer, supported by Cancer Council Australia (CCA).

C-145 - Age-Profiles Of Mammographic Density In Women From 22 Diverse Countries: Insights Into A Tissue-Specific Marker Of Breast Cancer Risk From The International Consortium On Mammographic Density

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Purpose: Mammographic density (MD) is radio-opaque (white) breast tissue on a mammogram and is a strong breast cancer risk factor. MD varies over time within women and this age-profile may be related to Pike's model of the breast tissue aging rate, with breast cancer risk being a function of accumulated breast tissue age. MD age-profiles have been studied in high breast cancer risk countries where westernized lifestyles prevail. In the International Consortium on Mammographic Density (ICMD), we investigated how MD is associated with age and menopausal transition across 22 countries, spanning the breast cancer incidence spectrum.
Methods: ICMD contains individual-level risk factor and MD data (read centrally using Cumulus) on 11755 breast cancer-free women in 40 ethnicity and location-specific population groups. Linear regression was used to estimate square-root percent MD (PMD) and absolute dense area (DA) in relation to age and menopausal status at mammography, adjusted for BMI, image type and population group.
Results: Mean (SD) age at mammography across ICMD was 52.5 years (8.2). 4890 pre and 6865 post-menopausal women were included. Overall, DA and PMD was lower in older women, with a difference in square-root DA per 10 years of -0.24 cm (95% confidence interval: -0.39,-0.08) at premenopausal ages, which was slightly larger at postmenopausal ages (-0.35 (-0.42,-0.27)). This association was present across all population groups and was more consistent for DA (between population group heterogeneity I^2=6.2%) than for PMD (I^2=41.5%). The difference in square-root DA between post and pre-menopausal women of the same age was pronounced (-0.52 (-0.63,-0.41): the equivalent of a drop from 16 cm^2 to 11.5 cm^2.
Conclusions: Lower PMD and DA with increasing age and particularly after menopausal transition were highly consistent and present across diverse countries, based on these cross-sectional data. They are likely to result from intrinsic biologically-driven changes.
Funding Source: NIH-R03CA167771

C-146 - An Evaluation Of Potentially Carcinogenic Pesticides And The Risks Of Non-Hodgkin Lymphoma (NHL) And Its Histological Sub-Types: An Analysis Of The North American Pooled Project (NAPP)

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Purpose: The International Agency for Research on Cancer (IARC) has classified numerous pesticides as possibly or probably carcinogenic. The purpose of this work was to investigate associations between carcinogenic pesticide use and the risks of NHL sub-types in the North American Pooled Project (NAPP).

Methods: The NAPP included 1690 NHL cases and 5131 controls from six Canadian provinces, and four Midwestern U.S. states. Pesticides were assigned a carcinogenic probability score (ranging from 0.1-1.0) based on a synthesis of assessments by IARC and the US Environmental Protection Agency. Nineteen pesticides were classified as “probably” carcinogenic (score ≥0.6) and 35 were “possibly” (score ≥0.5) carcinogenic. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression for NHL overall, and for follicular lymphoma (FL), diffuse large B-cell lymphoma (DLBCL), small lymphocytic lymphoma (SLL), and other.

Results: Compared to unexposed subjects, use of ≥5 pesticides (carcinogenic probability ≥0.5) was associated with significantly higher risks of NHL (OR=1.71, 95%CI:1.37-2.12; p-trend<0.0001). Similar positive trends in risk were observed for the use of ≥5 insecticides (carcinogenic probability ≥0.5) for NHL (OR=1.80, 95% CI:1.26-2.55), FL (OR=1.98, 95%CI:1.19-3.30), SLL (OR=2.34, 95% CI:1.10-5.00) and other (OR=1.41, 95% CI:0.69-2.88). Exposure to probably carcinogenic fungicides was associated with NHL overall (OR=1.90, 95%CI:1.22-2.95), DLBCL (OR=2.30, 95%CI:1.26-4.20), and other sub-types (OR=2.81, 95%CI:1.39-5.68). Dose-response relationships were attenuated for the herbicides, however use of 1 herbicide (carcinogenic probability ≥0.6) was associated with significantly higher odds of NHL (OR=1.28, 95%CI:1.02-1.60) and DLBCL (OR=1.51, 95% CI:1.11-2.07).

Conclusions: The risk of NHL and its subtypes increased significantly with the use of a greater number of potentially carcinogenic insecticides, fungicides and herbicides. The exposure response trends were quite striking and support of the hazard assessments of these agencies.

Funding source: Canadian Cancer Society Research Institute (#703055); U.S. National Institutes of Health Intramural Research Program, National Cancer Institute.

C-147 - Determination Of A Geographic Information System Based Indicator To Assess Environmental Dioxins Exposure In Lyon And Through Comparisons With An Atmospheric Dispersion Model Results

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Purpose
To investigate the association between environmental dioxin exposure and breast cancer in the French national E3N prospective cohort using a Geographic Information System (GIS), the purpose of the present study was to evaluate the accuracy of a GIS based exposure indicator (GISBEI) of the classification of participants historical dioxin exposure levels, through a comparison with dioxin concentrations computed by an atmospheric dispersion model.

Methods
Industrials sources, the main contributors for dioxin exposure over the study period (CITEPA, 2015), were selected and characterized using the Standardized Toolkit for Identification and Quantification of Dioxin and Furan Releases of the United Nation Environment Program. Atmospheric dioxin dispersion was modeled with SIRANE, an urban Gaussian model, for four years: 1996, 2002, 2007 and 2008. The SIRANE model performances were compared to weekly average dioxin concentrations measured within the Lyon urban area in 2007 and 2008.
Through a sensitivity analysis of the SIRANE results, we identified the meteorological and source parameters mostly affecting dioxin concentrations at the residences of the 300 study subjects. We further compared the correlation (Cohen's kappa coefficients) of study subjects estimated dioxin exposure levels (classified in quintiles) between the 2 methods, the SIRANE model and the GISBEI, for each year, and before and after integration of identified meteorological and source parameters into the GISBEI.

Results
Kappa coefficients for study subjects estimated dioxin exposure levels (classified in quintiles) were all below 0.55 for a GISBEI based solely on proximity and ranged from 0.71 to 0.82 after inclusion into the GISBEI of the meteorological and source parameters identified.

Conclusions
This study shows the advantages provided by the use of an atmospheric dispersion model in building and evaluating a GIS based indicator for historical environmental dioxin exposure assessment (1990-2008).

Funding sources:
Geo3N : ADEME, CLARA, UCBL
E3N : MGEN, LNCC, IGR, Inserm

C-148 - Pesticide Exposures And The Risk Of Multiple Myeloma In Men: An Analysis Of The North American Pooled Project (NAPP)

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Purpose: Multiple myeloma (MM) has been linked to agricultural activities, including pesticide exposures. Three case-control studies of haematological cancers were harmonized to form the North American Pooled Project (NAPP). The objective of this work was to evaluate associations between pesticide use and MM risk.

Methods: The NAPP included 547 cases and 2700 controls. Pesticide use was evaluated using different exposure metrics: ever/never; duration of use (years); and cumulative lifetime days (LD) (days/year × years of use). Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression adjusting for age, residence, use of proxy respondents, and medical conditions.

Results: Increased MM risk was observed for use of carbaryl (OR=2.02, 95% CI=1.28-3.21), captan (OR=1.98, 95% CI=1.04-3.77), and DDT (OR=1.44, 95% CI=1.05-1.97). Using the Canadian subset of data, we observed a more than 3-fold increase in MM risk (OR=3.18, 95% CI=1.40-7.23) for ≤10 LD of carbaryl use. The association was attenuated for >10 LD of carbaryl use (OR=2.44; 95% CI=1.05-5.64; ptrend=0.01). For captan, ≤17.5 LD of exposure was associated with a more than 3-fold increase in risk (OR=3.52, 95% CI=1.32-9.34), but this association was attenuated in the highest category of >17.5 LD (OR=2.29, 95% CI=0.81-6.43; ptrend=0.01). An increasing trend (ptrend=0.04) was observed for LD of DDT use (LD>22; OR=1.92, 95% CI=0.95-3.88).

Conclusions: We observed significant increases in MM risk for use of carbaryl, captan and DDT. IARC has classified DDT as probably carcinogenic to humans, and carbaryl was classified as likely carcinogenic in humans by the US EPA. IARC revised the classification of captan from a 'probable human carcinogen' to 'not likely carcinogenic' in 2004. This work will inform future hazard re-assessments by these agencies.

Funding: Canadian Cancer Society Research Institute Grant # 703055 and the U.S. National Institutes of Health Intramural Research Program of the National Cancer Institute.

C-149 - Effects Of Radon And UV Exposure On Skin Cancer Mortality ñ A Swiss National Cohort Analysis

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Purpose: Skin cancer incidence in Switzerland is among the highest in the world. In addition to exposure to ultraviolet (UV) radiation, radon alpha particles attached to aerosols can adhere to the skin and potentially cause carcinogenic effects. Exposure gradients in Switzerland are considerable due to large differences in geology and soil type (radon) and altitude (UV). We investigate the mutual effects of radon and UV exposure on skin cancer mortality.
Methods: Cox proportional hazard regression with age as the time axis was used to study the association between exposures and skin cancer mortality (IDC10: C43-44) in all Swiss adults aged >20 for the period 04 Dec 2000 to 31 Dec 2008 using the Swiss National Cohort. Exposures during the study period were modelled at address-level. Radon derived from our prediction model, validated with measurements from the Swiss Radon Database. Long-term erythemal weighted UV dose was modelled using daily maximum UV index measurements, monthly global radiation, and a digital terrain model. Cox models were adjusted for sex, civil status, language, education, job position, neighbourhood socio-economic position and UV exposure from outdoor occupation.
Results: The study included 4.3 million adults (mean age 48 years) and ~2300 skin cancer deaths (definitive primary cause). Radon and long-term UV exposure were not correlated (r =-0.01). We found the baseline hazard for radon decreased with age. Adjusting for the alternative exposure, hazard ratios ranged from 1.67 (95% CI: 1.17-2.38; at 20 years) to 1.16 (1.06-1.28; at 80 years) per 100 Bq/m3 radon and 1.09 (1.01-1.18; all ages) per 1 W/m2 in UV dose.
Conclusions: Our study suggests both UV and radon are relevant risk factors. A better understanding of the role of radon exposure in relation to skin cancer risk is of high public health relevance.
Funding source: Swiss National Science Foundation

C-150 - An Investigation Of Organochlorine Insecticide Use And The Risks Of Non-Hodgkin Lymphoma: Findings From The North American Pooled Project

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Purpose: Organochlorine insecticides are persistent, bio-accumulative compounds that are frequently used worldwide. Recently, the International Agency for Research on Cancer (IARC) classified several organochlorines as Group 1 and Group 2A carcinogens for non-Hodgkin lymphoma (NHL). However, some studies were limited by low statistical power and did not assess exposure-response relationships. In this analysis, we investigated self-reported organochlorine exposure with respect to NHL risk in a large population-based study: the North American Pooled Project (NAPP).

Methods: Four case-control studies conducted in Canada (1991-1994) and Midwestern U.S. (1981-1986) were pooled to form the NAPP, which includes 1690 NHL cases and 5131 controls. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for organochlorine use (ever/never exposed) and duration of use (years), with adjustment for demographic characteristics and NHL risk factors.

Results: Compared to unexposed subjects, statistically significant associations with NHL risk were observed among those reporting use of chlordane (OR=1.44, 95% CI=1.13-1.84), DDT (OR=1.32, 95% CI=1.10-1.58), dieldrin (OR=1.52, 95% CI=1.04-2.22), heptachlor (OR=1.47, 95% CI=1.02-2.11) and lindane (OR=1.69, 95% CI=1.31-2.17). A consistent exposure-response trend was observed for years of lindane use: OR>0 to 5=1.36, OR5 to >10=1.87, OR10 to >15=1.93, OR>15=2.01 (p-trend=<.0001). Increased risk of NHL was observed for >15 years of DDT use (OR=1.52, 95% CI=1.06-2.17, p-trend=0.001) Non-monotonic but positive trends in NHL risk with increasing exposure duration were also observed for chlordane (p-trend=0.03) and heptachlor (p-trend=0.04).

Conclusions: This analysis uncovered several statistically significant associations for organochlorine use and NHL risk. The increased sample size of the NAPP allowed us to estimate risk across more refined exposure levels and identify significant exposure-response trends for lindane. Overall, these findings contribute to the epidemiologic literature supporting the recent IARC classification.

Funding Source: Canadian Cancer Society Research Institute (#703055); U.S. National Institutes of Health Intramural Research Program, National Cancer Institute

C-151 - Pesticide Use And Risk Of Hodgkin Lymphoma: Results From The North American Pooled Project (NAPP)

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Purpose: The prevalence of haematological cancers is elevated in agricultural populations. It has been hypothesized that exposure to pesticides contributes to this risk. The purpose of this study was to investigate pesticide exposures and risk of Hodgkin lymphoma (HL) using pooled data from the North American Pooled Project (NAPP).

Methods: This analysis included 507 HL cases and 1563 controls from three population-based studies conducted in Midwestern USA (1981-86) and six provinces across Canada (1991-94). Odds ratios and 95% confidence intervals were estimated for self-reported pesticide use (never/ever) and duration of use (years) using logistic regression adjusted for age, sex, place of residence and respondent status.

Results: An increased risk of HL was observed for use of five or more insecticides (OR: 1.88, 95%CI: 1.08-3.27) relative to unexposed. Use of two or more carbamate insecticides (OR=2.45, 95%CI=1.03-5.84) was associated with more than double the risk of HL. An analysis of individual pesticides showed significant increasing trends of HL with duration of use of terbufos (>4.5 years, OR=3.34, 95%CI=1.27-8.78, p-trend=0.04) and lindane (>4.5 years, OR=2.08, 95%CI=0.95-4.56, p-trend=0.01). Ever use of carbaryl (OR=2.15, 95%CI=1.13-4.07) was associated with an increased risk relative to unexposed and a borderline significant increasing trend for HL was observed for duration of carbaryl use (p-trend=0.06). Several other insecticides were considered in the individual analysis but an exposure-response relationship with duration of use was not found. There does not appear to be an increased risk of HL with use of fungicides and herbicides evaluated.

Conclusions: Insecticide use, specifically use of terbufos, lindane, and carbaryl may increase the risk of Hodgkin lymphoma.

Funding: Canadian Cancer Society Research Institute Grant # 703055 and the U.S. National Institutes of Health Intramural Research Program of the National Cancer Institute.

C-152 - Exposure Assessment Of The Diesel Engine Exhaust Of Workers To Request Occupational Lung Cancer Approved

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This study was conducted to evaluate the occupational exposure of diesel engine exhaust(DE) of workers to request occupational lung cancer approved. DE exposure assessment was undertaken with regard to six cases that were asked to investigate for work related lung cancer to KCOMWEL from January 2013 up to January 2015. The jobs of 6 cases mentioned above were as follows; the unloading of fertilizer, garbage collection, indirect exposure to forklift emissions, fertilizer warehouse management, container transportation at port, and truck and bus driver. The respirable elemental carbon (REC) was used as surrogate exposure metric of DE. The REC was sampled on precleaned quartzfiber filter and then analyzed by thermo-optical carbon analyzer. Among 6 jobs, the fertilizer unloading job using an excavator had the highest REC concentration(52.0$\mu g/m^3$) of long-term personal sample. The personal exposure concentration of fertilizer warehouse management job was 20.8$\mu g/m^3$ and indirect exposure of forklift emissions in the tire industry were 14.7$\mu g/m^3$. The personal exposure concentration of the other tasks except above 3 jobs were below 10 $\mu g/m^3$. Based on this study, 6 cases were approved by occupational disease in Korea. The personal exposure data of 6 jobs in this study may not represent job exposure metrics of jobs because of a few sample sizes. It, however, has significant meaning that there was few such kind of the occupational exposure data in Korea until 2012 when DE was classified a human carcinogen by the IARC. The occupational exposure levels of REC can be affected by many factors such as tasks and working methods; the size and ventilation condition of the work space; the year, engine capacity, and emission regulation of vehicles, therefore, there is a need for accumulation of exposure evaluation data in many jobs and tasks to estimate the past exposure level and to evaluate work related lung cancer.

C-153 - Risk Of Endometrial Cancer In Patients With Antipsychotic Agents ñ A Nationwide Study In Taiwan

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Increasing evidence indicates the potential genotoxic or carcinogenic effects of antipsychotics which increase carcinogenesis or promote tumor progression. The risk of developing cancer must be considered by psychiatrists in their prescriptions. However, the association between antipsychotic agents-treated patients and risk of endometrial cancer is unclear. The aim of the study is to assess the risk of endometrial cancer after antipsychotic agents treatment. A case control study by analyzing data from the National Health Insurance Research Database (NHIRD) in Taiwan was designed to understand the relationship between antipsychotic agents and endometrial cancer. Insurance claims data for 6516 endometrial cancer patients were randomly selected from all insured women in the NHIRD. After the risk factors of endometrial cancer such as hypertension, hyperlipidemia, diabetes malleus, and polycystic ovaries were adjusted, there was a statistically significant increased risk of endometrial cancer in chronic haloperidol users compared to other antipsychotic-agents users. However, the chronic sulpiride user had a statistically significant decrease risk of endometrial cancer. Besides, the risk of endometrial cancer was significantly lower in the chronic haloperidol users with the history of progesterone treatment than in the chronic haloperidol users without the history of progesterone treatment. These findings suggest the most common antipsychotic agent, haloperidol, is associated with the increased risk of developing endometrial cancer. Haloperidol combined with progesterone treatment may consider as a solution for haloperidol-increased risk of endometrial cancer.

C-154 - Estimated Dietary Dioxin Exposure And Breast Cancer Risk Among Women From The French E3N Prospective Cohort

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Purpose: Dioxins are environmental and persistent pollutants mostly emitted from combustion facilities. Known to be endocrine disrupting chemicals, dioxins are suspected to increase breast cancer (BC) risk. Although diet is considered the primary source of dioxin exposure, no previous study has been published on dietary dioxin exposure in relation to BC risk. We aimed at assessing dietary dioxin exposure among women from the French E3N prospective cohort and estimating BC risk associated with this exposure.

Methods: The study included 63,830 women from the E3N cohort who completed a diet history questionnaire (DHQ) in 1993 and were followed until 2008. Dietary dioxin exposure was estimated by combining consumption data from the E3N DHQ and food dioxin contamination data from a French national monitoring program (CSHPF 2000). Hazard ratios (HR) and 95% confidence intervals (CI) were estimated by Cox models adjusted for BC risk factors.

Results: Mean dietary dioxin exposure was estimated at 1.3 ± 0.4 pg/kg body weight (BW)/day. A 0.4 pg/kg BW/day increase in dioxin intake was not associated with overall BC risk (HR=1.00; 95%CI: 0.96, 1.05). A significant decrease in risk of estrogen receptor negative (ER-)/progesterone receptor negative (PR-) tumors was observed among post-menopausal women in the upper quartile of estimated dioxin intake (HR for Q4 *vs.* Q1: 0.65; 95%CI: 0.45, 0.96; *P* for trend across quartiles=0.0463).

Conclusions: Overall, no association between estimated dietary dioxin exposure and BC risk was found among E3N women. Further studies should include both dietary and environmental exposures to determine whether low-dose dioxin exposure is associated with BC risk.

Funding sources: Lyon-UCBL, CLARA, ADEME. E3N: MGEN, LNCC, IGR and Inserm.

C-155 - Joint Effect Of Radiation And Nitrate Content In Groundwater ñ Major Factors Affecting Incidence Of Childhood Thyroid Cancer In Belarus After The Chernobyl Accident

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One of the most serious health consequences of the Chernobyl Nuclear Power Plant accident in 1986 was a dramatic increase in the incidence of thyroid cancer among those who were aged less than 18 years at the time of accident.

Among the factors that may increase the incidence of thyroid cancer, the following have been identified: radiation dose, young age at exposure, thyroid screening, iodine deficiency, and genetic predisposition.

Various screening programs conducted in 1990-2008 in Belarus have shown the prevalence of thyroid carcinoma among children of 0.19%-0.62% in different regions. The highest thyroid dose (320 mGy) was in children of Gomel Oblast. The doses in Mogilev and Brest Oblasts were 65 and 51 mGy, respectively. However, the results of ultrasound screening programs suggested that given comparable screening and thyroid radiation doses, the prevalence of pediatric thyroid cancer in Brest Oblast was substantially higher than in Mogilev Oblast (5.5 vs 1.5 per 100,000 PY).

Concentration of nitrate in groundwater in the early 1990's was 112 mg/L in Gomel, 40 mg/L in Mogilev, and 185 mg/L in Brest Oblast exceeding the MCL 2.5- and 4.0-fold in Gomel and Brest, respectively. Groundwater from open wells is the main source of drinking water in rural areas in Belarus. Study of the relationship between childhood thyroid cancer incidence, radiation thyroid dose and nitrate in groundwater in Belarus have shown that radiation dose was significantly associated with thyroid cancer incidence (P=0.029). Effect of radiation significantly varied according to nitrate concentration (P=0.004). (Drozd V et al., 2015).

Analytic epidemiological studies aimed at quantification of the joint effect of nitrate content in groundwater and radiation present a promising approach to understanding the impact and control of environmental factors on the growing incidence of thyroid cancer all over the world.

C-156 - Genitourinary Infections, Sexually Transmitted Infections And Prostate Cancer Risk: The EPICAP Study

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Purpose: Epidemiological studies have suggested that genitourinary infections (GUIs) and sexually transmitted infections (STIs) increase prostate cancer (PCa) risk. Chronic inflammation may explain these associations. We investigated the role of GUIs and STIs in the occurrence of PCa in the EPICAP study.
Methods: EPICAP is a population-based case-control study conducted in the *département* of Hérault, France between 2012 and 2014. All men residents in this *département* aged less than 75 years old who were newly diagnosed with a PCa were eligible to the study. Population controls were frequency-matched by 5-year age group to the cases. A total of 819 incident PCa cases and 879 controls were included. An in-person interview was conducted using a standardized questionnaire to obtain information on recognized or suspected risk factors for prostate cancer, as well as on history of GIUs (prostatitis, urethritis, orchi-epididymitis or acute pyelonephritis) and STIs (Gonorrhea, Trichomoniasis, Syphilis and other STIs). Odds Ratios (ORs) and their 95% Confidence Intervals (CIs) were estimated using multivariate unconditional logistic regression.
Results: Overall, 139 (18%) cases and 98 (12%) controls reported at least one GUI (OR=1.63, 95%CI, 1.22-2.17). The risk of PCa increased with the number of GUIs: OR=1.56, 95%CI, 1.15-2.13 for one and OR=2.47, 95%CI, 1.05-5.82 for two or more. Prostatitis and acute pyelonephritis were significantly associated with PCa (OR=1.53, 95%CI, 1.07-2.17 and OR=2.62, 95%CI, 1.27-5.42, respectively) while urethritis and orchi-epididymitis were not (OR=1.20, 95%CI, 0.65-2.22, OR=1.53, 95%CI, 0.87-2.69, respectively). Seven percent of the cases (n=58) and eight percent of the controls (n=72) reported a history of at least one STI (OR=0.79, 95%CI, 0.54-1.15).
Conclusions: Our results suggested that genitourinary infections, especially prostatitis and acute pyelonephritis, may play a role in the occurrence of PCa. The observed dose-response relationship supports the hypothesis of a role of chronic inflammation in prostate carcinogenesis.
Funding: LNCC, FDF, ANSES

C-157 - Melanocytic Nevi, Ambient UV Exposure And Thyroid Cancer Risk: The French E3N Prospective Cohort

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Purpose: Incidence rates have considerably increased worldwide for both differentiated thyroid cancer (DTC) and cutaneous melanoma, and two-way associations between these neoplasms have been described. Whether melanoma risk factors such as ultraviolet (UV) exposure and pigmentary traits are associated with DTC risk remains unknown.

Methods: Using Cox regression modeling, we prospectively analyzed the relations between self-reported pigmentary traits, childhood and adulthood residential UV exposure, and risk of DTC in 91,082 women from the E3N cohort, who were followed-up over 1990-2008 through biennial questionnaires. We used logistic regression modeling to assess associations of pigmentary traits and UV exposure with personal history of benign thyroid diseases. All statistical tests were two-sided.

Results: In models adjusted for age and DTC risk factors, number of nevi was positively associated with DTC risk (“very many” vs. “none”: Hazards Ratio=1.67, 95% Confidence Interval=1.03–2.73; Ptrend=0.01), independently of residential UV exposure or iodine intake. DTC risk was inversely associated with latitude (Ptrend=0.03) and positively associated with mean daily UV dose (Ptrend=0.02) at baseline, but not at birth, and only in women with dietary iodine below the median intake. Personal histories of dysthyroidism and of goiter/nodules were positively associated with number of nevi (Ptrend=0.0001 for both) and mean daily UV dose at baseline (Ptrend=0.0001 and 0.0003, respectively).

Conclusions: Our results suggest that number of nevi and residential UV exposure are associated with the risks of DTC and benign thyroid conditions. They point to novel pathways in thyroid cancer or melanoma etiologies and warrant replication.

Funding source: This work was supported by the Mutuelle Générale de l’Education Nationale (MGEN); the European Community; the French League against Cancer (LNCC); Gustave Roussy, the French National Institutes for Health and Medical Research (Inserm) and the French National Cancer Institute (InCA) (#2009-139). MK is supported by a Marie Curie Fellowship (#PIOF-GA-2011-302078)

C-158 - Gene Expression Profiling Of Buccal Epithelium Among Nonsmoking Women Exposed To Household Air Pollution From Smoky Coal

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Lung cancer rates in Xuanwei County are among the highest in the world for non-smoking females and have been causally associated with exposure to indoor smoky (bituminous) coal emissions. To understand the molecular effects of smoky coal exposure, we analyzed the global gene-expression profiles in buccal epithelial cells collected from healthy, non-smoking female residents of Xuanwei and Fuyuan who burn either smoky or smokeless coal. We identified a distinct gene expression signature, with enrichment of a number of pro-inflammatory genes, in the oral cells of non-smoking women exposed to smoky vs. smokeless (anthracite) coal. The gene expression signature was correlated with carcinogenic PAHs but not with non-carcinogenic PAHs and PM2.5 measured in personal air samples. In addition, there was substantial overlap between the gene expression signature found among smoky coal users and among tobacco users. Our findings provide biological insights into potential pathways associated with the elevated lung cancer risk observed in those exposed to smoky coal combustion.

C-159 - Elevated Bladder Cancer In Northern New England: The Role Of Drinking Water And Arsenic

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PURPOSE: Bladder cancer incidence and mortality rates have been elevated in northern New England for at least five decades. Our purpose was to identify the reasons for this excess with a focus on arsenic in drinking water from private wells, which are particularly prevalent in the region.
METHODS: In a population-based case-control study in Maine, New Hampshire and Vermont, we interviewed 1,213 bladder cancer cases and 1,418 controls to obtain information on known and suspected risk factors. Arsenic concentrations were estimated by statistical modeling based on measurements in water samples from current and past homes.
RESULTS: Bladder cancer risk increased with increasing water intake(P-trend=0.003). This trend was significant among participants with a history of private well use(P-trend=0.011). Among private well users, the trend with drinking water intake was apparent if well water was derived exclusively from shallow dug wells (which are vulnerable to contamination from manmade sources)(P-trend=0.002), but not if well water was supplied only by deeper drilled wells(P-trend=0.479). If dug wells were used prior to 1960, when arsenical pesticides were widely used in the region, heavier water consumers(>2.2 L/day) had double the risk of light users(<1.1 L/day)(P-trend=0.012). Among all participants, cumulative arsenic exposure from all drinking water sources, lagged 40 years, yielded a positive risk gradient(P-trend=0.004); among the highest exposed participants(97.5th percentile), risk was twice that in the lowest exposure quartile(OR=2.2;95%CI=1.3-3.9).
CONCLUSIONS: Our findings support an association between exposure to low-to-moderate levels of arsenic in drinking water and bladder cancer risk in New England. In addition, historical consumption of water from private wells, particularly from dug wells in an era when arsenical pesticides were widely used, was associated with increased bladder cancer risk and may have contributed to the New England excess.
FUNDING: Intramural Research Program of the US National Cancer Institute, Division of Cancer Epidemiology and Genetics.

C-160 - Environmental Dioxin Exposure Index And Breast Cancer Risk In A Case-Control Study Nested Within The French E3N Prospective Cohort: Considering Time Of Exposure In The Risk Estimate

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Purpose: To investigate breast cancer (BC) risk associated with environmental dioxin exposure, using statistical methods to consider temporal dimensions of exposure in the risk estimate.

Population: We designed a case-control study, nested within the E3N prospective cohort, that involves 98,995 French female volunteers, adherent to a health insurance plan (MGEN) and regularly followed-up since 1990 by self-administered questionnaires. Between 1990 and 2008, we identified 5,455 invasive BC cases that were matched to randomly selected controls on age, department of residence, menopausal status and existence of biological sample. For the present analysis, the study population was restricted to 525 cases and 952 controls living in the Rhône-Alpes region at baseline.

Methods: Assessment of environmental dioxin exposure was based on a detailed inventory of dioxin emitting sources and residential history of study subjects. For each participant, exposure was evaluated using a GIS (geographic information system)-based environmental dioxin exposure index including proximity to and technical characteristics of dioxin emitting sources, exposure duration, and wind direction and speed. First, BC risk associated with the environmental dioxin exposure index will be estimated with conditional logistic regression models. Second, using B-spline functions, we will analyze the relative weight of the exposure dose with respect to time and its association with BC risk. Models will be adjusted for BC risk factors and, when relevant, further adjusted for the number of years living in an urban area from birth to baseline.

Results: *Results will be presented and discussed at the IARC 50th Anniversary Conference.*

Conclusions: Our study may provide new ways of considering temporal dimensions for environmental exposures in disease risk assessment.

Funding sources: Lyon-UCBL, CLARA, ADEME. E3N: MGEN, LNCC, IGR, Inserm.

C-161 - The Canadian Partnership For Tomorrow Project: A Population Cohort For Health Research

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Purpose
In Canada, two in five people will develop cancer in their lifetime. Incidence rates for 'all cancers combined' and some specific cancers vary, with higher rates in the east than the west. Reasons for this geographic disparity are unclear, but may arise because of a complex interplay between modifiable risk factors, genetics and environment. The Canadian Partnership for Tomorrow Project (CPTP) brought together five provincial/regional cohorts to create a federated model with a streamlined infrastructure to support research.

Methods
Over 300,000 adults aged 30-74 provided health information and biological samples, as well as consenting to linkage with administrative databases, long-term follow up and use of their data/samples by 'approved researchers'. An ELSI committee addressed the ethical and legal aspects of access under a federated model, while a data harmonization committee ensured generation of harmonized core variables for CPTP. Comparative analyses were undertaken a priori to ensure that the CPTP approaches were interoperable with key international cohorts.

Results
CPTP participants reported a wide range of socio-demographic characteristics, and prevalence of chronic disease was broadly consistent with the population. Over 700 harmonized variables have been created to date, and biological samples have been obtained from 50% of the cohort. Under a controlled-access approach, the central Access Office supports an independent Access Committee. An interactive online portal allows researchers to browse the CPTP data dictionaries and facilitates electronic submission of access applications and tracking of the access process.

Conclusions
Even under a federated model, the CPTP accelerates research by leveraging existing efforts to create large, high quality datasets and biological sample repositories. CPTP will support research into how modifiable risk factors, genetics and environment interact to impact cancer risk, ultimately contributing to reducing the global burden of cancer.

Funding sources:
Available at: http://www.partnershipfortomorrow.ca/partners/

C-162 - The National Cancer Institute (NCI) Cohort Consortium

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An epidemiologic consortium is a group of scientists from multiple institutions who have agreed to cooperative research efforts involving, but not limited to, pooling of information from multiple population studies for the purpose of combined analyses, and is able to address scientific questions that cannot otherwise be addressed through the effort of investigators at a single institution. The National Cancer Institute (NCI) sees consortia as providing unique opportunities for advancing cancer epidemiology by virtue of the large sample size of study participants and the synergy resulting from the interdisciplinary expertise of the membership. First convened in 2000, the Cohort Consortium (CoCo) is one of the largest research consortia supported by the NCI; comprised of 57 U.S. and international cohorts, totaling over 7 million study participants. The purpose of CoCo is to serve as a research resource providing data and biospecimens to study gene-gene and gene-environment interactions in the etiology of cancer. The major initiatives are: 1) Breast and Prostate Cancer Cohort Consortium (BPC3). 2) Pancreatic Cancer Cohort Consortium. 3) African American BMI Working Group. 4) BMI and All Cause Mortality Pooling Project. 5) Diabetes and Cancer Initiative in the Cohort Consortium. 6) Lung Cancer Cohort Consortium. 7) Tumor Tissue Working Group. 8) Rare Cancers Vitamin D Pooling Project.
Basic demographic information and findings on these studies of the CoCo will be presented and information on how to participate in these initiatives. These important scientific findings would not have been possible without the formation of a large scale research collaboration, like the CoCo. Collaboration in the consortium enables investigators to share data and resources, expand study populations and create opportunities to pursue unique research studies. The CoCo is open to new research proposals and researchers are encouraged to contact the project principal investigators.

C-163 - Cesarean Delivery And Risk Of Infant Leukemia

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Introduction. Recent case-control studies have reported increased risks of pediatric acute lymphoblastic leukemia (ALL) among children born by cesarean delivery (CD). However, an association of CD with childhood leukemia has not been conclusively established and no previous study has examined the impact of CD on risk of infant leukemia specifically.
Methods. 443 infants diagnosed with acute leukemia, including both ALL and acute myeloid leukemia (AML), were identified at Children's Oncology Group (COG) institutions between January 1996 and December 2006. 324 controls frequency matched by year of birth were identified through random digit dialing and random selection from US birth registries. Mothers of cases and controls completed an interview including questions on mode of birth, information on labor and delivery, and birth characteristics. Odds ratios (OR) and 95% confidence intervals (CI) for risk of ALL and AML were estimated using multivariable unconditional logistic regression models, adjusted for year of birth, breastfeeding, birth weight, and maternal race.
Results. We observed a statistically significant association between CD and ALL (OR and 95% CI: 1.64 [1.09, 2.46]). We did not observe an association between CD and AML (OR and 95% CI: 1.20 [0.73, 1.98]).
Conclusions. Our analysis suggests an increased risk of infant leukemia following CD. Cortisol exposure is reduced among infants born by CD, particularly infants born by pre-labor CD, compared to those born vaginally. Cortisol may be beneficial among infants susceptible to ALL due to induction of apoptosis among preleukemic cells. Therefore, reduced cortisol levels in the first days of life among infants born by CD should be considered as a potential mechanism underlying this association. Additional mechanistic studies are needed to confirm causality and further understand the role of cortisol in reducing risk of infant leukemia.

C-164 - Cancer In The Population Near To A Rural-Urban Landfill In Tunja, Boyac·, Colombia

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INTRODUCTION Cancer is the third cause of adult mortality in Colombia and gastric cancer is the first local public health problem for cancer in Boyacá. Kidney cancer is astonishingly high in rural Pirgua population near to a waste urban place. Landfill leachate generated waste and It could be associated with the onset of cancer, maybe for the environmental risk to contaminate water, agriculture land and air. Our study aims to determine the relationship between the environment and digestive and renal cancer in a local place near to Tunja.
GENERAL OBJECTIVE: To evaluate the relationship between chronic exposure to wastes and prevalence of total, digestive and renal cancer in population next to the Pirgua´s landfill.
SPECIFIC OBJECTIVES:
1. Identify cancer prevalence in residents near the landfill.
2. Describe the atmosphere, water, sewage and hygiene of the population living near the waste and categorize their exposure level.
3. Analyze through surveys if there is any relationship between cancer and exposure to waste landfill.
METHODS: A description of the environment will take place with younger research group of medical students (GIBP); epidemiological information about the area, and for their variables such as morbidity and mortality of cancer, have been acquired by secondary data. The approach will be descriptive, analytical. We will apply a survey to a sample of the population in order to confirm the association between cancer and inhabit near landfill.
EXPECTED RESULTS: We expect the epidemiological identification of a population at increased risk for cancer incidence based on the assumption that the environment predetermine the onset of this disease.
KEYWORDS: cancer-leachate-pathological geography.

D-165 - The Skin Cancer Burden From Occupational Sun Exposure In Canada

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Purpose
Ultraviolet radiation (UVR) is a known human carcinogen and people who work outdoors are at particular risk of non-melanoma skin cancer (NMSC) due to sun exposure. This study estimated the attributable fraction (AF) of NMSC due to occupational sun exposure as part of a larger project to estimate the current burden of occupational cancers in Canada.
Methods
In order to calculate the AF, estimates of the proportion of workers ever exposed (PrE) during the risk exposure period (REP, 1961 – 2000), and relative risks (RR) for each of basal and squamous cell carcinomas (BCC, SCC) are required. To estimate the PrE, industry- and occupation-specific CAREX Canada estimates of prevalence and level of exposure were combined with historical Canadian employment data, labour force characteristics, and survival probabilities. RRs for BCC (RR=1.43) and SCC (RR=1.77) from recent meta-analyses were assigned to those in the moderate and high exposure groups, with the low exposed group considered not at risk for occupational NMSC.
Results
Approximately 2.6 million workers were ever exposed to solar UVR during the REP; 69% were in the high exposure group. The AF for NMSC was 10.4% for males, 1.3% for females, and 6.3% overall, which equated to a total of 4556 incident NMSC cases in 2011. Regarding the subtypes, 2846 BCC cases (AF = 5.3%) and 1710 SCC cases (AF = 9.2%) were attributable to outdoor work. Agriculture and construction made up the majority of cases by industry (51%).
Conclusions
Our study showed that a substantial burden of NMSC diagnoses in Canada may be attributed to working outdoors. We benefited from a more detailed exposure assessment than has been used in previous studies, but were challenged by the poorer quality of registry data for NMSC compared to other cancer sites.
Funding sources
Canadian Partnership Against Cancer, Canadian Cancer Society

D-166 - Occupational Formaldehyde Exposure And Risk Of Cancer At Selected Sites

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PURPOSE
To investigate risk of lymphohaematopoietic (LH), sino-nasal, and epipharyngeal cancers according to cumulative formaldehyde exposure.
METHODS
A cohort comprising more than 300 000 men from Finland and Sweden in 25 occupations identified as formaldehyde exposed was extracted from the Nordic Occupational Cancer Study (NOCCA). LH cancers were analyzed using partly overlapping categories. During follow-up from 1961–2003 in Sweden and 1970–2005 in Finland, altogether 7495 LH, 164 epipharyngeal, and 321 sino-nasal cancer cases were observed. Five controls per case were matched by age and country, and hazard ratios (HRs) were computed according to cumulative formaldehyde exposure with adjustment for relevant potential confounders (benzene, wood dust, nickel, and chromium). Exposure estimates were based on information of probability and level of exposure from the NOCCA Job Exposure Matrix.

RESULTS
For leukaemia, non-Hodgkin lymphoma (NHL), and multiple myeloma (MM), non-significant increases ranging from 9 to 23% were seen among the 10% with highest cumulative exposure. No association with exposure was seen for AML, but for CLL a borderline statistically significant risk elevation was observed (HR 1.29, 95% confidence interval [CI] 0.98-1.69). When a 10-year exposure lag was applied, HR for CLL was 1.37 (CI 1.04-1.82). Combining CLL, NHL and MM in the analyses, in accordance with newer classification schemes, we found a significant elevation of 11% (CI 1.00-1.23), increasing to 17% with a 10-year exposure lag (CI 1.04-1.32). For sino-nasal cancer, risk was significantly elevated only in the lagged analysis (HR 2.00, CI 1.07-3.75). No risk elevation was observed for epipharyngeal cancer.

CONCLUSIONS
Formaldehyde exposure appears to affect more LH cancer types than leukemia. The association with leukaemia was driven mainly by CLL. Sino-nasal cancer risk was doubled in the highest exposure group.

Funding sources
Nordic Cancer Union

D-167 - Employment In Natural Resource Based Industries And Prostate Cancer Risk In Northeastern Ontario, Canada

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Objective Prostate cancer is the most commonly diagnosed cancer in North American men and there continues to be limited knowledge on preventable risk factors. There are a number of occupational exposures in natural resource based industries that are suspected to be related to prostate cancer risk. This study investigates associations between employment in natural resource based industries and prostate cancer.
Methods Data were from a population-based, case-control study previously conducted in Northeastern Ontario. Incident cases (N=760) aged 45-85 years who were diagnosed between 1995 and 1998 were identified from the Ontario Cancer Registry. Controls (N=1632) were recruited from telephone listings and frequency-matched to cases by age. Lifetime occupational history was collected for all participants and logistic regression models were used to calculate odds ratios (OR) and 95% confidence internals (CI).
Results Elevated risks were observed for employment in forestry and logging industries (OR 1.87, 95% CI 1.32-2.73) and occupations (OR 1.71, 95% CI 1.24-2.35), which increased with duration of employment for ≥10 years. Elevated risks were also found for employment in wood products industries (OR 1.45, 95% CI 1.07-1.97) and paper and allied products industries (OR 1.43, 95% CI 1.03-2.00) and with duration of employment for ≥10 years. There were also few elevated risks in agriculture and mining related work, however these findings were not consistent across the study.
Conclusions There is evidence that prostate cancer risk may be associated with employment in several natural resource based industries, primarily in the forest industries. To further evaluate observed associations, studies should focus on natural resource based exposures.

D-168 - Estimates Of The Number Of Workers Exposed To Diesel Engine Exhaust By Industry In South Korea

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The aim of this study is to estimate the number of workers exposed to diesel engine exhaust (DEE) by industry and year in South Korea. The estimates of workers potentially exposed to DEE in South Korea were calculated by industry on the basis of the CARcinogen Exposure (CAREX) surveillance system. The data on the labor force employed in DEE industries were obtained from the 'Census on establishments' conducted by the Korea National Statistical Office from 1993 to 2013. The mean value of prevalence rates adopted by EU 15 countries was used as the primary exposure prevalence rate. We also investigated the exposure prevalence rates and exposure characteristics of DEE at 359 workplaces from 11 industries. Total workers exposed to DEE were estimated as 270,014 in 1993 and 417,034 in 2013 (2.2% of total labor force). As of 2013, the 'Land transport' showed the highest number of workers exposed to DEE, 174,359, followed by 'Personal and household services' with 70,298, 'Construction' with 45,555, 'Wholesale and retail trade and restaurants and hotels' with 44,005 and 'Sanity and similar services' with 12,584. Those five industries which have over 10,000 workers exposed to DEE accounted for 83% of total DEE exposure workers. Comparing primary prevalence rates used for preliminary estimation among 49 industries, 'Metal ore mining' had the highest rate of 52.6 %, followed by 'Other mining' with 50.0% and 'Land transport with 23.6%. The DEE prevalence rates we surveyed (1.3-19.8%) were higher than the primary prevalence rates. The most common emission sources of DEE were diesel engine vehicles such as forklift, truck and van. The 'Land transportation' was estimated to be the major industry. Our estimated number of workers exposed to DEE can be used to protect workers from potential exposure to DEE in Korea.

D-169 - Cancer Risks In A Population-Based Cohort Of 70,000 Canadian Agricultural Workers

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Purpose: Agricultural workers may be exposed to potential carcinogens including pesticides, sensitizing agents and solar radiation. Previous studies indicate increased risks of hematopoietic cancers and decreased risks at other sites, possibly due to differences in lifestyle or risk behaviours. We present findings from the Canadian Census Cohort, the largest national population-based cohort of agricultural workers.

Methods: Statistics Canada created the cohort using deterministic and probabilistic linkage of the 1991 Canadian Long Form Census to National Cancer Registry records for 1992-2010. Self-reported occupations were coded using the Standard Occupational Classification (1991) system. Analyses were restricted to employed persons aged 25-74 years at baseline (N=2,050,300), with follow-up until December 31, 2010. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards for all workers in agricultural occupations (n=70570; 49965 male), stratified by sex and adjusted for age at cohort entry, province of residence, and level of education.

Results: A total of 9800 incident cancer cases (7775 in males) occurred in agricultural workers. Among men, increased risks were observed for Non-Hodgkin lymphoma (HR=1.10, 95% CI=1.00-1.21), prostate (HR=1.11, 95% CI=1.06-1.16), melanoma (HR=1.15, 95% CI=1.02-1.31), and lip cancer (HR=2.14, 95% CI=1.70-2.70). Decreased risks in males were observed for lung, larynx, and liver cancers. Among female agricultural workers there was an increased risk of pancreatic cancer (HR=1.36, 95% CI=1.07-1.72). Increased risks of melanoma (HR=1.79, 95% CI=1.17-2.73), leukemia (HR=2.01, 95% CI=1.24-3.25) and multiple myeloma (HR=2.25, 95% CI=1.16-4.37) were observed in a subset of female crop farmers.

Conclusions: Exposure to pesticides may have contributed to increased risks of hematopoietic cancers, while increased risks of lip cancer and melanoma may be attributed to sun exposure. The array of decreased risks suggests reduced smoking and alcohol consumption in this occupational group compared to the general population.

Funding Source: Work Safety Insurance Board of Ontario (Grant #11024)

D-170 - Workplace Exposure To Diesel And Gasoline Engine Exhausts And The Risk Of Colorectal Cancer In Canadian Men

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Purpose: The International Agency for Research on Cancer (IARC) classified diesel exhaust as carcinogenic to humans (Group 1) and gasoline exhaust as a possible carcinogen (Group 2B) based studies of lung cancer, however the evidence for other sites is limited. We addressed this question by investigating exposure to diesel and gasoline emissions with respect to risk of colorectal cancer in men.

Methods: We used data from a population-based case-control study with incident cases of colon (n=931) and rectal (n=840) cancer and 1360 controls from 7 Canadian provinces conducted in 1994-1997. Lifetime occupational history and information on other risk factors was collected. Occupational hygienists, blinded to case-control status, assigned exposures to each job across 3 dimensions: concentration, frequency, and reliability. Logistic regression was used to estimate odds ratios (OR) and their 95% confidence intervals (CI), adjusted for age, province, use of proxy respondents, smoking, body-mass index, physical activity, intake of alcohol, processed meats, and occupational exposure to asbestos and aromatic amines.

Results: Among colorectal canccer cases, 638 (36%) were exposed to diesel and 814 (46%) were exposed to gasoline emissions. Relative to the unexposed, elevated risks were observed among subjects exposed to high concentration levels of diesel emissions for colorectal cancer (OR=1.65, 95% CI=0.98-2.80) and rectal cancer (OR=1.98, 95% CI=1.09-3.60), but not colon cancer (OR=1.35, 95% CI=0.72–2.54). Prolonged (>10 years) exposure at high concentrations was also associated with high risks of colorectal ((OR=1.90, 95% CI=0.85–4.23; p-trend=0.02) and rectal cancer (OR=2.33 95% CI=0.94–5.78; p-trend=0.02). No statistically significant associations were observed for gasoline emissions.

Conclusions: To our knowledge, this is largest population-based case-control study of diesel and gasoline exposure and colorectal cancer. Our findings suggest that sustained high-level exposure diesel emissions may increase the risk of rectal cancer.

Funding Source: Workplace Safety and Insurance Board (Ontario) - Grant #10011

D-171 - Occupational Exposure To Endotoxin And Lung Cancer Risk: Results Of The ICARE Study

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Purpose: We investigated the role of occupational exposure to endotoxin in lung cancer risk in a French population based case-control study.
Methods: Lifelong work histories of 2926 cases and 3555 controls were collected using standardized questionnaires. Estimation of endotoxin exposure was based on a publication issued by the Institut National de Recherche et de Sécurité (INRS), which reported measurements in biological aerosols workstations. Several exposure-related variables were created: intensity (<1000UE/m³; >1000UE/m³), total duration (years), life time cumulative exposure (UE/m³*years) and time since cessation (years). Smoking history was combined into a comprehensive smoking index (CSI) that included mean number of cigarettes/ day, duration and time since cessation. Odds ratios (OR) and 95 % confidence intervals (CI) were estimated using unconditional logistic regression models and controlled for main confounding factors including CSI.
Results: We found an inverse significant association between high endotoxin exposure and lung cancer risk (151 cases/336 controls; OR=0.64, 95% CI=0.5-0.82). The main activity sectors entailing high exposure included dairy, cattle, poultry and pig farms. In contrast, a statistically significant positive association was found for low exposure (OR=1.33, 95% CI=1.08-1.64) (eg. sawmills, wool industry, meat processing). Using restricted splines cubic models, we observed that the association between cumulative endotoxin exposures and lung cancer risk departed significantly from linearity. In addition, the risk decreased with duration and increased with time since cessation, irrespective of the exposure intensity. Analysis by subgroups showed an interaction with tobacco consumption, and light smokers appeared to be more sensitive to endotoxin protective effect.
Conclusions: Our findings suggest that high exposure to endotoxin confers protection against lung cancer.

Funding source: Fondation de France

D-172 - Pesticide Exposure And Prostate Cancer Risk In The AGRICAN Cohort

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Purpose: Farming and pesticide use are regularly associated with increased prostate cancer risk. Our aim was to identify occupational risk factors related to pesticide exposure associated with prostate cancer risk among men enroled in the large prospective cohort AGRICAN.
Methods: Data on lifetime agricultural exposures (13 types of crops, 5 livestock and their related tasks including pesticide use and re-entry tasks) were collected from the enrolment questionnaire. We used a simplified version of the crop-exposure matrix PESTIMAT to assess exposure to organochlorine insecticides. From enrolment (2005-2007) to 2009, 1672 incident prostate cancer cases were identified from cancer registries.
Results: A greater prostate cancer risk was observed among men treating cattle with insecticides, mainly those having the largest stock (≥150 cattle: HR 1.59, 95% CI 1.02-2.48; p for trend= 0.01). A slight increased risk was observed among male pesticide users (HR 1.10, 95% CI 0.97-1.25). Among fruit growers, harvesting also increased prostate cancer risk, up to two-fold for the largest area. We observed a borderline significant increased prostate cancer risk associated with exposure to organochlorine (HR 1.15, 95% CI 0.99-1.32) without linear relationship with duration of exposure. Eight out of the 18 active ingredients of organochlorine studied significantly increased prostate cancer risk and a linear relationship with intensity of exposure was observed for 6 of them (aldrin, chlordane, dieldrin, DDD, toxaphene and HCH).
Conclusions: This work provides new data on the association between pesticide exposure and prostate cancer risk and emphasize the need to consider other uses or exposures (insecticides on animals and re-entry tasks), use of protective gloves and specific active ingredients to study cancer risk associated to pesticide exposure.

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D-173 - Lifetime Prevalence Of Occupational Exposures To Carcinogens In France: Providing Input To Estimate Cancer Attributable To Carcinogens At Work Place

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Purpose
A previous study reported that 3.7% of cancer mortality in France was attributable to occupational carcinogen exposures although this study did not comprehensively assess lifetime carcinogen exposure. The aim of this study was to estimate the proportion of the French population ever exposed to occupational carcinogens, and use these estimates as input to calculate attributable fractions.

Methods
To account for a biological latency of 10 to 50 years between carcinogen exposure and cancer incidence, we estimated lifetime exposure over the period 1965-2005. The prevalences of cross-sectional occupational exposures were obtained from the SUMER surveys (Surveillance Médicale des expositions aux risques professionnels) which contained data on 50,000 French workers for the years 1994, 2003 and 2010. Using an established method, lifetime occupational exposures were estimated using data from French labour surveys to estimate national changes in the number of workers and sector-dependent employment turnover rates.

Results
We estimated the lifetime exposure to 59 physical and chemical carcinogens and occupations classified as group 1 or 2A by IARC Monographs. For example, between 1965 and 2005, 1.8% of the French male population had worked as painters. By comparison, a UK study using the same methodology indicated a higher proportion of painters: 5.8% of males had been a painter within the same period. The UK study showed that 1.2% of lung cancers were related to painting, an estimate that is expected to be lower in France due to lower exposure.

Conclusions
This study seeks to estimate the lifetime exposure to occupational carcinogens in France. They will provide the necessary input to estimate the fraction of cancers attributable to occupational exposures in the country in 2015, enabling comparisons with other countries. These results provide a vital evidence base for planning national strategies to ensure healthy working conditions.

Funding source: Institut National du Cancer, France

D-174 - Night Work And Risk Of Breast Cancer Defined By Receptor Status: The CECILE Study

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Purpose:
In 2007, volume 98 of the IARC monographs concluded that “shift work that involves circadian disruption” was probably carcinogenic to humans (group 2A). Since the publication of the monograph about fifteen epidemiological studies on night shift work and breast cancer have been published with mixed results. Only few studies however have investigated shift work in relation to breast cancer subtypes defined by Estrogen (ER) or Progesterone (PR) receptor and Human Epidermal growth factor Receptor 2 (HER-2) status.
Methods:
We explored the association of night work with breast cancer subtypes, defined by ER, PR and HER2 status in a case-control study in France including 975 cases and 1317 controls. Night work was defined as work schedule covering at least the entire time span from 11:00 pm to 5:00 am. Odds ratios (OR) contrasting women who had ever vs never worked at night were calculated using logistic regression models adjusting for potential confounders.

Results:
The association of night work with breast cancer was stronger for ER, PR and HER2-positive tumors (OR 1.49, 1.48 and 1.91, respectively) than in the ER, PR and HER2-negative counterparts (OR 0.86, 1.12, 1.56). Stratification by menopausal status showed that these associations were restricted to premenopausal women (OR 2.04, 1.98, 2.80, respectively). The odds ratio for the ER or PR-positive and HER2-positive subtype of breast cancer in premenopausal women was 3.30 (95%CI 1.42-7.67).
Conclusions:
This study provides evidence that night work might be associated with specific subtypes of breast cancer, and supports findings in other studies. The strongest association was seen in premenopausal women for the breast cancer combining positive hormone receptors (ER+ or PR+) and HER2+.

Funding Source:
National Institute of Cancer (INCa), Fondation de France, French Agency for Environmental and Occupational Health Safety (AFSSET), French National Research Agency (ANR), Ligue contre le Cancer

D-175 - SYN-JEM: A Quantitative Job-Exposure Matrix For Five Lung Carcinogens

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Objective – The use of measurement data in occupational exposure assessment allows more quantitative analyses of possible exposure-response relations. We describe a quantitative exposure assessment approach for five lung carcinogens (i.e. asbestos, chromium-VI, nickel, polycyclic aromatic hydrocarbons (by its proxy benzo(a)pyrene (BaP)) and respirable crystalline silica). A quantitative job-exposure matrix (JEM) was developed based on statistical modelling of large quantities of personal measurements.
Methods – Empirical linear models were developed using personal occupational exposure measurements (n=102 306) from Europe and Canada, and auxiliary information like job (industry), year of sampling, region, an a priori exposure rating of each job (none, low and high exposed), sampling and analytical method, and sampling duration. The model outcomes were used to create a JEM with a quantitative estimate of the level of exposure by job, year and region.
Results – Decreasing time trends were observed for all agents between the 1970s and 2009, ranging from -1.2% per year for personal BaP and nickel concentrations to -10.7% for asbestos (in the time period before an asbestos ban was implemented). Regional differences in exposure concentrations (adjusted for measured jobs, years of measurement, and sampling method and duration) varied by agent, ranging from a factor 3.3 for chromium-VI up to a factor 10.5 for asbestos.
Conclusion – Time-, job-, and region-specific exposure levels were estimated for four (asbestos, chromium-VI, nickel and RCS) out of five considered lung carcinogens. Large amounts of personal occupational exposure measurement data and statistical modelling, making the best use of all available information, appear to be essential in order to successfully derive a quantitative JEM to be used in community-based studies.

D-176 - Lung Cancer Burden Of Occupational Exposure To Radon In Canada

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Purpose: Estimate the proportion of Canadians exposed to radon in all occupational environments and calculate lung cancer cases attributable to these exposures.

Methods: Radon exposure for workers in high-risk occupations (e.g. underground mining) and indoor workers were assessed separately. High-risk workers who were likely to have exposure >800 Bq/m3 were identified by occupational hygienists, by occupation and industry, from the 2006 Canadian census. Indoor workers were also identified by industry and occupation, by first excluding outdoor workers exposed to solar radiation in the CAREX Canada SUNJEM, then removing workers in well-ventilated workplaces by expert assessment. To account for the increased likelihood of radon exposure on lower floors, building height adjustment factors were applied to reduce exposure population in urban areas. The exposure distribution of these indoor workers was modeled, by province, using radon measurements from a survey of federal buildings in Canada.

Combining the exposure assessment above and the population model developed for the Canadian Occupational Cancer Burden project, we estimated the fraction of lung cancers in 2011 attributable to occupational radon exposure during 1961 – 2001. Relative risks were calculated using the BEIR VI exposure-age-concentration risk model.

Results: Approximately 4.4 million indoor and 26,000 high-risk Canadian workers were exposed to radon from 1961-2001. The majority (79%) of exposed indoor workers had exposures below 50 Bq/m3. In total, 67 new cases of lung cancer in 2011 were attributable to occupational radon exposure in Canada, representing 0.25% of incident lung cancers.

Conclusions: Lung cancer attributable to occupational radon exposure is low in Canada. Most exposure and disease burden are associated with low radon concentrations, below the WHO reference level of 100 Bq/m3.

Funding Sources: Canadian Cancer Society, Canadian Partnership Against Cancer.

D-177 - Exposure To Crude Oil And Ultraviolet Radiation And Risk Of Skin Cancer In 25 000 Offshore Oil Industry Worker

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Purpose
To examine prospectively the risk of skin cancer by anatomical site according to dermal exposure to crude oil, benzene, mineral oil, and ultraviolet radiation in 25 000 offshore oil industry workers traced in the Cancer Registry of Norway 1999–2012.

Methods
Different metrics of exposure were developed according to expert-based intensity estimates (job-exposure matrices) covering dermal exposure to crude oil, mineral oil, and dermal and inhalatory exposure to benzene, and according to self-reported solar exposure. Hazard ratios (HRs) were derived by Cox regressions adapted to a stratified case-cohort design with 95% confidence intervals.

Results
A total of 112 cases of cutaneous melanoma and 63 cases of squamous cell carcinoma were observed. Dose-related risk patterns were seen for skin cancer on the hand (melanoma and non-melanoma combined, 1 melanoma and 7 squamous cell carcinomas) according to duration of exposure to crude oil, or according to duration of benzene exposure. For the highest exposed tertile (15 years+ of crude oil exposure) compared with the unexposed, the HR was 5.4 (95% CI 0.8–39, 4 cases), and the P_{trend} across categories was 0.029, adjusted for sunburns and education. No such trend was found for mineral oil. When anatomical site was disregarded, those reporting ≥ 4 sunburns/year compared to none had increased risks of melanoma (HR 4.5, 95% CI 1.4–15, 4 cases) and squamous cell carcinoma (HR 8.1, 95% CI 1.9–33, 3 cases).

Conclusions
Our study suggests that skin cancer can be induced by dermal exposure to crude oil in the upstream oil industry.

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Cancer Registry of Norway Research Fund

D-178 - A Job-Exposure Matrix For The Assessment Of Alkylphenolic Compounds

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Introduction: Alkylphenolic compounds are ubiquitous chemicals with endocrine disrupting properties used as surfactants but having a wide range of other applications. Biologic matrices commonly used in epidemiologic studies, such as blood serum or plasma are not sensitive enough and susceptible to contamination. To overcome these limitations, we developed a job-exposure matrix (JEM) to assess occupational exposure to alkylphenolic compounds in the MCC-Spain study, and that can be used in many other epidemiological studies.
Methods: The MCC-Spain study on cancer involved more than 10,000 participants in 12 Spanish provinces. Occupational history was assessed for all jobs held for at least 1 year, and more than 28,000 occupational registries were collected. To construct the JEM, we consulted multiple sources of information, and performed interviews with nine key people from industry and academia. Three hygienists coded frequency (minority/majority of workers involved) and intensity of exposure (including dispersive processes, with shaking, or aerosol generation, or otherwise) to alkylphenolic compounds for all the 390 ISCO-88 job titles by periods of time.
Results: We identified 57 (14.6%) out of 390 ISCO-88 job titles with potential exposure to alkylphenolic compounds. In 6 of jobs deemed as exposed, exposure depended on the economic sector. Nonylphenol ethoxylates were the compounds most commonly involved (33 job titles). Use of alkylphenolic compounds varied greatly over time; while they are still used in the plastic and rubber industry, their use began to decline before 1995 in domestic cleaning agents. Preliminary results on associations between alkylphenolic compounds and cancer in the MCC-Spain will be presented at the conference.
Discussion: We built a JEM to assess exposure to alkylphenolic compounds, taking into account changes in use over time, and different types of alkylphenolic compounds, that can be a valuable tool for exposure assessment in epidemiologic research on the health effects of these chemicals.

D-179 - Frequency And Level Of Asbestos Exposure In Ovarian Cancer Patients: A Multicenter Study

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Purpose : Ovarian cancer is the fifth most common cancer and the fourth cause of cancer death in women in Europe. Its etiology is still not fully understood. Following the conclusion by IARC in 2009 on a causal relation between asbestos exposure and ovarian cancer, we examined the frequency and level of asbestos exposure in ovarian cancer patients.
Population : A descriptive multicenter cases study among patients with histologically-confirmed ovarian cancer between January 2010 and December 2012, and managed in one of three specialized hospitals in Lyon, France.
Methods : Individual, medical and occupational data were collected by a standardized questionnaire administered by phone. Exposure levels were assessed by an industrial hygienist using national and international classifications. Assessment included direct asbestos exposure at work, indirect exposure via nearby colleagues working with asbestos, and occupational environmental exposure. Familial exposure was assessed based on questions relating to family members' occupations. We compared the frequency of asbestos exposure among our cases to the data from a cross-sectional survey conducted in 2007 by the French Institute for Public Health Surveillance in a representative sample of 10,010 subjects, involving 5,252 women from the French population aged 25 to 74 years in 2007.
Results: The 162 patients (mean age of 58 years; response rate 50%) reported on average 2.4 different jobs (median overall working duration 27.1 years). The prevalence of occupational asbestos exposure was 18% (median duration 14 years), almost 5% of patients had non-occupational exposure, 4% through their relatives, and 1% through environmental sources. Lifetime prevalence of occupational asbestos exposure was significantly higher compared to asbestos exposure of women of the same age in the French general population (4%).
Conclusion: Future research should investigate the association between asbestos exposure and histology subtypes as well as mechanisms involved using genetic and molecular biology techniques.
Funding: INCa/ANSES

D-180 - Trend Of Mesothelioma Incidence In Lombardy, Italy, 2000-2029

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Purpose: In Italy, where asbestos has been extensively used from 1946 to 1992, mortality from pleural mesothelioma is expected to peak in 2012-24. Using data of the MM registry of the Lombardy Region, North-West Italy, the most populated and industrialised Italian region, we analysed time patterns in the period 2000-2012 and made projections for the period 2013-2029.
Methods: We selected all incident cases of MM with first diagnosis between 2000 and 2012. We fitted categorical Poisson age-cohort models using 5-year categories for age at diagnosis and birth cohort. The gender-specific age and cohort regression coefficients were then applied to population data to calculate projections of the numbers of MM cases in the years 2013 to 2029. Statistical analyses were performed with Stata 13.
Results: In 2000-2012 we recorded 4,435 MM cases, 2,846 in men and 1,589 in women. Occupational asbestos exposure was more frequent in men (73.6%) than in women (38.2%). The average number of MM cases per year was still increasing (+2.6% in men, +3.3% in women). A maximum of 416 MM cases (266 men, 150 women) is expected in 2019. We forecast there will be 6,809 more cases (4,379 in men, 2,430 in women) in the period 2013-2029, for a total of 11,244 MM cases (7,225 in men, 4,019 in women) in 30 years.
Conclusions: This study documented a high MM burden in both genders in the Lombardy Region, reflecting extensive asbestos exposure in the past. Incidence rates are still increasing and a downturn of MM occurrence is expected to occur after 2019. Documenting mesothelioma occurrence may help to increase awareness of dangers of asbestos exposure in countries that still use it but where its health effects are still overlooked.
Funding source: Lombardy Region; Ministry of Health and INAIL; Associazione Italiana per la Ricerca sul Cancro.

D-181 - Night Work And Prostate Cancer Risk: Preliminary Findings From The Proteus Case-Control Study In Montreal, Canada

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Background: In 2007, IARC classified shift work involving circadian disruption as a probable human carcinogen. Human evidence, mostly based on breast cancer, was judged as limited. A handful of studies have suggested an association between night work and prostate cancer (PCa) risk.
Purpose: To assess the association between night work, as defined by an IARC Working Group in 2010, and PCa risk.
Methods: PROtEuS, a population-based case-control study, was conducted in Montréal, Canada. Subjects included 1,933 incident PCa cases aged ≤ 75, diagnosed across French hospitals in Greater Montreal in 2005-2009. Concurrently, 1,994 population controls were randomly selected from French-speaking men on the electoral list. In-person interviews elicited in-depth information on each job held over the lifetime, including work schedules. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CI) for the association between night work and PCa risk, taking into account several potential confounders.
Results: 23% of cases and 21% of controls had held a night job (3 hours of work between midnight and 5:00 am), for at least 1 year. The average cumulative duration of night work was 7.8 ± 8.2 years for cases and 8.7 ± 8.7 years for controls. Compared to men having never held a night job, those who did had an OR for PCa of 1.05 (95%CI 0.88-1.25). The OR for high grade (Gleason 7 [4+3]) PCa was 1.09 (95%CI 0.85-1.38). There was no evidence of a duration-response trend. Excluding men working rotating shifts from the unexposed category did not alter findings. Nor did exclusion of controls not recently screened for PCa.
Conclusions: These preliminary findings provide little support to the hypothesis that night work plays a role in PCa development. In-depth analyses are underway.
Funding: Canadian Cancer Society, Cancer Research Society and the Quebec Government

D-182 - Methodological Approaches For Estimating The Number Of Cancers Caused By Occupational Exposure In Canada

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Objectives
In recent years, several projects quantifying the burden of occupational cancer were conducted with increased methodological sophistication. We present the methods for incorporating more detailed exposure assessments and risk-relationships in the estimation of the attributable fraction (AF), developed for the Canadian Burden of Occupational Cancer project funded by the Canadian Cancer Society.

Methods
This project builds upon methods from a recent UK burden study to derive AFs using: relative risks (RR) from review of the literature, detailed assessment of the prevalence and level exposure developed by CAREX Canada, historical exposure trends, and a population model constructed from Canadian data. The methodological approach for each exposure-cancer site pair is adapted according to the level of detail in the available epidemiology and exposure data. The framework had three possible approaches: Scenario A (overall exposed/unexposed), Scenario B (categorical exposure-response) and Scenario C (quantitative exposure-response).

Results
An example of the most advanced approach (Scenario C) is crystalline silica. Approximately 780,000 workers were exposed to silica 1961-2001, with 46% in the highest exposure group. We incorporated annual exposure decreases of 4.1%, from an analysis of the Canadian Workplace Exposure Database. Based on the calculated cumulative exposure and the dose-response curve from Steenland et al. 2001, we estimated mean RRs of 1.36, 1.46, and 1.57 for the low, medium, and high exposure groups respectively. Estimated AFs for silica-related lung cancers were: 4.4% for males (549 cases), 0.2% for females (24 cases), and 2.4% overall (573 cases). Over half of the cases (56%) were from the construction industry.

Conclusions
We sought to increase the validity of the burden estimates by using Canadian exposure and population data. The methodological enhancements in incorporating detailed epidemiology and exposure assessment further increases the validity of estimates for specific industries and occupations, facilitating targeted risk reduction strategies to prevent occupational cancers.

D-183 - Nonlinear Low Dose Hematotoxicity Of Benzene; A Pooled Analyses Of Two Studies Among Chinese Exposed Workers

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Impairment of the hematopoietic system is one of the primary adverse health effects after exposure to benzene. We previously have shown that benzene at lower levels of exposure (<1 ppm) effect the blood forming system. Here we extend these analyses by detailed modeling of the exposure response association of benzene and its major metabolites (i.e. catechol, muconic acid, phenol, and hydroquinone) on peripheral white blood cell counts (WBCs) and its major cell-subtypes (i.e. granulocytes, lymphocytes, and monocytes) using two previously published cross-sectional studies among occupationally exposed Chinese workers. Clear non-linear exposure response associations were observed between air benzene concentrations and WBCs and its cell-subtypes with a larger than proportional decrease in cell counts at lower than at higher levels of benzene exposure (exposure range 0.1 – 100ppm). This association was largely similar in shape (supralinear) when the analyses were repeated with the measured benzene metabolites and as such enzymatic saturation processes do not seem to explain the observed non-linearity. An analyses on the risk of having a WBC count below 4000 cells/ul showed that this association was essentialy linear. Together, these results suggest that the non-linearity in the observed hematological effects may be explained by increased cell proliferation, while the risk of having a WBC count below 4000 cells/ul is a result of both hematotoxicity and failure to compensate for this effect.

D-184 - Update On Progress With An Update To The British Rubber Industry Study Cohort And With An International Pooled Study Of Rubber Industry Cohorts

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Here we present progress on an update of a British cohort of rubber industry workers and for an international pooled cohort study coordinated by the International Agency for Research on Cancer.
The UK cohort consists of 40,867 men aged 35+ who were employed in the British rubber industry on 1 February 1967. The previous analysis found an excess of bladder cancer mortality where exposure to antioxidants may have occurred. An excess of lung cancer was observed in the total industry. We have received research governance clearances from ethics, Health Research Authority Confidentiality Advisory Group, Office for National Statistics' Microdata Release Panel, the Health and Social Care Information Centre (HSCIC) Data Access Advisory Group for England and Wales and Public Benefit and Privacy Panel for Scotland for mortality and cancer incidence follow-up. The cohort is currently being traced for mortality by HSCIC and we plan to present preliminary results at the meeting in June.
Preliminary results will be presented on trend analyses for UK-exposure information from the EXASRUB database, which will develop exposure models specifically for the British industry. Sensitivity analyses to investigate the assumptions made as part of the exposure assessment will also be carried out.
The international pooled study anticipates pooling data from Great Britain, Poland, Germany, Holland and Sweden, making this not only the largest ever evaluation of cancer risks in the rubber industry, but also the first large investigation using quantitative exposure assessments for a number of potential carcinogens pertinent to this industry. We will report on progress with the international pooled study.

E-185 - Dental X-Rays And The Risk Of Cancers Of The Head And Neck Region: A Systematic Review And Meta-Analysis

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Purpose
Dental radiography, a common source of low-dose diagnostic radiation exposure in the general population, has been associated with the risk of thyroid cancer and tumours of the salivary glands and brain. We synthesised the published data to assess the association between dental x-rays and risk of developing these cancers.
Methods
We carried out a systematic literature search of observational epidemiological studies from inception up to 2 November, 2015 using electronic databases Embase (Ovid), Medline (Ovid and PubMed) and Web of Science. Studies were eligible for inclusion if they reported the association as an odds ratio/relative risk, or contained sufficient information for calculating the effect size. Meta-regressions were fitted using the statistical software Stata. Heterogeneity was assessed with I2 and Cochran's Q. Quality of the studies was assessed using the Newcastle-Ottawa Scale.
Results
The literature search identified 1319 articles; of these, 71 were obtained in full text for further assessment, and 23 were selected for inclusion in the synthesis. Six studies assessed the association with thyroid cancer, three with tumours of the salivary glands, six with glioma, and eight with meningioma. The meta-regression analysis showed that exposure to dental x-rays was significantly associated with an increased risk of thyroid cancer (OR=1.74, 95% CI: 1.34-2.26). An increased risk of meningioma (based on 3 studies) was observed for repeated (5+) dental x-rays (OR=1.62, 95% CI: 1.14-2.30). There was no significant association with any other cancer of the head and neck region.
Conclusions
Our review further supports the existing hypothesis that exposure to dental x-rays is associated with an increased risk of thyroid cancer. Although the risk at the individual level is likely to be low, the proportion of the population exposed is large. Thus, the notion that low-dose radiation exposure through dental radiography in the general population is safe warrants further investigation.

E-186 - Radiation Doses From Pediatric CT Scans In Great Britain (1978-2008): A Survey Of Individual Exposures And A Risk Assessment Of Potential Subsequent Cancers

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Background: Despite the great medical benefits, there are concerns that use of computed tomography (CT) can increase risk of cancer, especially in children. This study aims to assess individual exposures in children or young adults scanned in Great Britain and projecting the potentially radiation-induced cancers from the 1980's to the current time.

Methods: Individual scan parameters were collected for 1,073 CT scans performed in 1978-2008 in 36 hospitals in patients before 20 years of age. Organ doses were estimated using experimentally validated dose conversion coefficients. Lifetime cancer risks were projected using dose-response models derived from data for the Japanese atomic bomb survivors and for patients exposed to X-rays (RadRAT risk assessment tool), and using national cancer and mortality statistics. Total numbers of cancer were projected up to 2014 using data of the Diagnostic Imaging Dataset (Office for National Statistics, England) and trends in CT use reported in a previous survey in the UK.

Results: In 2000-2008, organ doses per exam and subsequent lifetime cancer risks were 50-70% lower than in 1978-1989. In 2000-2008, the projected lifetime risks varied from 3 to 9 per 10,000 head scans and 9 to 45 per 10,000 body scans according to the age at scan. We calculated that 57 cancers (90% uncertainty interval: 34-97) might be induced over the patients' lifetime by the 103,000 scans performed in England in 2014 in individuals under 20 years of age.

Conclusion: There have been reductions in dose per CT exam in pediatric CT since 1995, but a more widespread use of CT has increased collective exposure. This study projected numbers of possibly radiation-induced cancers, resulting both from reduced individual doses and an increased frequency of use.

Funding sources: NCI intramural research program, UK Department of Health, Cancer Research UK

E-187 - Studying The Association Between Uranium Exposure And Cancer By Integrating Dosimetry, Radiobiology And Epidemiology: The CURE Project

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Introduction
Uranium is a radionuclide emitting alpha particles, and therefore has potential to be carcinogenic. However, direct evidence that would allow for a proper quantification of the carcinogenic effects of uranium in humans is limited. Especially, most available epidemiological studies suffer from major limitations. New studies borrowing strengths from enhanced epidemiological datasets on the one hand, and from modern biology approaches on the other hand, will have higher potential to improve the characterization of the biological effects of uranium exposure and the quantification of subsequent cancer risk.

Methods
CURE (Concerted Uranium Research in Europe) was a 18-month concerted action supported by the European Commission, involving 9 European institutes. It aimed to elaborate a collaborative research project on the biological and health effects of uranium contamination, integrating epidemiology, biology and dosimetry. A work-package was dedicated to each of these disciplines with strong interactions, and a further working group on uncertainty was constituted. A strong focus was put on cancer effects.

Results
Protocols were developed for pooled analyses of existing cohorts of uranium miners (40,000) and uranium processing workers (40,000) in Belgium, the Czech Republic, France, Germany, and the United Kingdom. To allow for the study of dose-response relationships, protocols were developed to calculate organ doses due to uranium exposure using state-of-the art dosimetric methods. Feasibility studies for molecular epidemiology were worked out for sub-cohorts, and standardized protocols were developed for the measurement of several biomarkers relevant to cancer effects. Methods were proposed to estimate the impacts of uncertainties at several steps of the project.

Conclusions
Based on CURE protocols, a multidisciplinary research project will be proposed to improve the characterization of the biological effects associated with uranium exposure, and the quantification of related cancer risk.
Funding source
European Commission, through the 7th Framework Program Network of Excellence DoReMi (http://www.doremi-noe.net/)

E-188 - EPI-CT: Epidemiological Study To Quantify Risk For Paediatric Computerized Tomography And To Optimize Doses

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Purpose – The increasing worldwide use of paediatric computed tomography (CT) led to increasing concerns regarding the iatrogenic effects of ionizing radiation on children. Recent national studies on paediatric CT reported increased risks of childhood leukaemia and brain cancer. Uncertainties on the risk estimates remain as these studies often lack information on the medical history of the patients and exposure assessment was based on group-average approaches, rather than on individual data. A large European cohort study (EPI-CT) has been set up to further evaluate the potential risk of cancer associated with CT exposures in childhood.

Methods –EPI-CT uses a common protocol implemented in Belgium, Denmark, France, Germany, the Netherlands, Norway, Spain, Sweden and the United Kingdom. Demographic information and technical data on CT are obtained from records of radiology departments. Passive follow-up is conducted by linkage to population-based registries. Individual organ doses are estimated via a simulation approach which produces alternative realizations of doses. The feasibility of studying different biomarkers of radiation sensitivity at young ages was also tested.

Results – This study is unique because of its size (more than a million patients), sophisticated dosimetry and the attention paid to characterise possible bias factors including missing doses from other procedures or missed CTs, confounding by SES and by indication. It will strengthen the scientific evidence on the effects of low doses of ionizing radiation in young people.

Conclusions – To ensure that CT scanning remains beneficial, radiation dose should be kept as low as possible while ensuring sufficient diagnostic quality. Reducing exposure from CT scanning will impact the global cancer burden since the number of procedures increases worldwide.

Funding sources: This work was supported by the European Community's Seventh Framework Programme (FP7/2007–2013) (grant number 269912). Complementary funding from ministries, national institutions and cancer associations was obtained in participating countries.

E-189 - Perinatal And Early Life Risk Factors For Childhood And Adolescent Melanoma

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Purpose: Melanoma, the deadliest form of skin cancer, is the 2nd most common cancer diagnosed under 30 years of age in the US, where more than 75,000 new melanomas occur annually. Nearly 9,000 will occur in California. Known risk factors for melanoma have been assessed from studies in adults over 50 years, so current knowledge may not reflect important contributors to pediatric, adolescent, and young adult melanoma, which represents early onset disease likely to have distinct age-specific risk factors or windows of susceptibility that differ from older adults. Striking gender differences by age exist, where younger females are at much greater risk of melanoma than men, and in older adulthood the opposite is true.
Methods: We conducted a population-based, case-control study of Californians (1,396 melanoma cases and 27,920 controls, obtained by linking cancer registry data to birth records) to investigate the association of melanoma and early life risk factors, including early life ambient ultraviolet radiation(UV) and infant birthweight, along with interactions by age and race/ethnicity.
Results: Higher UV exposure was significantly associated with 26-43% higher odds of melanoma depending on age at diagnosis, but particularly for ages 15-19yrs. High birthweight versus normal birthweight was associated with 20% increased odds(OR:1.20;95%CI:1.03-1.41), while low birthweight appeared protective(OR:0.58;95%CI:0.42-0.80) after adjustment. Among Hispanic persons, odds of melanoma at ages 0-5 were 3 times the odds of melanoma at ages 25-29 (OR:3.05;95%CI:1.50-6.17).
Conclusions: Higher birthweight and UV in early life are important melanoma risk factors for early onset disease. Early UV exposure may play a particularly strong role in melanomas at ages 15-19, while persons of Hispanic background may be more likely to get a melanoma in early childhood than as a young adult.
Funding: This work was supported by the NIEHS R21ES018960, R21ES019986, P30ES007048, by the NCI and the NICHD under grant R01CA158407.

E-190 - Radiation Doses From X-Ray Guided Cardiac Catheterizations In Children And Young Adults In The UK

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Purpose: Cardiac catheterizations are x-ray guided procedures used to diagnose and treat both congenital and acquired heart conditions. The radiation doses can be relatively high, raising concerns over the increased risk of developing cancer.

Methods: A cohort of around 13,000 patients who underwent cardiac catheterizations in the UK, while aged under 22 years, was established. Individualised, examination specific dose estimates were calculated using Monte Carlo computer simulations, based on exposure indicators recorded at the time of each procedure. Cohort members were matched with the National Health Service Central Registry (NHSCR) to determine cancer incidence.

Results: 109 malignancies of all types were observed, verses 37 expected (SIR=2.94, 95% CI: 2.41, 3.56). Leukaemia (SIR=4.3, 95% CI: 2.87, 6.18), lymphoma (SIR=5.92, 95% CI: 4.04, 8.38) and cervical cancer (SIR=9.32, 95% CI: 4.55, 16.89) were also significantly raised. Half of these malignancies developed in patients who were identified as having undergone organ transplantation. Removing these patients, who made up around 5% of the cohort, reduced the SIR to 1.67 (95% CI: 1.25, 2.18). There was little suggestion of a clear relationship between cumulative radiation dose and excess risk of developing cancer. Most malignancies developed outside the thoracic region, with no cases of lung, breast, oesophageal or stomach cancer being identified. Considering only cases developing 5 years (solid cancers) or 2 years (leukaemia) following the first recorded exposure, the SIR was reduced to 2.13 [95% CI: 1.48, 2.97].

Conclusions: Children and young adults undergoing cardiac catheterizations appear to have a significantly higher incidence of cancer than the general population. This appears to be mainly due to factors other than radiation. The impact of transplantation on risk must be taken into account in medical radiation epidemiological studies. Further studies following enlargement of the cohort will follow.

Funding source: British Heart Foundation

E-191 - In Utero Exposure To Ionising Radiation And Cancer Risk In The Southern Urals, Russian Federation

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Background: Limited evidence is available on whether in utero exposure to low-dose ionizing radiation increases the risk of cancer over the lifetime.
We report on the analyses of two in utero exposed population cohorts from the Southern Urals (Russian Federation).

Methods: The respective cohorts comprised 8466 offspring of female workers of a large nuclear facility (the Mayak Production Association) and 11,470 offspring of women living in areas along the Techa River contaminated by nuclear accidents and nuclear waste from the same facility, with detailed dosimetry. Excess relative risk (ERR) and relative risks (RR) models were used to estimate the hematological and solid cancer risks over the lifetime associated with in utero exposure, adjusted for post-natal exposure, age, sex and ethnicity.

Results: The combined cohort totaled 700,504 person-years at risk over the period of hematological malignancies incidence follow-up, yielding 58 incident cases. The adjusted risk of hematological malignancies was increased in subjects who received elevated in utero doses (ERR: 1.27; 95% confidence interval [CI]: -0.20 to 4.71, for doses above 80 mGy), and the risk increased consistently per 100 mGy of continuous exposure in utero (ERR: 0.77; 95% CI: 0.02 to 2.56).
During the 554,411 person-years at risk in the solid cancer analyses, 369 cases were observed, showing a RR of 0.72 (95% CI = 0.39 to 1.22) for in utero doses above 80 mGy.

Conclusions: The results suggest a positive association between in utero exposure to ionizing radiation and risk of hematological malignancies up to age 60, but the small number of outcomes precludes firm conclusions. There was no evidence of an association between solid cancer risk and in utero radiation exposure in the current data. Continuation of cancer follow-up in this unique combined cohort is important given the relatively young age of cohort members with respect to cancer.

F-192 - Effects Of Cigarette Smoking, Green Tea Consumption, MicroRNA-29b, And Its Target DNMT3B On Lung Cancer Development

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Green tea can prevent cancer. However, its inhibitory mechanisms on smoking-induced lung cancer are unclear. In the tumor development, the increased expression of DNA methyltransferase (DNMT) was observed, and this expression was downregulated by increased micro (miR)-29b expression. Especially, cigarette smoke and tea polyphenols might influence the DNMT3B expression by regulating the miR-29b expression. Therefore, we designed a case-control study to evaluate the effects of cigarette smoking, green tea consumption, and expressions of miR-29b and DNMT3B in the development of lung cancer. A total of 71 lung cancer patients and 71 healthy controls were recruited to measure expressions of miR-29b and DNMT3B mRNA in whole blood by real-time polymerase chain reaction in the present study. Questionnaires were administered to obtain the epidemiological and clinical characteristics. Results revealed, among healthy controls, smokers had a significantly lower miR-29b expression than nonsmokers. After adjusting the effects of confounding factors, compared to the subjects with the combination of higher miR-29b expression/lower DNMT3B mRNA expression, subjects with other combinations of miR-29b and DNMT3B mRNA expression had a 3.36-fold (95% C.I. = 1.11-10.17) increased risk for lung cancer development. Significant interactions of smoking with miR-29b and with DNMT3B mRNA expression on lung cancer development were observed; respectively. Significant interaction of green tea consumption and DNMT3B mRNA expression on lung cancer development was also observed. Our study suggested smoking might reduce the miR-29b expression. Smokers with lower miR-29b expression and higher DNMT3B mRNA expression, and green tea nondrinkers with higher DNMT3B mRNA expression were susceptible for lung cancer development.

Keywords: green tea, smoking, lung cancer, miR-29b, DNMT3B

F-193 - Smoking And Risk Of Breast Cancer According To Hormone Receptor Status In A Racially/Ethnically Diverse Population

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Purpose: To examine the risk of breast cancer from smoking for women diagnosed with Estrogen Receptor (ER) +, ER-, Progesterone Receptor (PR) + and PR- tumors.
Methods: From 1993 to 2010, we followed 83,300 women who were enrolled in the Multiethnic Cohort Study at 45–75 years of age. We identified cancer cases via linkage to the Surveillance, Epidemiology, and End Results Program cancer registries that covered the states of Hawaii and California through December 2010. We used Cox proportional hazards models to estimate hazard ratios (HR)s and 95% confidence intervals (CI) while adjusting for a priori selected confounders. .
Results: During a mean follow-up of 14.6 years, 4,484 women developed invasive breast cancer, of whom 560 (12.5 %) had unknown status for hormone receptor. Altogether, 3,183 (71.0%) women were diagnosed with ER+, 730 with ER-, 2,541 (56.7%) with PR+ and 1,151 with PR- breast cancer. Women who had smoked for more than 5 years before their first childbirth had an overall HR for ER+ breast cancer that was 31% higher (95% CI 1.11- 1.54) compared with parous never smokers. The corresponding HR for ER- breast cancer was 0.99 (95% CI 0.68 - 1.44). Among women who had a PR+ tumor status, the risk was 26% higher (HR = 1.26, 95% CI 1.05 - 1.52) and for PR- breast cancer 25% higher (HR = 1.25, 95% CI 0.95 - 1.64). The $P_{interaction}$ by tumor status was 0.22 for ER+/ER- tumors and 0.63 for PR+/PR- tumors.
Conclusions: For parous women who had smoked more than 5 years before their first childbirth, we found a smoking-related increase in breast cancer risk for both ER+ and PR+ tumors. These risks did not differ significantly by hormone receptor positive and negative tumors.
Funding source: Grant U01 CA164973 from the US National Cancer Institute.

F-194 - Smoking And Risk Of Lung Cancer, According To Cell Type By Gender In A Norwegian Cohort Of 600,000 Participants

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Purpose
In Norway in 2013 lung cancer (LC) was the second most common cancer among men and the third most common cancer among women. Trends by histological type have shifted over time and in 2013 adenocarcinoma was the most frequent subtype, and squamous cell carcinoma ranked second. The purpose of the study was to examine by gender LC incidence overall and by subtype according to smoking history in a Norwegian prospective cohort.

Methods
We followed 585,583 Norwegian men and women born between 1897 and 1975, recruited from three different cohort studies conducted from 1974 to 2003, by linkage to national virtually complete registries through December 2013. We used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals for the association between ever versus never smoking status at enrolment and LC histological subtypes. We used multivariable analyses stratified by birth cohort and cohort study, and tested for heterogeneity by BMI, attained education and physical activity.

Results
During 11.6 million person-years, with a median follow up of 20 years, LC occurred in 3.714 men and 2.820 women. Among men 38% and 25% of the LC cases were adenocarcinoma and squamous cell carcinoma, respectively. For women the corresponding figures were 40% and 13%, respectively. Among men, ever smokers had an increased adenocarcinoma risk (HR= 6.93; 95% CI: 5.36-8.94), compared with never smokers. For women, this HR was 6.38 (95% CI: 5.25-7.76). For squamous cell carcinoma the HR was 35.16 (95% CI: 18.22-67.84) for men, and 37.94 (95% CI: 18.77-76.70) for women.
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Conclusions
Our findings suggest that, in Norway, adenocarcinoma is the most frequent LC cell type in both men and women, and that squamous cell carcinoma is more strongly associated with ever smoking in both sexes.

Funding: The project is supported by the Northern Norway Regional Health Authority.

F-195 - Tobacco, Alcohol And Head And Neck Cancer In Three Brazilian Regions

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Objective. In this case-control study, we compared the probabilistic reasons of risk of smoking and alcohol consumption in the Head and Neck Cancer (HNC) in three Brazilian regions: Midwest, Southeast and South. Method. The study included 1.594 cases of HNC and 1.292 hospital controls. Odds ratio and respective intervals with 95% confidence were estimated by unconditional logistic regression with adjustment for age, sex, education, consumption of fruit and vegetables, smoking (for exam of alcohol effect) and alcohol consumption (for exam of smoking effect). It was also calculated the attributable proportion risk (APR) of tobacco and alcohol in the HNC. Results. The effect of smoking in HNC was more significant in the population of the Midwest compared to those of the Southwest and South. On the other hand, the alcohol abuse induced major risk of HNC in the population of Southwest and Midwest of Brazil. Conclusion. These results suggests distinct profiles of culture and customs in the populations that influence the patterns of consumption of tobacco and alcohol.

F-196 - Mentioning Smoking On Death Certificates: Health Benefits Of Quitting In The Hong Kong Mortality Case-Control Study

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Purpose: Evidence on the benefits of stopping smoking in developing countries to help curb the growing tobacco epidemic is scarce and urgently needed. Mortality case-control study has yielded timely evidence on the hazards of smoking. We aimed to investigate its application on quitting. **Methods**: The Lifestyle and Mortality study was a case-control study that included 81% of all deaths age 30+ years in 1998 in the death registries of Hong Kong by interviewing relatives. Cases were deaths from smoking-related causes (N=19,526) and controls were deaths from non-smoking related causes (N=6,076) following Sitas et al 2013. Unconditional logistic regression yielded adjusted odds ratios (AORs) of all smoking-related causes and cancers by duration of quitting and age at quitting (both compared with continued smoking), adjusting for sex and age at death. **Results**: For duration of quitting, the AORs (95% CI) for all smoking-related causes, were 0.73 (0.58-0.93) in quitters who had stopped smoking for 5-9 years, 0.71 (0.60-0.84) for 10+ years, and 0.49 (0.44-0.56) in never smokers. The corresponding figures for cancers were 0.68 (0.52-0.90), 0.65 (0.54-0.80) and 0.36 (0.32-0.42). For age at quitting, the AORs for all smoking-related causes were 0.80 (0.66-0.95), 0.77 (0.52-1.15) and 0.49 (0.43-0.56) for quitting at the age of 45-64 years, 25-44 years and never smoking. The corresponding figures for cancers were 0.73 (0.59-0.89), 0.67 (0.43-1.03) and 0.36 (0.31-0.42). **Conclusions**: Graded benefits of quitting were observed using the mortality case-control study, which could be a quicker and cheaper alternative to cohort studies in examining the hazards of smoking and benefits of quitting. Smoking history should be recorded during death registration for long-term sustainable monitoring. This change is unlikely to be adopted by governments, unless this is recommended by WHO. Strong advocacy is needed. **Funding**: HK Health Services Research Committee (631012) and HK Council on Smoking and Health.

F-197 - The Fraction Of Cancers Attributable To Tobacco In Wales, In 2013

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Purpose:
In 2011, a landmark study estimated that 42.7% of all cancers each year were attributable to lifestyle and environmental factors in the UK (Parkin et al. 2011). This information has been an important component in influencing public health decisions. However, there is a wide variation in exposure prevalence between UK-constituent countries. In addition, the cancer epidemiology evidence-base is constantly changing – new aetiological effect sizes have emerged, or become more robust, since 2010.
New calculations are required to establish UK country-specific estimates to inform local public health decisions, and incorporate the most up-to-date risk factor evidence.

Methods:
The proportion of cancers attributable to tobacco in Wales was calculated. Cancer types with sufficient evidence in humans for smoking, voluntary and involuntary, as judged by the International Agency for Research on Cancer (IARC) were used.
Smoking exposure data was obtained from 2002 to estimate attributable cancers in 2012 – for current smokers, cohabitation with a smoker and workplace exposure. Systematic reviews were conducted to identify the highest-quality evidence available for tobacco aetiological effect sizes.

Results:
We expect there will be some differences in the proportion of cancers caused by tobacco in Wales compared to the UK; these differences will be explored for multiple cancer types. Research is ongoing at Cancer Research UK to establish estimates for further lifestyle and environmental factors in Wales.

Conclusions:
By using country-specific exposure prevalence, and the latest risk factor estimates, local estimates of the proportion of cancers caused by lifestyle and environmental factors can be derived. These specific estimates will provide valuable information for health organisations in how to tailor public health interventions, and help predict areas for greatest impact.

F-198 - Effects Of Active And Passive Smoking On Human Papillomavirus Infection And Cervical Intraepithelial Neoplasia Grade 2 Or Worse In China: A Pooled Analysis

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Purpose: We performed a pooled analysis to examine cigarette smoking and household passive smoke exposure in relation to the risk of HPV infection and CIN2+.
Methods: Data were pooled from 12 cross-sectional studies for cervical cancer screenings from 10 provinces of China in 1999 – 2007. A total of 16,949 women were analyzed, along with 2,531 HPV positive women and 410 CIN2+ cases. Pooled odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression models controlling for sexual and non-sexual confounding factors.
Results: There was an excess risk between active smoking and HPV infection and CIN2+. Adjusted OR for ever smokers vs. never smokers was 1.45 (95% CI: 1.10-1.91), for HPV infection and 1.89 (95% CI: 1.03-3.44), for CIN2+. Passive smoking had a slightly increased risk on the HPV infection with adjusted OR 1.11 (1.00-1.24), but no statistical association was observed between passive smoke exposure and CIN2+.Compared with the neither active nor passive smokers, both active and passive smokers had a 1.57-fold (95% CI: 1.14-2.15) increased risk of HPV infection and a 1.99-fold (95% CI: 1.02-3.88) risk of CIN2+.
Conclusions: Our large multi-center cross-sectional study found active smoking could increase the risk of overall HPV infection and CIN2+ adjusted by passive smoking and other factors. Passive smoking mildly increased the risk of HPV infection but not the development of CIN2+ following infection. An interaction exists between passive tobacco exposure and active smoking for HPV infection and the CIN2+ risk, but needs to be confirmed in further prospective studies including more cases.
Funding source: Our work was supported by the National Natural Science of Foundation of China (No 81322040).

F-199 - Calculating Baseline Risk For Non-Drinkers From Population Lifetime Risk Estimates: Communicating Alcohol Guidelines

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Purpose: National guideline limits for the consumption of alcohol should be communicated using robust calculations of risk of disease at different levels of consumption. Using population lifetime risk figures as the baseline for these calculations overestimates the risk for alcohol drinkers, because population lifetime risk includes all levels of exposure, from non-drinkers to heavy drinkers. We present a methodology to calculate a reasonable baseline (lifetime risk for non-drinkers), using the recently revised UK alcohol consumption guidelines as an example, and present the differences in absolute risk for alcohol drinkers when calculated using the general population, or non-drinkers, as the baseline.

Methods: Risk figures based on two baselines were compared. The first uses UK 2012 lifetime risk estimates for all cancer types classified by IARC as caused by alcoholic beverages: breast (female), colorectal, laryngeal, liver, oesophageal, oral cavity and pharyngeal cancers. The comparator was a non-drinkers baseline calculated by applying the population distribution of a range of drinking levels to the relative risks (RRs) for those drinking levels, and combining them to find the lifetime risk for non-drinkers which, when used as the baseline to calculate lifetime risk for different levels of drinking, gives a total population lifetime risk as near as possible to the general population baseline.

Results: The two different baselines generated markedly different lifetime risk estimates for all cancer types. The largest differences were found in cancer types where the relative risk with alcohol consumption is higher, and in populations where higher alcohol intake levels are more common.

Conclusions: Reasonable baseline lifetime risk estimates can be produced using population distribution of risk exposure and relative risk at each exposure level. This methodology can be applied to other risk factors, such as tobacco or overweight, where exposure prevalence and RRs are known.

Funding source: Cancer Research UK.

F-200 - Trends In Incidence And Mortality From Lung Cancer, São Paulo, Brazil

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Purpose: estimates from the International Agency for Research on Cancer, indicate approximately 1.8 million new lung cancer (LC) in 2012 alone. This study aimed to verify trends in incidence and mortality from lung cancer in São Paulo.
Methods: incident lung cancer cases (code C34 in ICD-10) from 1997 to 2012 were obtained from the Population-based Cancer Registry in São Paulo. Deaths were obtained from DATASUS database for the same period (1997 to 2012) and ICD-10 code (C34). The incidence and mortality rates (per 100,000) were calculated based on the population provided by IBGE and adjusted for the world population of SEGI. The trend analyzes were carried out for incidence, mortality and age groups (40-49, 50-59, 60-69, ≥70 years), using the Joinpoint software. The results were presented as annual percent change (APC).
Results: 27,107 incident cases (62.5% in men) and 23,842 deaths (63.9% in men) occurred in the period. There was a significant reduction in incidence of -7.6%/year and 3.5%/year in men and women, respectively. This pattern was seen for all age groups and both sexes. In regards to mortality, decreasing trends, though less pronounced (2.3%/year), were observed for men. As for women, mortality has been increasing 0.7% annually. This increase is more accentuated in women aged 50 and older. Mortality remained stable for women aged 40-49 years.
Conclusion: the important reduction in incidence of lung cancer for both sexes, which seems to be a related to the decreasing trends in tobacco smoking prevalence in the Municipality of São Paulo, a result of anti-tobacco policies.
Funding source: Conselho Nacional de Desenvolvimento Científico e Tecnológico and Fundação de Amparo à Pesquisa do Estado de São Paulo.

F-201 - A Common Variant On 2q31.3 Reduces Lung Cancer Risk Among Light Smokers: Transdisciplinary Research In Lung Cancer Consortium

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Heavy smoking increases the risk of lung cancer(LC) by 50-fold. However, the lifetime risk of LC is between 15-20% even among heavy smokers, raising the question whether there may be protective factors that mitigate the carcinogenic risk of smoking. Previously, we have shown significant gene-smoking interactions on chromosome 15q25.1, with genetic variants in this region associated with minimal increased risks of LC among never smokers, but substantially increased risks among smokers. Studies contrasting LC risk between heavy and light smokers have not been conducted, and little is known about protective factors that may reduce LC risk for certain smokers.

To identify genetic factors that may reduce LC risk by levels of smoking, we conducted a genome-wide case-only analysis to detect gene-smoking interactions for LC, comparing heavy(≥30 cigarette pack-years) versus light smokers(<30 cigarette pack-years). The case-only design provides improved power for detecting interactions provided there is no correlation between the genetic and the environmental factors in the underlying population. Genotype data for 4,639 heavy smoker cases and 1,824 light smoker cases were meta-analyzed from 7 studies within the Transdisciplinary Research in Cancer of the Lung(TRICL) consortium.

The most significant gene-smoking interaction was found on 2q31.3 with rs62180069(P=5x10-8; OR=0.76). This SNP lies between the SCHLAP1 gene encoding the SWI/SNF complex antagonist associated with prostate cancer 1 and the UBE2E3 gene. While this variant showed no association with risk of LC among heavy smokers(OR=1.03; 95% CI:0.94-1.13), it significantly lowered the risk of LC among light smokers(OR=0.85; CI:0.78-0.93). There was no evidence of gene-smoking correlation among controls and no evidence of heterogeneity in the associations across studies.

Our large-scale meta-analysis identified a protective genetic variant for LC that reduces the risk of disease among light smokers. Further studies are needed to characterize the biological mechanism underlying the interaction between rs62180069 and smoking behavior.

F-202 - Screening And Brief Intervention For Distress, Alcohol And/Or Tobacco Consumption: An Epidemiological Study In An Oncology Surgical Department

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Purpose: Alcohol and tobacco consumption have been shown to reduce treatment efficacy, increase side effects, encourage relapse and/or secondary cancers and affect the quality of life of patients being treated for cancer (Barrault et al, 2012). Despite scientific, clinical and political incentives, alcohol and/or tobacco screening and brief intervention (SBI) services are poorly implemented in primary health care settings. This study aims to describe the clinical characteristics (distress and consumption) of cancer patients included in a SBI pilot program in a surgical department in Bordeaux. To our knowledge, this is the first epidemiological study on alcohol/tobacco SBI in a cancer treatment center in France.

Methods: A descriptive analysis of clinical and epidemiological data of cancer patients admitted in the surgical department and consenting to participate to the SBI pilot program (consisting of a single brief motivational interview) at Institut Bergonié from September 2014 to August 2015.

Results: Among the 252 screened patients (94% women; mean age 55 ± standard deviation of 14.1 years, range 18 to 91 years; 81% treated for primary cancer, 48% for breast cancer), almost one in two (49%) patients presented with emotional distress. Twenty-six percent were tobacco smokers, 20% presented a risky alcohol use and 49% were regular alcohol consumers.

Conclusions: The results are consistent with epidemiological studies of alcohol/tobacco use on the general population showing that people continue their risky behavior after a cancer diagnosis. It also demonstrates that distress is common among this population. These data strongly support that helping people identify and cope with their risky behavior and emotional needs should be a part of routine health care in a cancer setting, in order to reduce morbidity-mortality from cancer. Further research is needed to measure the efficacy of SBI in this context.

Founding source : Ligue Nationale Contre le Cancer (2013-2016)

F-203 - Qat Use And Oesophageal Cancer In Ethiopia: A Pilot Case-Control Study

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Purpose of pilot study:
To assess the feasibility for a multi-center case-control study of oesophageal cancer (OC) in Addis Ababa and to generate preliminary estimates on the association between the occurrence of OC and suspected (qat use) and established (tobacco and alcohol) risk factors.
Methods:
All consenting OC cancer patients seeking cancer treatment in Addis Ababa University Teaching Hosptal or diagnostic services in two endoscopy clinics in the city between May 2012 and 2013 were enrolled. Two controls (hospital, hospital visitor) were matched to cases on sex, age (± 5 years) and place of residence. A face-to-face structured questionnaire was administered. Odds ratios (OR) with 95% confidence intervals (95% CI) were calculated using conditional logistic regression.
Results:
Findings are reported on a total of 206 participants, including 73 OC cases and 133 controls (40 hospital and 93 healthy visitors). Only 8% of OC cases enrolled resided in Addis Ababa. Ever tobacco use (OR: 3.31, 95% CI: 0.53, 20.6; p=0.20) and ever alcohol use (OR: 2.30, 95% CI: 0.32, 16.5; p=0.41) were associated with elevated risk of OC as compared to never users, although confidence intervals were wide. Our study showed no overall excess risk of OC in association with ever qat use (OR: 0.95, 95% CI: 0.22, 4.22), but an association in non-tobacco users. Other factors associated with increased risk of OC included low consumption of green vegetables and high salt intake, education and religion.
Conclusions:
We report for the first time tobacco, alcohol and qat-associated OC risk estimates in Ethiopia, though based on an unrepresentative pilot study. A large case-control study, with proper sample size, and enrolment of cancer cases at health facilities from the country side (where the majority of cases occur) is needed to confirm findings, particularly of qat chewing and elevated OC risk in non-tobacco users.

F-204 - Fraction Of Cancers Attributable To Tobacco Smoking In France

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Purpose: To estimate the population attributable fraction (PAF) and associated numbers of cases for various cancer sites in France in 2012 due to both active and domestic passive tobacco smoking.
Methods: We extracted age- and sex-specific population and national estimates of cancer incidence for France, and incidence rates of lung cancer among never-smokers and risk estimates for smoking and various cancers from the American Cancer Prevention Study (CPS II). For active smoking, we applied the Peto-Lopez method to estimate the PAF for lung cancer and applied the Levin's formula to estimate the PAF for other sites. Using survey-based smoking prevalence in France and marital status data to calculate the proportion of non-smokers living with an ever-smoker partner. Using the relative risks for second-hand smoking we estimated the PAF for lung cancer due to domestic passive smoking.
Results: Among cancer sites included, 47,892 (52%) and 12,645 (26%) cancer cases for men and women between age 35 to 84 respectively in France in 2012 were attributable to tobacco smoking. Among males, tobacco smoking accounts for 23,693 lung (PAF 89%), 6,279 oral cavity & pharyngeal (82%), 3,405 bladder (42%), and 2,820 kidney (39%) cancer cases. Among females, it is responsible for 7,045 lung (68%), oral cavity & pharyngeal (49%), 773 colorectal (5%) and 767 ovarian (19%) cancer cases. Domestic passive smoking is responsible for 47 (4.5%) and 62 (2.8%) lung cancer cases among male and female never-smokers in France.
Conclusions: Tobacco smoking is responsible for over 40% of the cancer cases from major cancer sites. More effective tobacco control programmes are therefore essential to reduce the cancer burden in France.
Funding Sources: French National Cancer Institute

F-205 - Trends In Incidence And Mortality From Tobacco-Related Cancers, São Paulo, Brazil

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Purpose: Tobacco smoking is the most important modifiable risk factor for cancer. According to WHO, there is one billion smokers worldwide and half of them will die from tobacco-related illnesses. The aim of the present study was to assess trends in incidence and mortality of tobacco-related cancers in São Paulo, Brazil, between 1997 and 2012.
Methods: We selected topographies for which there is sufficient evidence, for their association with tobacco: head and neck (oral cavity, pharynx, nasal cavity and accessory sinuses, larynx), esophagus, stomach, colon-rectum, liver, pancreas, lung, cervix, ovary, urinary tract and myeloid leukemia. Incident cases were provided by the Population-based Cancer Registry of São Paulo and deaths were obtained from the Department of Informatics of the Unified Health System. The incidence and mortality rates were calculated based on the population provided by Brazilian Institute of Geography and adjusted for the world population of SEGI. The trend analyzes were carried out according to sex, using the Joinpoint software. The significance level was set at 5%.
Results: Some 195,332 newly (53.2% in men) diagnosed cases and 114,745 deaths (57.3% in men) occurred from tobacco-related cancers between 1997 and 2012. Incidence decreased for head and neck, esophageal, gastric, pancreatic, colorectal, lung, urinary tract (men only), cervical, ovarian cancer and myeloid leukemia and increased for liver in women. As for mortality, head and neck, esophageal, gastric, cervical, ovarian cancers and myeloid leukemia significantly decreased, whereas, liver and colorectal cancers in men and lung in women have shown increasing trends.
Conclusion: Important reductions in the burden of several tobacco-related cancers may reflect, to some extent, decreasing trends in tobacco-smoking prevalence in São Paulo, which in turn is a result of anti-tobacco efforts in Brazil. Increasing trends for some cancers indicate that other risk factors might be becoming gradually important in this context.

F-206 - Geographical Patterns And Time Trends In Prevalence Of Cigarette Smoking And Water-Pipe Use In Iran: Analysis Of Pooled Data Of Six Consecutive Rounds Of National Survey, 2004-2011

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PURPOSE: To estimate the prevalence of daily use of tobacco products including cigarette and water-pipe in Iran, and to investigate the geographical patterns and time trends of tobacco use in Iran.
METHODS: We pooled the data of six consecutive rounds of STEPS survey in Iran from 2004 to 2011, to obtain a representative sample of about 4,000 Iranian adults aged 15-64 years for each province (30 provinces). Complex sample survey analysis was utilized to estimate percentages with daily cigarette smoking, daily use of water-pipe, and dual use of the products over the years of study at both national and province levels by gender, residential area, and age-groups. We also employed a multiple logistic regression model to estimate Odds Ratio (OR) and 95%CIs to evaluate the trends over time.
RESULTS: The total prevalence of cigarette-only smokers, water-pipe-only users, and dual smokers were estimated 10.7%, 2.2%, and 0.4% in Iran, respectively. The prevalence of the daily use of water-pipe significantly decreased from 2004 to 2011 (OR=0.9; P<0.0001). For cigarette smoking, no significant trend was observed over the years of study (OR=1.0; P=0.898). The prevalence of daily cigarette smoking ranged from 6.3% in Bushehr province in the southern Iran to 14.6% in West Azerbaijan province in the northwestern part of the country. In addition, the percentage with daily use of water-pipe ranged from 0.6% in Ilam province in the western part of Iran to 12.4% in Bushehr in the southern Iran.
CONCLUSION: We used national data and conducted a large study and reported pattern of tobacco consumption in overall and by type of tobacco use in Iran. Geographical pattern of smoking was opposite to the pattern of water-pipe consumption. Research is needed to evaluate health impact of waterpipe use in Iran, in particular, in the high prevalence provinces.

F-207 - Attitudes Toward The Tobacco Epidemic Among Gender And Sexual Minority Groups In The United States

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PURPOSE: Approximately 4% of adults in the United States self-identify as Lesbian, Gay, Bisexual, or Transgender individuals (LGBT), corresponding to about 9 million adults. There is reason to believe that cancer risk in this group is higher than the general population. However, few studies have examined how individuals from sexual and gender minorities perceive tobacco use and its health consequences. To address this gap, we conducted a community tobacco survey at local non-governmental organizations, health care facilities, and during the 2014 and 2015 editions of the Houston Pride Parade and Festival.
METHODS: A cross-sectional survey (20 items) examined tobacco use, health risk perception, attitude toward the tobacco industry, sexual orientation, and other socio-demographic factors. Trained surveyors used a paper-and-pen instrument, and results from 279 completed surveys from self-identified LGBT individuals were analyzed.
RESULTS: The mean age of participants was 31 years (SD=11.0). The majority self-identified as gay (22%) and transgender (42%). Current cigarette use (every day or some days) among respondents was high (26%). However, there was no strong perception among study participants of high tobacco use prevalence among gender and sexual minorities. Most of the participants either agreed or strongly agreed with accepting sponsorship money from the tobacco industry for LGBT organizations/events/establishments. Interestingly, most of the respondents agree that there is too little emphasis on smoking as a health issue in the LGBT community.
CCONCLUSION: These preliminary findings confirm the high prevalence of tobacco use among gender and sexual minority groups. While these high rates are cause for concern, this effort provides important information that will be used for targeting interventions to prevent and reduce tobacco use in this vulnerable population in the state of Texas.

F-208 - A Comprehensive Review Of Cigarette Smoking And Cancer Treatment: A World Health Organization Tobacco Use Knowledge Summary

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Purpose: This WHO Tobacco Knowledge Summary aims to qualitatively summarize the evidence for the adverse effects of post-diagnosis smoking on cancer treatment and its outcomes. The resulting summary will serve as a tool to involve healthcare providers in the fight against smoking in the cancer population.
Methods: We searched for systematic and comprehensive reviews regarding the effects of post-diagnosis smoking on cancer treatment and its outcomes in three databases, PubMed, Web of Science, and Cochrane Library. Inclusion and exclusion criteria were then used to select the articles for review.
Results: Out of 1,020 identified articles, 14 review articles were selected for appraisal. The preliminary review showed evidence of the adverse impact of post-diagnosis smoking on treatment outcomes including progression, recurrence, and survival. The evidence of adverse impact was strong for lung and head and neck cancers, and to a lesser degree, bladder and breast cancers. Data were scarce for non-tobacco-related cancers. The adverse clinical outcomes among patients who continue to smoke after diagnosis can be explained by increased treatment-related complications, altered drug metabolism, or nicotine-induced cell proliferation and inhibition of cell apoptosis, all of which can lead to reduced efficacy of systemic therapy and radiotherapy.
Conclusions: This preliminary review revealed evidence that continued smoking after a cancer diagnosis has negative impacts on cancer treatment and its outcomes, suggesting the need for effective smoking cessation interventions during the course of cancer treatment. Current evidence is limited to few specific types of cancer and treatment. More prospective studies are needed to evaluate both biological and clinical effects of post-diagnosis smoking on different types of treatment and its outcomes, particularly for non-tobacco-related cancers.
Funding source: This work was supported by the European Commission FP7 Marie Curie Actions – People – Co-funding of regional, national and international programmes.

F-208-1 - Gender and Adolescent Attitudes Towards Tobacco Use in 3 Middle Eastern Countries

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Purpose:
The purpose of this paper is to use data collected in the 2009 and 2010 Egypt, Jordan, and Morocco Global Youth Tobacco Surveys (GYTS) to understand the factors that contribute to youth smoking. In response to the growing burden of cancer, greater understanding of gender and geographic/cultural differences in smoking attitudes and behaviors among the youth will inform cancer prevention programs in these countries.
Methods
This study uses GYTS data from Egypt, Jordan, and Morocco in 2009 and 2010. GYTS is a nationally representative survey of 13-15-year-old students using a consistent and standard protocol. Current smoking status is defined as using any tobacco product, such cigarette smoking or hookah use, on at least one day during the 30 days preceding the survey. Associations were computed using SAS software.
Results
Significant differences were observed between boys and girls in all three countries in attitudes and beliefs about tobacco use. While differences between boys and girls were seen in all three countries, the differences were greater in Egypt and Jordan compared with Morocco. Girls were generally more likely than boys to have negative opinions about tobacco use. For example, girls (34.6%) were more likely than boys (25.7%) to say that smoking makes girls and boys look less attractive. Girls (48.5%) were also more likely than boys (35.6%) to believe that exposure to cigarette is harmful. However, there were also differences by country. In Jordan, girls (54.4%) were more likely to believe that exposure to cigarette smoke is harmful compared with girls in Morocco (45.0%) and Egypt (49.1%).
Conclusion
By understanding the attitudes, knowledge and risk behaviors in youth smoking, Ministries of Health and relevant organizations can better design, implement, and evaluate tobacco control and cancer prevention programs in these countries, especially among adolescents.

POSTERS

MECHANISMS

MECHANISMS - Genetics and (epi)genomics

G-209 - Genetic Requirement Of Telomerase-Negative Cancers

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Purpose - Telomere maintenance is required for chromosome stability, and telomeres are typically elongated by telomerase following DNA replication. In both tumor and yeast cells that lack telomerase, telomeres are maintained via an alternative recombination mechanism. Previous studies have indicated that yeast Sgs1 and Top3 may work together to remove highly negative supercoils that are generated from recombination. However, the mechanism by which cells eradicate highly positive supercoils during recombination remains unclear.
Methods - Using various telomeric assays, the ability of telomere recombination in topoisomerase deficient cells was evaluated in yeast and in human.
Results - In the present study, we demonstrate that Top2 is involved in telomere-telomere recombination. Disturbance of telomeric structure by RIF1 or RIF2 deletion alleviates the requirement for Top2 in telomere-telomere recombination. In human telomerase-negative ALT (alternative lengthening of telomere) cells, TOP2α or TOP2β knockdown decreases ALT-associated PML bodies, increases telomere dysfunction-induced foci and triggers telomere shortening. Similar results were observed when ALT cells were treated with ICRF-193, a TOP2 inhibitor. Importantly, ICRF-193 treatment blocks ALT-associated phenotypes in vitro, causes telomere shortening, and inhibits ALT cell proliferation in mice.
Conclusions - Taken together, these findings imply that TOP2 is involved in the ALT pathway, perhaps by resolving the highly positive supercoil structure at the front of the helicase. Inhibition of topoisomerase II may be a promising therapeutic approach that can be used to prevent cell proliferation in ALT-type cancer cells.
Funding source - Ministry of Science & Technology of Taiwan

G-210 - CCDC26, CDKN2BAS, RTEL1, And TERT Polymorphisms In Pediatric Brain Tumor Susceptibility

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Purpose: The role of genetic polymorphisms in pediatric brain tumor (PBT) etiology is poorly understood. We hypothesized that single nucleotide polymorphisms (SNPs) identified in genome-wide association studies (GWAS) on adult glioma would also be associated with PBT risk.
Methods: The study is based on the Cefalo study, a population-based multicenter case-control study. Saliva DNA from 245 cases and 489 controls, aged 7-19 years at diagnosis/reference date, was extracted and genotyped for 29 SNPs reported by GWAS to be significantly associated with risk of adult glioma. Data were analyzed using unconditional logistic regression. Stratified analyses were performed for two histological subtypes: astrocytoma alone and the other tumor types combined.
Results: The results indicated SNPs CDKN2BAS rs4977756 (p=0.036), rs1412829 (p=0.037), rs2157719 (p=0.018), and rs1063192 (p=0.021), were associated with an increased susceptibility to PBTs, whereas TERT rs2736100 was associated with a decreased risk (p=0.018). Moreover, the stratified analyses showed a decreased risk of astrocytoma associated with RTEL1 rs6089953, rs6010620, and rs2297440 (ptrend=0.022, ptrend=0.042, ptrend=0.029, respectively) as well as an increased risk of this subtype associated with RTEL1 rs4809324 (ptrend=0.033). In addition, SNPs rs10464870 and rs891835 in CCDC26 were associated with an increased risk of non-astrocytoma tumor subtypes (ptrend=0.009, ptrend=0.007, respectively).
Conclusions: Our findings indicate that SNPs in CDKN2BAS, TERT, RTEL1, and CCDC26 may be associated with the risk of PBTs. Therefore, we suggest that pediatric and adult brain tumors might share common genetic risk factors and similar etiological pathways.
Funding source: Swedish Council for Working Life and Social Research (2004-0504; 2007-0224), Swedish Research Council (K2008-70X-15366-04-3), Swedish Cancer Society (09 0666), Swedish Childhood Cancer Society (PROJ06/050; PROJ09/086), Swedish Radiation Protection Authority (SSI P 1572), Danish Strategic Research Council (2103-05-0006; 2064-04-0010), Swiss Federal Office of Public Health (05.001626), Swiss Research Foundation on Mobile Communication (A2006.18), Swiss National Science Foundation (PDFMP3_122873), Research Council of Norway (175163/V40).

G-211 - DNA Methyltransferase 3B -149 Genetic Polymorphism Modulates Lung Cancer Risk Elicited By Smoking

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Cigarette smoking can increase stability of DNA methylation, hypermethylation of tumor suppressor genes, and sensitivity for carcinogens, thus subsequently lung cancer will be developed. DNA methyltransferase 3B (DNMT3B) is the key methyltransferase in DNA methylation regulation. Especially, green tea might lower incidence of cancer through the inhibition of DNA methyltransferase activity. Here, we designed a hospital-based case-control study to evaluate the influence of smoking, green tea consumption, and genetic polymorphism of DNMT3B -149 on the risk of lung cancer. A total of 190 lung cancer patients and 380 healthy controls were collected in this study. Questionnaires were administered to obtain demographic data, smoking status, green tea consumption, vegetables and fruits intake, exposure to fumes of cooking, and family history of lung cancer. Genotypes for DNMT3B -149 were identified by polymerase chain reaction. Results showed smoking, green tea consumption, exposure to fumes of cooking, family history of lung cancer, and polymorphism of DNMT3B -149 were significantly associated with development of lung cancer. Compared with nonsmokers who carrying DNMT3B -149 CT genotype, smokers who carrying DNMT3B -149 TT genotype had a higher odds ratio of 2.89 (95% C.I. = 1.17-7.12), and the interaction of smoking with DNMT3B -149 genotype on the risk of lung cancer was statistically significant. However, the test for the interaction between green tea consumption and DNMT3B -149 genotype on lung cancer risk was not significant. Our results suggested that DNMT3B -149 TT genotype with higher promoter activity might increase lung cancer risk elicited by smoking.

G-212 - Local DNA Demethylation Defines HNF4A Promoter Choice During Hepatocyte Differentiation

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Background:
Hepatocellular carcinoma (HCC) is commonly preceded by a chronic disease leading to damage of the liver architecture. During liver injury, hepatic progenitor cells (HPCs) are essential for tissue regeneration through an activation process called “ductular reaction”. Interestingly, poorly differentiated hepatocytes are observed in inflammatory hepatitis and the degree of HPCs’ activation is correlated with the degree of inflammation. Because of its role in determining cellular fate, DNA methylation may have an important function during the process of HPC differentiation.
Results:
To understand the role of DNA methylation during hepatocyte differentiation, we profiled approximately 450k methylation sites at different time points in the progression from progenitor to hepatocyte stages using the bipotent liver progenitor HepaRG cell line. The top most significant differentially methylated region (DMR) was the P1 promoter of HNF4A, a master transcription factor of hepatocyte differentiation. Progressive demethylation of HNF4A P1 was highly correlated with increased expression of P1-dependent isoforms of HNF4A. Gene expression of the TET1 and TET2 demethylases was increased during the early transition towards differentiation. Moreover, TET1 was significantly enriched during this transition at the HNF4A DMR locus, and proximal ligation assays revealed the colocalization of the pioneer hepatocyte transcription factor FOXA2 and TET1 demethylase during differentiation.
Conclusion:
These data supports a model where liver progenitors are poised for targeted demethylation at specific genomic locations involved in terminal stages of hepatocyte differentiation. In addition, intragenic methylation may have a role in controlling cellular programs through isoform switching with a potential role of TETs enzymes in this process.

G-213 - Mendelian Randomization Analysis Of 5p15.33, Telomere Length And Lung Cancer Risk: Results From 14,324 Cases And 10,783 Controls In The Transdisciplinary Research in Cancer of the Lung (TRICL) Group Of The International Lung Cancer Consortium (ILCCO)

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Purpose: Telomere length (TL) has been consistently associated with lung cancer risk, but the direction of this effect remains controversial. To elucidate the causal relationship between TL and lung cancer, we compared results from an observational study and a Mendelian Randomization (MR) analysis, where we developed novel genetic instruments for TL and tested their association with lung cancer in 20 pooled TRICL/ILCCO studies.

Methods: The observational analysis estimated odds ratios (OR) for TL, measured using qPCR, in 1128 cases and 928 controls. To develop novel TL instrumental variables (IVs), variants identified through deep-sequencing of 5p15.33 (*TERT*/*CLPTM1L*) were genotyped in 900 controls. Variants meeting MR criteria were combined into a single IV. Six SNPs from previously identified TL genes (*ACYP2*, *TERC*, *NAF1*, *OBFC1*, *DHX35*, *RTEL1*) were used as additional IVs. Associations with lung cancer for all IVs were estimated using data from 14324 cases and 10783 controls, and applied in a likelihood-based MR model to estimate the causal effect of TL.

Results: The observational analysis suggested that longer TL was inversely associated with lung cancer risk (OR=0.94, p=0.04), especially squamous carcinoma (OR=0.77, $p=1.1\times10^{-4}$). In the first MR stage, we identified 8 5p15 SNPs associated with TL ($p<5\times10^{-3}$), including 6 novel rare variants, not previously reported. The combined 5p15.33 IV was reliably associated with TL ($\beta=0.15$, $p=1.8\times10^{-7}$) and explained 2.3% of TL variance. Using this instrument and 6 other SNPs as IVs, our MR analysis showed that longer TL predisposes to increased lung cancer risk (OR=1.77, 95% CI=1.32-1.54), especially for adenocarcinoma (OR=2.02, 95% CI=1.29-3.71).

Conclusions: This largest MR analysis of TL and lung cancer, using individual-level data and novel genetic instruments, demonstrates that longer TL is associated with increased lung cancer risk. Previously reported inverse associations for long TL were likely due to residual confounding and reverse causation.

Funding Source: CIHR (CGS-137441)

G-214 - Functional Analysis Of Novel Germline TP53 Variants

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Purpose: Li-Fraumeni Syndrome (LFS) is a rare autosomal dominant familial cancer syndrome, characterized by multiple malignancies and frequent germline alterations in *TP53*. In this study, we highlight four unclassified exonic p53 variants detected in patients with a suspected diagnosis of LFS. Given the unknown clinical significance of these variants, we sought to uncover their impact on p53 function and tumor development.

Methods: Using site-directed mutagenesis, we generated pCMV-plasmids carrying the aforementioned p53 mutants. *TP53*-null H1299 and SAOS-2 cells were subsequently assayed using the Dual-Luciferase Assay to examine p53 transactivation levels. The tumor suppressive capacity of these p53 variants was also assessed by colony formation and Western blotting.

Results: We report for the first time the discovery of two novel functional variants in codons 191(c.572C>G; p.P191R) and 360 (c.1079G>T; p.G360V), located, respectively, in the DNA binding domain and in a linker region near the tetramerization domain of *TP53*. Our data revealed that while the P191R variant decreased the transactivation levels of several p53 targets (RGC, p21 and BAX), it failed to segregate with disease status. The G360V variant, on the other hand, behaved in a paradoxical fashion by causing a stark upregulation in the activity of the same p53 response elements. This enhanced tumor suppressive effect was also observed at the level of colony formation and caspase-3 activation.

Conclusions: We report the discovery of two novel functional p53 polymorphisms, P191R and G360V, which may act as phenotypic modifiers in LFS. While the P191R led to a decrease in p53 transactivation, the G360V variant caused a dramatic activation of p53 response elements. In the future, the enhanced transactivation effects of G360V-p53 may prove useful in designing more efficacious p53-based gene therapies.

Funding source: Canadian Institutes of Health Research (#MOP-300105).

G-215 - Identification Of Gene Expression Profile Of Laryngeal Squamous Cell Carcinoma

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Laryngeal squamous cell carcinoma (LSCC) is a common head and neck cancer, being one of the most incidence tumors in the world, especially in developing countries, such as Brazil. The main risk factors for LSCC are tobacco and alcohol consumption and it usually occurs in patients older than 60 years. Similarly to others head and neck tumors, LSCC is a major health problem because of poor prognosis and slight improvement in the five-year survival during the past four decades. Aiming to better understand the molecular changes present in LSCC, we carried out a gene expression profile analysis using the Affymetrix Human Exon 1.0 ST microarray chip. To this end, 14 tumor tissues were compared with 12-matched non-malignant surrounding mucosa, resulting in 245 up-regulated and 449 downregulated genes in tumor. Principal component analysis and Bayesian hierarchical clustering showed that the global gene expression profile observed in tumors is distinct from that their adjacent mucosa. Enrichment analyses of the differently expressed genes (DEG) were performed in order to understand which molecular changes are occurring and which molecules were responsible for this gene expression profile. Moreover, aiming to identify the main altered cellular signaling pathways, we analyzed our data in KEGG database and was the signaling pathways related to cellular adhesion, drug and xenobiotics metabolism, immune and inflammatory response, pathways related to cancer, among others, were pointed out as the most altered. In addition, the transcription factors regulators analysis identified the transcriptional factors E12, AP1, FOXO4, NFAT, LEF1, CHX10 and MAZ as possible gene expression main regulators in laryngeal tumors. Further, to this purpose, 54 microRNAs were observed as possible candidates involved with the regulation of DEG. Funding Source: Ministério da Saúde; Swiss Bridge.

G-216 - Comprehensive Germline Genetic Analysis Of Mexican Patients With Predisposition To Inherited Breast Cancer By Massive Parallel Sequencing

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Breast cancer is the neoplastic disease with the highest incidence and mortality worldwide and nearly 10% of the cases are due to inherited pathogenic alleles in cancer predisposing genes such as *BRCA1* and *BRCA2*. However, in the Mexican population the spectrum of inherited breast cancer susceptibility not caused by *BRCA1/2* pathogenic alleles has not been explored. To this aim, we evaluated the presence of germline pathogenic alleles in the coding sequence and splice sites of 143 cancer susceptibility genes in 69 Mexican female patients with cancer that were selected for family cancer history, following inclusion criteria based on the guidelines of the National Comprehensive Cancer Network. In these patients we defined pathogenic variants using data from international databases of normal populations and cancer patients, annotation information and technical parameters. Pathogenic alleles (stopgain/loss, frameshift indels) were found in *BRCA1* (8.7%, 6/69), *BRCA2* (2.9%, 2/69), *FANCC* (2.9%), *MSR1* (2.9%), *FANCL* (1.4%, 1/69), *SDHB* (1.4%) and *TSC2* (1.4%). Private or rare missense variants with unknown clinical significance (VUS), but defined as pathogenic in ClinVar or by algorithms assessing evolutionary conservation and deleterious structural changes at protein level, were found in single patients in the genes *AIP, ANTXR1, APC, ATR, CD96, CYP21A2, ERCC3, ERCC6, FANCA, FANCB, FANCE, LIG4, LYST, MSH6, MSR1, MTAP, PDE11A, PDGFRA, PMS2, POLE, PTCH1, RAD50, RHBDF2, RUNX1* and *WRN*. These patients did not have other pathogenic alleles, suggesting a potential contribution of these VUS to disease susceptibility. In 29 patients we did not find any potential pathogenic variant. This study contributes to identify new susceptibility alleles that can predispose to inherited breast cancer in the Mexican population and highlights the necessity of expanding genetic tests for hereditary breast cancer to broader gene panels. This work was supported by PAPIIT UNAM (IA204215).

G-217 - Characterization Of Tumor Initiating Cells In Esophageal Squamous Cell Carcinoma

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The presence and role of tumor initiating cells (TICs), also known as cancer stem cells, in esophageal squamous cell carcinoma (ESCC) are still poorly understood, mostly because of the lack of good biomarkers for their identification. Therefore, this study aims to isolate and characterize the TICs in ESCC. We first performed a sphere formation assay in order to isolate the possible TICs in four ESCC cell lines, using a stem cell-specific medium in non-adherent conditions. RT-qPCR analysis was performed to evaluate the expression of 26 genes, comparing the spheres with their respective parental cells. To investigate whether the possible TICs presented a re-differentiation capacity and were able to generate a cell population with the same morphological and molecular features of the parental cells, we dissociated the spheres and plated the cells in parental's condition. To ensure that the differential expression of the possible markers is not a consequence of the exposure to the stem cell-specific medium, parental cells were plated in adherent conditions in the presence of this specific medium. All ESCC cell lines were capable of forming spheroids. CXCR4, ITGA6, ABCG2 and NANOG showed an overexpression in this condition and were identified as possible TIC markers in TE1 and TE11, but only CXCR4, ITGA6 and ABCG2 were confirmed in TE13. In the re-differentiation assay, all sphere-derived ESCC cells were capable of forming populations with morphological and gene expression profiles similar to parental cells. Finally, ESCC cells cultured in adherent conditions in the presence of stem cell-specific medium showed ITGA6 upregulation, suggesting that this is not a good TIC marker . In conclusion, our data show that CXCR4 and ABCG2 could be possible markers for TICs in ESCC and must be tested for TIC's population enrichment in xenografic NOD-SCID mouse tumorigenesis assay. Funding sources: CNPq and FAPERJ.

G-218 - Characterization Of The Expression Profile Of APOBEC And TET Families In Esophageal Squamous Cell Carcinoma

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Esophageal squamous cell carcinoma (ESCC) is one of the main histological types of esophageal cancer worldwide and in Brazil. Although its high incidence and mortality rates, the mechanisms that lead to ESCC development are still poorly understood. Our group has shown before that alterations of DNA methylation are a common event in ESCC and may preceed the first genetic alterations, however what leads to this deregulation is still unkown. The specific pattern of DNA methylation depends on the balance between methylation and demethylation processes. We have shown that ESCC shows an overexpression of *DNMT3B* in comparison with normal surrounding mucosa, but genes from the demethylation machinery were not evaluated. More recently, APOBEC proteins (cytosine deaminases), related to the generation of genetic variability, have been implicated also in active DNA demethylation as well as TET proteins, which are involved in the hydroxylation of 5-methylcytosine. However, data regarding expression and regulation of APOBEC and TET families in ESCC is limited. Therefore, the aim of this study is to evaluate the expression profile of *APOBECs* and *TETs* and their regulation in ESCC patients. We analyzed the expression of these genes in tumor and matched surrounding normal tissue from up to 18 ESCC patients by RT-qPCR. *APOBEC3A1*, *APOBEC3B*, *APOBEC3D*, *APOBEC3FA* and *APOBEC3G* were found overexpressed in ESCC when compared with matched surrounding mucosa whereas *TET2* was found downregulated. Additionally, *APOBEC3B* was able to distinguish surrounding mucosa from tumor with 94.44% sensitivity and 100% specificity while *APOBEC3D* distinguished theses two tissues with 88.89% sensitivity and the same specificity. Our results suggest that the deregulation of the APOBEC family of genes is a common feature in ESCC and could be involved in the aberrant methylation profile previously observed. Funding source: Ministério da Saúde, FAPERJ.

G-219 - Pooled Analysis Of Methylome Data Identifies A DNA Methylation Signature Highly Predictive For HPV Status In Head And Neck Squamous Cell Carcinomas

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Purpose. Oncogenic human papilloma viruses (HPV) have been found to be causally associated with a subset of head and neck squamous cell carcinomas (HNSCC). Several lines of evidence argue that some viruses including HPV may promote tumour development via an ‘‘epigenetic strategy’’, although the precise underlying mechanisms remains poorly understood. In this study we aimed to address whether HPV affects the DNA methylome in HNSCCs and if any specific methylation signature can be used for differentially diagnosis with HNSCCs associated with other aetiologies.
Methods. DNA methylation raw data from Illumina 450k platform of two different cohorts (TCGA and University College of London, UCL) were retrieved and analyzed together with a subset of cases from a French cohort for which we generated data from the same platform. A total of 326 cases were analyzed, of which 63 were HPV (mainly subtype 16) positive. Machine learning algorithms were used to identify a DNA methylation signature able to identify a HPV specific signature and the signature was tested on the entire cohort of French cases.
Results. After normalization of the data, global methylation profiles were able to distinguish HPV positive from HPV negative cases .We identified a signature of only 5 CpGs which was able to discriminate between the two groups of tumours with a sensitivity of 90-95% and a specificity of 98%. Conclusions. HPV infection is associated with a specific DNA methylation signature with higher predictive value of HPV status compared with current detection methods in HNSCCs. These results have an important relevance for the early diagnosis and treatment of these tumours. DNA methylation signatures may be used to identify and improve the understanding of the carcinogenic mechanisms of different environmental exposures.
Funding source. This research was funded by the INCA, PAIR VADS programme and by the Epigenetics Group at IARC.

G-220 - Identification Of Novel Long Non-Coding RNAs Deregulated In Hepatocellular Carcinoma Using RNA-Sequencing

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Purpose. Functional characterization of long non-coding RNAs (lncRNAs) and their pathological relevance is still a challenging task. Abnormal expression of a few long non-coding RNAs have been found associated with hepatocellular carcinoma, with potential implications for both improvement of the understanding of molecular mechanism of liver carcinogenesis and discovery of biomarkers for early diagnosis or therapy. However, the understanding of the global role of lncRNAs during (HCC) development is still in its infancy.
Methods. In this study, we produced RNA-Seq data from 23 liver tissues (controls, cirrhotic and HCCs) and applied a statistical and gene network analysis approach to identify and characterize expressed lncRNAs.
Results. We detected 5,525 lncRNAs across different tissue types and identified 57 differentially expressed lncRNAs in HCC compared with adjacent non-tumour tissues using stringent criteria (FDR<0.05, Fold Change>2). Using weighted gene co-expression network analysis (WGCNA), we found that differentially expressed lncRNAs are co-expressed with genes involved in cell cycle regulation, TGF-β signalling and liver metabolism. Furthermore, we found that more than 20% of differentially expressed lncRNAs are associated to actively transcribed enhancers and that the co-expression patterns with their closest genes change dramatically during HCC development.
Conclusion.Our study provides the most comprehensive compendium of lncRNAs expressed in HCC, as well as in control or cirrhotic livers. Our results identified both known oncogenic lncRNAs (such as H19 and CRNDE) and novel lncRNAs involved in cell cycle deregulation and liver metabolism deficits occurring during HCC development. Future studies to understand the functional importance of these newly identified lncRNAs in cancer development and progression are warranted.
Funding source. This research was funded by the Epigenetics Group at IARC.

G-221 - The Role Of p53 And SP1 In DNMTs Gene Regulation

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TP53 mutations are the most frequent alterations found in tumors and the loss of its encoded protein activity can lead to genetic instability. Epigenetic alterations have recently been recognized as key events in tumors development. DNA methylation is an epigenetic mechanism characterized by the methylation of cytosines in CpG dinucleotides and catalyzed by the DNA methyltransferases (DNMTs). The aim of this project is to evaluate the role of p53 and SP1 (transcription factor overexpressed in a wide range of tumor and p53 partner in the regulation of some genes) in *DNMTs* gene regulation. The possible gene regulation of DNMTs by p53 may be an important indicator of the interaction between genetic and epigenetic mechanisms involved in tumors development. *DNMTs* mRNA (qRT-PCR) and protein expression (Western blotting) were evaluated in the esophageal squamous cell carcinoma cell lines TE-1 (TP53 temperature sensitive mutant: 32°C - WT p53 and 37°C - mutant p53) and TE-13 (p53 null) and in the colorectal carcinoma cell lines HCT116 p53 + / + and HCT116 p53 - /-. DNMTs and SP1 expression levels were higher in cell lines presenting null or mutant p53. TP53 silencing led to DNMTs increased expression in cells expressing mutant p53 whereas in p53 competent cells, the opposite effect was observed. Transfection with a p53 expression vector and treatment with the DNA alkylating agent methyl methanesulfonate resulted in augmentation of DNMTs levels only in p53-competent cells. SP1 silencing led to a reduced DNMTs expression in p53-deficient cells and increased in p53 wild-type cells. Conversely, transfection of SP1 expression vector resulted in the opposite effect. Together, these data show that p53 and SP1 play a role in *DNMTs* gene regulation, in a dose-dependent manner, and further experiments are needed to understand the mechanisms by which this regulation occurs. Financial support: CNPq, CAPES and MS.

G-222 - Genome-wide DNA Methylation Markers Of Lifestyle Exposure And Pre-Diagnostic Breast Cancer Risk

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Purpose
Identifying potential of DNA methylation changes in peripheral blood as a marker of lifestyle exposure and cancer risk is gaining importance. In the present study we assessed whether epigenome-wide DNA methylation measured in peripheral blood samples obtained before onset of the disease is associated smoking status and with increased risk of breast cancer.
Methods
The study cohort included 470 female incident breast cancer cases and matched controls embedded in a large nested case–control cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC) study. DNA methylation levels were measured across 485,777 CpG sites using the Infinium HumanMethylation450 BeadChip kit. The bioinformatics and biostatical analyses were performed using R (version 3.2.2)/Bioconductor packages.
Results
We identified 748 CpG sites and 8 regions that were differentially methylated in smokers compared to non-smokers (FDR ≤ 0.05). We observed a marked reversibility of methylation changes after smoking cessation, although 4 CpG sites in 2 genes (ALPPL2 and AHRR) remained differentially methylated up to 22 years after smoking cessation.
Higher epigenome-wide methylation at CpG island was associated with risk of breast cancer (OR per 1 SD =1.20, 95 % CI: 1.03-1.40). We examined whether epigenetic age acceleration (EAA) which refers to epigenetic age acceleration adjusted for abundance measures of blood cell counts predicts development of breast cancer. EAA was found to be a significant prognosticator of breast cancer incidence (P = 0.041) at the time of the blood draw. The result becomes even more significant when restricting the analysis to subjects that developed breast cancer within 10 years of follow up (P=0.013).
Conclusions:
Thus, our study demonstrates that prospectively collected blood based DNA methylome changes may serve as potential markers of lifestyle exposure and breast cancer risk.

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G-223 - Assessment Of Polymorphisms Of Tumor Suppressor Gene Lysyl Oxidase Among Nepalese Patients Of Oral Submucous Fibrosis

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Background: Oral submucous fibrosis (OSF) is a chronic, insidious disease associated with significant functional morbidity and an increased risk for malignancy. The common hypothesis for OSF pathogenesis is the increase of collagen synthesis or reduced collagen degradation in oral sub-epithelial tissues because of chemical, physical/inflammatory irritation. Although available epidemiological evidence indicates that chewing of areca-nut is an important risk for developing of OSF, not all chewers develop OSF. However, no genetic study has been done till date on OSF in Nepalese population.

Objective: To explore genetic variability of tumor suppressor genes among the OSF patients and to find relationship between OSF and tumour suppressor gene-lysyl oxidase's polymorphism among patients attending BPKIHS

Methods: A total of 46 samples were collected from 26 patients with OSF and 20 age-sex matched patients undergoing extraction of third molar served as control. A detailed medical, dental history and oral examinations was recorded. Punch biopsy was taken using 6mm punch then was sent to molecular biology laboratory for genetic analysis.

Results: Only 39 samples were suitable for analysis by PCR-RFLP. The mean age was 30.9±12.09. Out of 39 samples, 27 were OSF cases and 12 were control. The fingerprinting analysis revealed three different genotypes ie homozygous G/G allele, A/A allele and heterozygous G/A alleles showed one, two and three bands respectively after pstI digestion. Further analysis showed that heterozygous allele G/A was predominantly found in case and control whereas genotype A/A and G/A were found in control and case respectively. Analysis of demographic information documented that habit of smoking/chewing tobacco was predominantly found in genotype G/G as compared to others.

Conclusion: This study explored possible genetic marker of OSF in Nepalese population. However, further studies with large number of samples are required to validate these developed simple molecular tools which are easy to perform and analyse.

G-224 - Alterations Of MET-HGF Pathway In Esophageal Squamous Cell Carcinoma

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Esophageal cancer is among the most incident and lethal malignancies in the world and presents two main histological subtypes. Between them, squamous cell carcinoma of the esophagus (ESCC) corresponds to 80% of the cases. The development of ESCC in Brazil has been extensively correlated with tobacco and alcohol, but the molecular mechanisms involved are poorly understood. Among the most promising signaling pathways in gastrointestinal tumors, the hepatocyte growth factor (HGF) pathway and its receptor MET stands out. Thus, the aim of this study is to evaluate whether alterations of this pathway could contribute to ESCC development. To this end, tumor and normal surrounding tissue were collected from thirty patients diagnosed with ESCC. The evaluation of HGF and MET expression was performed by RT-qPCR using primers that discriminate the two splicing variants of MET. The methylation status of MET intragenic CpG sites was assessed by pyrosequencing. Only variant 2 of MET showed a significant variation in expression, which was increased in tumors. Thus, this variant was chosen as the focus of our study. From a ROC curve analysis, it was observed that the differential expression of this variant was able to distinguish with 93.1% of sensitivity and 86.21% of specificity tumors from surrounding tissue. We also performed the analysis of HGF expression and found its greatest expression in tumor tissue compared with its surrounding mucosa. The methylation analysis of MET intragenic CpG sites revealed a hypermethylation in ESCC. Thus, our data suggest that both the pathway receptor MET and its ligand HGF are upregulated in ESCC, which may represent potential diagnostic markers and/or new therapeutic targets. Furthermore, we show for the first time a deregulation of DNA methylation in MET gene body, which could be correlated with a preferential expression of splicing variant 2. Funding sources: Ministério da Saúde, CNPq, FAPERJ.

G-225 - DNA Methylation Associated With DNMT1 Overexpression As A Probable Cause Of Esophagin Loss In Esophageal Cancer

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Esophageal cancer (EC) is the sixth most frequent cancer and is the sixth leading cause of cancer-related deaths worldwide. Squamous cell carcinoma (ESCC) correspondes to 80% of the cases. A previous study from our group showed a gradual loss of esophagin (SPRR3) expression in malignant transformation of the healthy esophagus into ESCC. However, molecular mechanisms studies involved in SPRR3 silencing are limited. The aim of this study is to examine DNA methylation as regulatory mechanism of esophagin expression in ESCC. For this, three CpG sites of esophagin gene were analyzed by pyrosequencing in esophageal cancer cell line (OE21) treated with the demethylating agent decitabine, and in tumor and matched normal surrounding mucosa from patients with ESCC. RT-qPCR was performed to evaluated esophagin and DNMT1 expression in the same samples. Our results demonstrate that decitabine treatment was able to induce SPRR3 demethylation in a time and dose-dependent manner in OE21, correlated with an increased mRNA expression. The methylation of CpG sites analyzed was significantly higher in tumors in comparison with the adjacent tissues (A, p=0.0017; B, p=0.0002; C, p=0.0103). The ability of SPRR3 methylation to distinguish the adjacent mucosa from tumor samples using ROC curve analyses was significant for each of the CpG sites examined (A, sensitivity and specificity=84.62%, P=0.003; B. sensitivity=93.33% specificity=86.67%, P<0.0001; C, sensitivity and specificity=80.0%, P=0.0017). We observed an inverse correlation between esophagin methylation and its mRNA expression for CpG sites evaluated (A, p<0.0001; B, p=0.0022; C, p=0.0006). In order to investigate the mechanisms that could be involved in SPRR3 hypermethylation, we evaluated DNMT1 expression, which was higher in tumors with this profile (A, p=0,0028; B, p=0.0157; C, p=0.0080) and inversely correlated with SPRR3 expression (p=0.0009). Our data suggest DNA methylation induced by DNMT1 as a possible mechanism for esophagin silencing in ESCC. Funding Source: FAPERJ and MS/INCA.

G-226 - Evaluation Of Desmoglein 1 Alterations In Esophageal Carcinogenesis

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Esophageal cancer is one of the ten most frequent types of tumors with a five-year survival lower than 20% in Brazil and worldwide. Squamous cell carcinoma (ESCC) is the main histological subtype and is usually diagnosed in late stages, leading to an ineffective treatment. This panorama shows the urgency in understanding the mechanisms that lead to ESCC development. A previous study from our group showed that DNA methylation alterations are common in ESCC and affect pathways like cell adhesion, as evidenced by the promoter hypermethylation of Desmoglein 1 (*DSG1*), which encodes a desmosomal cadherin. Based on this, the aim of this study is to evaluate the regulation of *DSG1* in ESCC. Initially, we treated the ESCC-derived cell line OE21 with the demethylating agent decitabine and observed a dose and time-dependent demethylation of *DSG1* promoter by pyrosequencing, which was accompanied by an increase of mRNA expression (RT-qPCR). We also performed the same analyses in tumors and matched normal surrounding tissue from 36 ESCC patients. Our data showed that ESCC samples show a higher methylation and a lower *DSG1* expression in comparison with the surrounding tissue. In addition, we analyzed DSG1 protein expression in ESCC and showed that normal esophageal tissue presents a predominant membrane expression. In tumors, we observed different expression patterns, varying from complete expression loss to cytoplasmic staining with a few regions of membrane expression. A new *DSG1* isoform, which loses the transmembrane domain, has been predicted, but not yet validated. We were able to detect the mRNA expression of this isoform using specific oligonucleotides and this could explain the cytoplasmic expression observed in ESCC. In conclusion, our data shows an inverse correlation between *DSG1* methylation and expression *in vitro* and *in vivo* and suggests that the full-length DSG1 is lost in ESCC. Funding source: Ministério da Saúde, CAPES.

G-227 - Aberrant Promoter Methylation Of ESR1 Gene Is Associated With Inferior Survival In Surgically Resected Non-Small Cell Lung Cancer (NSCLC)

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Purpose: We have previously reported that the aberrant promoter methylation in several tumor suppressor genes in NCSLC tumor tissue was associated with clinico-pathological features of NSCLC. The aim of the current study was to assess whether promoter methylation in these genes was associated with 5-year survival in this population.
Methods: Primary tumor samples (n=65) and corresponding nonmalignant lung tissues (n=65) were obtained from NSCLC patients who underwent curative surgery at the Institute for lung diseases, Clinical Center of Serbia. DNA was extracted and the samples were shipped to the University of Minnesota, where promoter methylation in seven genes (RASSF1A, CDH13, MGMT, ESR1, DAPK, SOX1 and HOXA9) was analyzed by using bisulfite pyrosequencing. Cox proportional hazards models were used to analyze the associations between gene methylation status and overall patient survival.
Results: In the Cox proportional hazards model, ESR1 methylation in tumor tissue was associated with significantly poorer survival, with hazard ratio of 1.09 (95% confidence interval 1.02-1.16, p=0.01). This effect was independent of TNM stage, which was also a predictor of survival. No significant survival differences were associated with methylation in other genes tested in either of the two tissue types.
Conclusion: Our study suggests that high ESR1 promoter methylation may be associated with inferior survival in NSCLC patients. Caution is warranted due to small sample size and a modest effect observed. Further studies are needed to confirm whether ESR1 promoter methylation could be utilized as a prognostic biomarker of NSCLC survival.

Funding source: International Organization for Cancer Prevention and Research (IOCPR)

G-228 - DNA Methylation Levels Measured Globally And At LINE-1 DNA Repetitive Elements In Pre-Diagnosis Peripheral Blood-Derived DNA And Risk Of Colorectal Cancer

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Purpose: The aim of this study was to associations between colorectal cancer (CRC), overall and by molecular subtype, and DNA methylation measured at LINE-1 DNA repetitive elements and globally from the mean CpG methylation levels of the Illumina HumanMethylation450k array.
Methods: A nested case-control study was conducted within the Melbourne Collaborative Cohort Study. Cases were diagnosed with CRC during follow-up (until 2010). Controls were selected using risk set sampling with age as the time variable, and matched by sex, year of baseline attendance, country of birth and baseline sample type for DNA (Guthrie card, lymphocytes, buffy coat). Tumours were characterised for microsatellite instability (MSI) and CpG island methylator phenotype (CIMP). Bisulphite converted DNA from baseline blood samples was assayed for LINE-1 methylation using pyrosequencing and at more than 485,000 CpG sites across the genome using the Illumina HumanMethylation450k Beadchip array. Global methylation was estimated by calculating the mean beta values across all CpG sites. We estimated odds ratios (ORs) and their 95% confidence intervals (CI) per standard deviation increase using conditional logistic regression with adjustment for potential confounding variables.
Results: DNA methylation values were obtained for 824 CRC cases and 824 matched controls (50.6% female; mean age at blood draw=59.8 ± 7.6 years). No association with CRC risk overall was observed for mean global methylation levels or for LINE-1 (OR=0.93; CI=0.76-1.14; p=0.49 and OR=0.86; CI=0.67-1.12; p=0.23, respectively). However, when stratified by CIMP status, increasing levels of LINE-1 methylation were associated with a 2-fold increased risk of CIMP positive CRC (OR=2.34; CI=1.02-5.35; p=0.04). A weaker, but consistent, association was observed for CIMP positive CRC in regard to mean global methylation (OR=1.67; CI=0.89-3.12; p=0.11).
Conclusions: Higher levels of LINE-1 methylation measured in peripheral blood-derived DNA were associated with CIMP-positive CRC.
Funding source: NHMRC (1027505)

G-229 - Effect Of Leptin Gene Methylation On Colorectal Cancer Chemoresistance

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Introduction: Colorectal cancer (CRC) is one of the most common tumors all over the world. Obesity, considered a risk factor of CRC, is characterized by a high level of secreted cytokines from adipose tissue. Among these inflammatory molecules, leptin is considered the key mediator for CRC cancer development and progression by activation of mitogenic and anti apoptotic signaling pathways. Gene expression can be significantly modulated by alterations in DNA methylation patterns.
Objectives: The aim of this study is to investigate the impact of leptin gene methylation on CRC prognosis and sensitivity to chemotherapy.
Materials and Methods: The study involved 70 CRC tissue samples collected from King Abdullah University Hospital (KAUH) from which only 53 was analyzed because of bisulfate fragmentation and low yield of DNA extracted from FFPE tissues. A total of 22 blood samples were collected from healthy volunteers and enrolled as a control group. Leptin promoter methylation was analyzed by methylation specific PCR after bisulfate conversion. Results and Discussion: Results revealed that the incidence of leptin gene methylation was significantly higher in CRC patients in comparison to that of controls ($P<0.05$). The correlation between patient's demographics and leptin gene methylation was not significant ($P<0.05$). However, a significant correlation between leptin gene methylation status and early cancer stages (I, II and III) was found in male but not in female ($p<0.05$). Moreover, a significant correlation was found between leptin promoter methylation and early tumor localization T1-2 ($p<0.05$). The correlation between epigenetic regulation of leptin and chemosensitivity was not significant.
Conclusion: Taken together, these results suggest the possibility to use leptin gene methylation as a biomarker for the evaluation of CRC prognosis and metastasis.

G-230 - Alterations Of MGMT, P15, TP53 And DNMT3A Genes In Acute Leukemias Patients

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PURPOSE: Epigenetic changes play a significant role in development and progression of acute leukemia. Literature data indicate that especially important seems to be hypermethylation of p15 and MGMT genes. For the development and prognosis of acute leukemias is also important to evaluate mutation of DNMT3A and TP53 genes. The aim of the study was to determine whether the MGMT and p15 promoter hypermethylation and DNMT3A and TP53 mutations have an impact on development acute leukemias.
METHODS: The clinical data of 55 patients diagnosed with AML or ALL between 1998 and 2003 were retrospectively analyzed. DNA was extracted from bone marrow of the patients with acute leukemia. The methylation status of MGMT was evaluated by methylation-specific PCR (MSP). Combined bisulfite restriction analysis (COBRA) was used to detect p15 methylation level. Mutation analysis of DNMT3A (R882H) was performed by PCR-RFLP method. Exons 5-8 of TP53 mutation was detected by sequencing.
RESULTS: We have found that p15 methylation and TP53 mutation was detected significantly more often in patients with AML than patients with ALL. Age at diagnosis was higher for patients with MGMT methylation. There were no significant relationships between type of leukemia and DNMT3A mutation and MGMT methylation. No significant differences were observed between age and survival in patients with or without DNMT3A and TP53 mutation and p15 methylation.
CONCLUSION: Epigenetic changes can be exploited in the clinics as biomarkers for acute leukemias.
FUNDING SOURCE: This study was supported by the grant of the National Science Center, Poland, no. 2011/01/B/NZ4/03345.

G-231 - DNA Methylation Analysis Of Plasma Circulating Cell-Free DNA By Targeted-Deep Sequencing Reveals Potential Epigenetic Biomarkers For High-Risk Monitoring And Detection Of Liver Cancer

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Purpose: Tumor-derived cell-free circulating DNA (cfDNA) isolated from the plasma and serum of individuals with cancer has been shown to contain cancer-associated genetic and epigenetic alterations. Epigenetic changes (such as DNA methylation) are tumour specific and appear early in tumor development, thus they can provide particularly attractive markers with broad application in diagnostics and risk assessment. However, reliable detection of DNA methylation changes in body fluids has proven to be technically challenging. With the recent development of high-throughput sequencing technologies there has been a growing interest in cfDNA that has the potential to be used in the context of developing of non-invasive biomarkers.
Methods: Here, we applied massively parallel semiconductor sequencing to assess the methylation of a panel of genes in plasma circulating cell-free DNA (cfDNA), also to evaluate the potential of these genes as novel biomarkers for hepatocellular carcinoma (HCC) in two different case-control studies, in France and in Thailand (HCC cases, chronic liver disease cases and controls). We also analysed a set of HCC and adjacent tissue samples as well as different liver cell lines to further compare with 'The Cancer Genome Atlas' (TCGA) data.
Results: Methylation in cfDNA was detected for FBLN1, PSMA7, PXDN and VIM, with substantial differences in methylation patterns between cases and controls. Further, the average methylation level across analysed CpG-sites was associated with higher odds of HCC for VIM for French cases and for Thai cases, and lower odds of HCC for FBLN1.
Conclusions: Together, our study provides evidence that deep sequencing is a suitable method for analysing methylation profiles in cfDNA, and that changes in methylation levels of specific genes in cfDNA are associated with HCC which may represent useful plasma-based biomarkers for improved diagnosis accuracy and patient surveillance.
Funding source: Ligue Nationale Contre le Cancer (Comité du Rhône)

G-232 - Identification Of A Transcription Factor Able To Alter The Cellular Identity And The Methylation Landscape Of Breast Cancer

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Purpose: despite the numerous advances, breast cancer (BC) is still the most common cancer affecting women. Lowly methylated regions (LMRs), non-CpG *loci* that contain specific transcription factor (TF) motifs, have been suggested to act as regulators that define cellular identity but have not been reported in BC. Here, we aimed to identify the key subtype-specific TFs that shape BC methylome.
Methods: we selected subtype-specific LMRs using whole bisulfitome data available at TCGA. Differentially methylated regions (DMRs) within these LMRs were selected by comparing tumors and normal tissues in a larger TCGA cohort assessed by arrays. Finally, we predicted the most relevant TFs able to bind these DMRs. Additionally, we decided to overexpress the main TF identified in basal BC in MCF7, a luminal (epithelial) cell line to see whether it could induce a basal-like (mesenchimal) phenotype and modulate the methylome *in vitro*.
Results: we found 1,185 hypomethylated DMRs for basal subtype *in silico* that were enriched in EBF1 motifs. The methylation levels of the EBF1 motif-containing regions showed a strong negative correlation with the expression of 719 genes, including *BTS2*, *CD74* and *SLPI*, putative oncogenes known to be specific for basal and/or poor outcome BC. Finally, *in vitro* overexpression of EBF1 was able to induce an epithelial-to-mesenchimal transition-like phenotype in the MCF7 cells, and to modify the methylation of 1072 *loci in vitro* (with a significant overlap with those targets found *in silico*).
Conclusions: EBF1 is able to change the methylation levels *in vitro* and seems to affect the molecular identity of the cells, leading to a more mesenchimal phenotype that could be translated into a more aggressive presentation of the disease.
Funding source: IARC Postdoctoral Fellowship (FP7–People–COFUND) and Postdoctoral Fellowship - Education Department of the Basque Government to NF-J during the first and the second year, respectively.

G-233 - Micro-RNA And mRNA Integrative Analysis Uncover Potential Diagnostic And Prognostic Markers In Penile Carcinomas

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Purpose. Integrative analysis of transcriptomic and epigenetic profiles is a powerful method to identify molecular drivers of cancer development and progression. Aiming to contribute with the identification of molecular drivers, we investigated penile carcinomas (PeCa), a rare disease associated with high mortality and morbidity rate.
Patients and Methods. miRNA expression was performed using the TaqMan Human MicroRNA Array v2.0 (Applied Biosystems) in 23 PeCa tissues and 12 non-neoplastic penile tissue (NPT). Previously reported transcriptome expression results (Kuasne et al. Clin Epigenetics. 2015 Apr 18;7:46) were integrated with miRNA data.
Results. Eighty-one miRNA and 2,697 mRNAs differentially expressed were identified comparing tumor and non-neoplastic tissues. Integrative analysis revealed that 255 mRNAs were specifically regulated by 68 miRNAs in PeCa. For data confirmation, 8 miRNAs and 8 mRNAs were evaluated by RT-qPCR in an array-independent set of cases (PeCa=36; NPT=27) confirming the results. Molecular diagnostic classifiers with MMP1, MMP12 and PPARG transcripts were able to distinguish tumors from NPT with 92% of sensitivity and 83% of specificity. Similarly, three miRNAs (hsa-miR-31-5p, hsa-miR-224-5p, and hsa-miR-223-3p) were able to discriminate tumors from NPT (82% of sensitivity and 74% of specificity). Higher MMP1 expression levels were able to predict lymph node metastasis more efficiently than clinical-pathological data.
Conclusion. To our knowledge, this is the first integrative analysis of miRNA and mRNA expression data in PeCa. The findings revealed molecular markers involved in the development of PeCa. Furthermore, MMP1 overexpression was as predictive marker of lymph node involvement and could be useful in the clinical practice.
Financial support: FAPESP and CNPq.

G-234 - Breast Cancer Molecular Subtypes And Risk Factors In Premenopausal Latin American Women: The PRECAMA Study

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Purpose
Breast cancer (BC) encompasses heterogeneous pathologies that can be further subtyped by genomic alterations. BC genomic subtypes have been associated with different outcomes, but how this molecular heterogeneity relates to risk factors and etiology remains largely unknown. In Latin America (LA), there is a high incidence rate of breast cancer in premenopausal women. The PRECAMA study, a multicenter population-based case-control study that includes tumor sample collections, was developed to characterize the molecular features of premenopausal BC and their link to risk factors.

Methods
Pathological tumor samples collected in Chile, Colombia, Costa Rica and Mexico were analyzed for molecular profiling. Immunohistochemistry (IHC) was performed centrally for ER, PR, HER2, KI67, EGFR, CK56 and p53 protein markers. Targeted deep sequencing was done on genomic DNA extracted from formalin-fixed paraffin-embedded (FFPE) tumor tissues and their paired blood samples to screen for somatic mutations in eight genes frequently mutated in BC (AKT1, CDH1, ERBB2, NOTCH1, PIK3CA, PTEN, RB1, TP53). Statistical differences between BC subtypes defined by their IHC and mutation profiles were analyzed by Chi-2 tests using R software.

Results
The genes analyzed were mutated at frequencies similar to those described in databases covering European and North American populations. As expected, *TP53* mutations were more frequent in HER2 and triple-negative IHC subtypes while PIK3CA was more frequent in ER positive tumors. Interestingly, a high proportion of *TP53* G:C>T:A mutations was observed in *TP53* in PRECAMA cases compared to other series.

Conclusions
These preliminary results suggest common pathways but possible differences in mutagenic processes giving rise to these tumors. The analysis of a larger number of cases in the near future will allow investigating associations between risk factors and specific molecular features.

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G-235 - The Genetics Of Gene Expression In Human Pancreatic Tissues

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Purpose: To understand the influence noncoding germline variation exerts on the regulation of gene expression in pancreatic tissues and to explain the underlying molecular mechanisms of pancreatic cancer risk loci.
Methods: We sequenced RNA from 95 histologically normal pancreatic tissue samples and tested associations between ~6million germline variants and the expression of ~17,000 genes. We included 115 tumor derived pancreatic tissue samples from the Cancer Genome Atlas (TCGA) pancreatic cancer dataset for comparison. Allele specific expression (ASE) was tested for heterogeneous loci at coding regions within each individual after taking into account the expected allele imbalance.
Results: We identified 484 cis-eQTL genes in histologically normal tissues and 237 cis-eQTL genes in tumor tissues (FDR<0.1). We observed significant enrichment of eQTLs within noncoding regulatory regions, which was more prominent in pancreatic cancer cell lines as compared to other tissues in the ENCODE data. The eQTLs were enriched in promoters for normal (3.8-fold) and tumor (4.6-fold) tissue eQTLs as compared to non-eQTL SNPs. Enrichment of eQTLs was seen in genic regions and for 5'UTRs, this was more prominent in the tumor tissue (21-fold) as compared to the normal tissues (10-fold). A common pancreatic cancer risk locus on 9q34.2 in the ABO gene demonstrated a regulatory effect on ABO expression in both normal (P=5.8x10-8) and tumor (P=8.3x10-5) tissues, with replication in the GTEx pancreatic samples (n=149, P=3.0x10-12). The ASE analyses further identified 1,286 genes with ASE in normal tissues after adjusting for multiple testing (P<1x105), including 36.8% of the cis-eQTL genes.
Conclusions: We have identified eQTLs representing potential functional regulatory variance in the pancreas and generated a dataset for further studies on regulation of gene expression in pancreatic tissues, which not only elucidates gene regulatory mechanisms in the pancreas, but also aids in interpreting pancreatic cancer GWAS findings.
Funding source: NCI/NIH intramural funding.

G-236 - Modeling Cancer Driver-Like Events Using In Vitro Carcinogen Exposure And Immortalization Assays

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Purpose
Cancer genomes harbor mutational spectra that document exposures to external factors and endogenous events underlying the tumor development. Information on candidate cancer driver alterations is accessible from public compendia of somatic mutations, yet much of this knowledge remains hypothetical and of little mechanistic insight. Simple, robust and rapid systems are thus needed for well-controlled experimental investigations of functional impact of carcinogenic exposures on the genome and on cancer cell growth.

Methods
We devised barrier bypass-clonal expansion (BBCE) assays based on cultured primary mouse embryonic fibroblasts which upon carcinogen exposure circumvent senescence, a selective pressure barrier, and immortalize. Exomes of the resulting clones are sequenced and analyzed to decipher both the mutational signatures and the putative functional driver events selected and enriched for during the outgrowth phase.

Results
Using the BBCE assays, we tested the global mutagenic effects of several known human carcinogens. We obtained 25 independently arising cell lines, altogether harboring 16,061 acquired mutations of which 7,615 were non-synonymous. As in human cancers, the alterations affected pathways regulating DNA damage response, DNA repair, cell cycle, cell death, transcription and chromatin structure, and multiple developmental signaling pathways. Forty-eight genes listed in the COSMIC Cancer Gene Census were recurrently mutated across the BBCE cell line panel, including well-established oncogenes (HRAS, KRAS, ABL1, EGFR) and tumor suppressors (APC, ATM, BRCA2, PTCH1, TP53). A number of epigenetic and chromatin regulators also acquired recurrent mutations. Data will be presented describing a customized pipeline to prioritize candidate driver events, followed by systematic genome editing or pharmacological manipulation of select genes and assessment of the resulting phenotypic and molecular traits.

Conclusions
In summary, our BBCE approach may yield new mechanistic insights into driver-like events underlying cancer development.

Funding source
International Agency for Research on Cancer; ITMO CANCER – INSERM Plan Cancer 2015.

G-237 - Selected miRNAs And Their Target Genes Alterations In Primary Glioblastoma Patients

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PURPOSE: Glioblastoma (GB) carries complex genetic alterations resulting in a different molecular and epidemiological profile. There is increasing evidence that the altered miRNA expression plays an important role in GB development. The aim of the study was to examine expression of selected miRNAs and to assess the relationship between miRNA expression and alterations of their target genes and clinical features in primary GB.
METHODS: Tumor samples were obtained from 49 patients with primary glioblastoma. We used qPCR method for evaluation of miR-125b, -181, -21, -34a and -648, TP53 and MGMT expression level. For TP53 and MGMT protein expression we used immunohistochemistry. We used sequencing analysis for detection of TP53 mutations (5-8 exons). Additionally we used MS-PCR method for analysis of MGMT methylation status.
RESULTS: We found that TP53 mRNA level was negatively correlated with miR-34a level in patients with IHC-detected TP53 overexpression, whilst TP53 mRNA level was positively correlated with miR-34a level in patients without IHC-detected TP53 overexpression. MGMT mRNA was negatively correlated with miR-125b level only in patients without MGMT methylation. MGMT mRNA level in MGMT-methylated patients was significantly lower than in patients without MGMT methylation. We found a tendency towards a worse survival of patients with MGMT methylation.
CONCLUSION: Expression of the microRNAs and their potential target genes are dysregulated in GB. Epigenetic modification of MGMT gene may play an important role in regulation of MGMT transcription and may be a prognostic factor for survival of glioblastoma patients.
FUNDING SOURCE: This study was supported by the grant of the National Center of Science, Poland, 2011/01/B/NZ4/03345.

G-238 - Genome Methylation In Papillary Thyroid Cancer

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Purpose: Papillary thyroid carcinoma (PTC), a usually indolent disorder, is the most frequent thyroid cancer. However, a number of patients present disease progression, for which there are no effective therapeutic options. In this study, the methylation profile was integrated with the large-scale expression gene data of PTC and surrounding normal tissue (NT) aiming to identify putative molecular drivers.
Methods: Forty-one PTC obtained from patients treated with total thyroidectomy and radioiodine therapy were included in this study. The BRAF V600E mutation was evaluated by pyrosequencing method. The microarray platform Methylation 450 Human Infinium®BeadChip (Illumina) was performed in all 41 paired samples. The data were analyzed with wateRmelon package. Thirty-four PTC evaluated by gene expression arrays (Sure Print G3 8x60K; Agilent Technologies) were integrated with the methylome data. Six genes were selected to be confirmed using pyrosequencing and qRT-PCR in 94 PTC and 50 NT samples. The findings were submitted to in silico pathway analysis (IPA and KOBAS).
Results: The BRAF genotyping analysis resulted in 28 cases BRAF V600E. A total of 6,070 probes differentially methylated were identified in PTC samples: 5,425 CpG sites hypomethylated and 645 hypermethylated ($p<0.05$ and $|\Delta\beta|=0.15$). An unsupervised hierarchical clustering analysis revealed one cluster with cases presenting poor prognosis (recurrence, male sex, tumors >1cm and extrathyroidal extension). Integrative analysis between expression and methylation data revealed 214 genes with significant negative correlation ($p<0.05$). We suggested
that ERBB3, FGF1, FGFR2, GABRB2, HMGA2 and RDH5 genes are associated with PTC development being regulated by methylation. In silico analysis indicated the involvement of FGF signaling pathway associated to PTC.
Conclusion: These findings suggest that methylation is one mechanism involved in the regulation of the altered gene expression in PTC. Putative molecular drivers were identified that can be useful in the clinical practice.
Financial Support: FAPESP 2008/57887–9 and CNPq 573589/08–9.

G-239 - A Gene Pathway Approach To Study The Biological Effects Of Vitamin D On Colorectal Tumourigenesis

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Purpose: Biological plausibility, extensive experimental evidence and strong supportive data from prospective observational studies point towards a protective effect of higher circulating vitamin D [25(OH)D] levels against colorectal cancer (CRC) development. However, it is unclear whether or to what extent this association is modified by variation in genes involved in 25(OH)D metabolism and signaling.
Methods: 939 tagging single nucleotide polymorphisms (SNPs) in the vitamin D pathway [including genes related to vitamin D metabolism, mineral homeostasis, and vitamin D receptor (VDR) genomic effects] were analyzed in 1,420 CRC cases and 1,420 matched controls from the European Prospective Investigation into Cancer and Nutrition (EPIC) study using a custom Illumina Goldengate genotyping assay. Multivariable odds ratios and 95% confidence intervals were calculated using conditional logistic regression. The adaptive rank-truncated product (ARTP) method implemented in R-package PIGE was used for pathway analysis.
Results: 100 SNPs in 29 genes related to vitamin D metabolism (CYP24A1/CYP2R1/CYP3A4/GC, etc.), mineral homeostasis (CASR), and genomic effects (VDR/RXRA, etc.) were statistically significantly associated with CRC risk (raw P-values < 0.05), but lost significance after correction for multiple testing. Among controls, 34 SNPs [including 6 SNPs previously identified to be associated with 25(OH)D in GWAS] in 17 genes were statistically significantly associated with season-adjusted concentration of 25(OH)D (raw P-values < 0.05; all non-significant after multiple testing correction). Pathway analyses showed no statistically significant effects on CRC risk for either individual genes or genes grouped into distinct pathways. However, the data suggested that risk associations with genes in vitamin D metabolism pathways may depend on interactions with circulating 25(OH)D (P = 0.06).
Conclusions: The findings from this prospective nested case-control study suggest that common genetic variation in an array of genes related to vitamin D metabolism likely have little influence on the vitamin D-CRC risk association in Western Europeans.

G-240 - Establishing A Causal Effect Of Epigenetic Changes On Risk Of Cancer

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Demethylation at AHRR is a sensitive indicator of cigarette smoking. AHRR has also emerged as the site where DNA methylation is most strongly (and inversely) associated with lung cancer risk. We used Mendelian randomization to establish whether methylation at AHRR has a causal effect on lung cancer, which may mediate the carcinogenic effects of tobacco smoke. This approach uses the random assortment of alleles at conception to circumvent confounding and reverse causation.

We identified two independent genetic variants, rs2671915 and rs2672766, robustly associated with AHRR (cg05575921) methylation in ~1,000 individuals from the Accessible Resource for Integrative Epigenomic Studies (ARIES) which were then used to establish a causal effect of methylation on lung cancer in ~75,000 individuals from the International Lung Cancer Consortium (ILCCO).

For each variant, we calculated the odds ratio (OR) for disease per unit increase in AHRR methylation by the Wald ratio (βGD/βGP), where βGD is the OR for disease per copy of the effect allele in ILCCO and βGP is the unit change in methylation per copy of the effect allele in ARIES, which were then combined in fixed effects meta-analysis.

We found no strong evidence for a causal effect of AHRR DNA methylation on total lung cancer risk (OR = 1.05 (0.93, 1.18) per unit increase in methylation) nor for adenocarcinoma (OR = 0.94 (0.79, 1.13)), although a causal effect was seen for squamous cell carcinoma (OR = 1.35 (1.11, 1.63)).

Results suggest that previous findings implicating increased AHRR methylation with decreased cancer risk are likely to be confounded and rather increased AHRR methylation may increase squamous cell carcinoma risk, which is more in line with the action of AHRR as a tumour suppressor. This approach can be extended to establish the causal role of methylation in mediating associations between other risk factors and cancer.

G-241 - Germline BRCA1 and BRCA2 Mutations In High-Risk Patients In Medellin, Colombia

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Purpose. Germline mutations in BRCA1 and BRCA2 account for 30-50% of inherited breast cancers and 40% of ovarian cancers. Three founder mutations and a few sporadic mutations have been identified in Colombia. The pattern of mutations in different regions of the country remains largely unknown. This study describes the frequency and type of germline mutations in BRCA genes in patients undergoing genetic testing for Hereditary Breast and Ovarian Cancer syndrome (HBOC) in a Comprehensive Cancer Center in Medellín, Colombia.
Methods. We enrolled 45 women referred to the Genetics Service of the Instituto de Cancerología Las Americas who were tested for HBOC or HBOC and other hereditary cancer syndromes according to NCCN 2015 guidelines. Full BRCA1/2 sequencing and detection of large rearrangements or multi-gene panel testing including BRCA1/2 were performed by Myriad (12 BRCA1/2 comprehensive tests and 33 myRisk panels).
Results. Seven patients (15.5%) carried deleterious mutations (5 in BRCA1 and 2 in BRCA2). Among these, one was a novel mutation (BRCA2: c.9246dupG), two were not reported in Colombian women (BRCA1: c.213-12A>G, BRCA2 del exons 15-16), and none were previously described Colombian founder mutations. Six mutation-carriers had a history of breast cancer (median age of diagnosis of 35.3 years), one of ovarian cancer and five had family history of breast and/or ovarian and/or pancreatic cancer. No deleterious mutations were found in other genes and 14/33 (42.4%) multi-gene panels reported variants of unknown significance in other genes.
Conclusions. We found a novel BRCA2 mutation and two BRCA1/2 mutations not previously reported in Colombia. This suggests the necessity of performing full gene sequencing and large rearrangement testing of BRCA1/2 in our population, which currently is not widely done. We propose the creation of an open access Colombian database of genetic variants in high-penetrant cancer genes.
Funding Source. Instituto de Cancerología Las Américas.

G-242 - Role Of GSTM1 And GSTT1 Copy Number Variations In Differentiated Thyroid Cancer Risk In Europeans From Metropolitan France And Melanesians From New-Caledonia

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GSTM1 and *GSTT1* are involved in the detoxification of various exogenous and endogenous substances. Copy number variations (CNVs) or deletion of these genes can lead to increase or decrease of enzyme activities. *GSTM1* and *GSTT1* deletions have been associated to risk of several cancers. We investigated whether CNVs of *GSTM1* and *GSTT1* influenced the risk of differentiated thyroid carcinoma (DTC) and whether they modify the association between DTC risk and previously described risk factors including body mass index (BMI), tobacco smoking, alcohol intake and reproductive factors such as age at menarche and numbers of pregnancy.
We analyzed *GSTM1* and *GSTT1* CNVs in 505 cases and 622 controls of European descent and, 156 cases and 114 controls of Melanesian descent from 2 population-based case-control studies conducted in Metropolitan France and in New Caledonia.
GSTM1 and *GSTT1* CNVs were not associated to DTC risk in Europeans and Melanesians. However, they modulated the association between DTC risk and BMI, alcohol drinking or tobacco smoking in both populations.
The OR contrasting BMI>25 to BMI≤25 kg/m² was stronger in *GSTT1* non-carriers (OR(95%CI)= 2.87(1.14-7.22)) than in *GSTT1* carriers (OR(95%CI)= 1.41(1.00-0.99)); the corresponding ORs in Melanesians women were 5.9(1.61-21.53) and 0.87(0.31-2.46), respectively. The strongest association of BMI with DTC was observed among Melanesians women deleted for *GSTM1* and *GSTT1* (OR(95%CI)= 9.36(2.09-41.84)).
In Europeans and Melanesians, we reported an inverse association between alcohol consumption and DTC risk that was stronger among subjects with deletion of *GSTM1*, *GSTT1 and* both *GSTM1*/*GSTT1*. Regarding cigarette smoking, we reported an inverse association with DTC risk among *GSTM1*/*GSTT1* non-carriers, whereas a positive association was reported among carriers of at least 2 copies of *GSTM1*/*GSTT1*. No effect modification was observed for reproductive factors.
Our results suggest that *GSTM1* and *GSTT1* genotypes modify the association between DTC risk and BMI, cigarette smoking and alcohol drinking.

G-243 - DNA Methylation Markers Of Early Stage Invasion Strategies In Primary Malignant Melanoma

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Purpose: the high mortality rate of melanomas is primarily due to the aggressive metastatic capacity of the tumours. Studies performed so far have accordingly aimed at examining the metastatic disease, while melanomagenesis remains unclear. Because epigenetics provides a valuable tool for biomarkers that can serve as targets for early detection, we attempted to characterize the DNA methylation markers of primary melanomas, which associated with local invasion.
Methods: studying the invasive potential of multiple cell lines derived from primary melanomas was followed by subcultures of invasive clones. Epigenome-wide paired analyses were done in invasive and non-invasive clones by Illumina Methylation arrays; to gain a functional view of the epigenetic changes, we studied gene expression patterns by Affymetrix arrays.
Results: we described a methylation pattern associated with invasion, which involved promoter hypermethylation and decreased expression of genes playing a role in proliferation. Several methylation changes were visible for genes responsible for the mesenchymal transition strategies. Gene body methylation changes affecting TEAD1 master transcription factors and genes of amoeboid transition pathways were also detected. Experimental validation of both the methylation and gene expression results are in progress as well as in silico validation, using the publicly available data. As a next step, we will apply melanoma tissues – from nevi through in situ and to vertical growth phase tumours – in order to infer at which point the invasiveness related methylation changes occur.
Conclusions: our study can contribute to a conceptual change of shifting the focus from therapeutic interventions of the metastatic tumours towards promoting early detection as well as more accurate prognostication of melanomas.
Funding source: the research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of the TÁMOP-4.2.4.A/2-11/1-2012-0001 ‘National Excellence Program’; by IARC Postdoctoral Fellowship and Marie Curie Actions-People-COFUND.

G-244 - Lung Cancer OncoArray Project Identified New Lung Cancer Susceptibility Loci

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Background: Genome-wide association studies(GWAS) have identified several lung cancer loci in *CHRNA3/5, TERT, HLA, BRCA2, CHEK2* and more, although much of its heritability remains unexplained. With comprehensively characterize lung cancer genetic susceptibility, the investigators in Transdisciplinary Research of the Lung(TRICL), International Lung Cancer Consortium(ILCCO) and Lung Cancer Cohort Consortium(LC3) launched the Lung Cancer OncoArray project. **Method:** In collaboration with NCI GAME-ON Network, a customized OncoArray with cancer-specific contents and genome-wide backbone was developed. A total of 18,251 lung cases and 15,220 controls from 29 studies were genotyped. Standard QC procedures were applied resulting in 17,889 cases and 14,969 controls with European ancestry, and imputation was performed based on 1000 genome reference panel. The associations were estimated by unconditional logistic regression under log-additive model. To maximize the statistical power, we conducted a combined analysis with previous GWAS data, adding to a total of 28,082 cases and 54,395 controls. The effects by histological subtypes and smoking status were evaluated and the heterogeneity was assessed based on Q and I^2 statistics. **Results:** We identified 10 novel lung cancer loci with p-value less than $5x10^{-8}$ and odds ratios ranged from 0.83 to 1.85, including those in 1p31($p=6.77x10^{-11}$), 2p15($p=1.92x10^{-9}$), 6p25($p=1.54x10^{-8)}$, 8p12($p=2.06x10^{-10}$), 10q24($p=3.22x10^{-9}$), 11q23($9.84x10^{-11}$), 12p13($1.19x10^{-10}$), 15q21($p=2.65x10^{-8}$), 19q13($p=9.12x10^{-19}$) and 20q13($p=6.05x10^{-9}$). The genetic region in 1p31, 11q23, 15q21 and 19q13 were associated with lung cancer risk overall, while 2p15 and 12p13 were associated with squamous cell carcinoma. The rest were predominately associated with lung adenocarcinoma. Notably these regions encode genes related to cancer biology(*NRG1*, *IRF4*), tobacco metabolism(*CYP2A6*), and telomere regulation(*RTEL1, OBFC1*). **Conclusions:** Based on the largest collaborative analysis for lung cancer genetics to date, we identified additional novel loci specific for histological subtypes. Independent validation and functional characterization are currently underway. These results further our understanding of lung cancer etiology overall and for specific histological subtypes.

G-245 - Exploring Mechanisms Linking Glucose Levels And Cancer-Related Phenotypes In Healthy People: A Recall By Genotype Study

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Purpose
Extensive epidemiological studies have suggested a link between western lifestyle factors that worsen glycemic control and cancer [1-5]. Despite growing evidence that hyperglycemia contributes to cancer progression and compromises the effectiveness of treatment, the mechanisms by which raised glucose contributes to increased cancer progression is not fully established. Previous in vitro studies found that IGFBP-2 expression was increased in hyperglycemic conditions through the acetylation of histones associated with IGFBP-2 promoter [6, 7]. Furthermore, it was found that up-regulation of IGFBP-2 and down-regulation of PTEN levels mediated hyperglycemia-induced chemoresistance [6, 7]. The aim of this RBG study implemented in a population cohort is to evaluate the impact of genetic variants associated with fasting glucose levels on circulating IGFBP-2 protein levels in healthy individuals.

Methods
We will recall 100 healthy participants from the Avon Longitudinal Study of Parents and Children study (ALSPAC) from each tail of the genotypic risk score for glucose for the measurement of IGFBP-2 expression by enzyme-linked immunosorbent assay (ELISA) and acetylation of histones associated with the IGFBP-2 promoter by Chromatin immunoprecipitation assay (ChIP).

Results
Samples of 50 participants from each tail of the genotypic risk score for glucose in ALSPAC yields groups capable of delivering reliable contrasts in glucose levels based on iteratively simulating a random draw of differing proportions of the 5% tails (a=0.01. power>80%).

Conclusions
This study has the potential to improve our understanding of the causal relationship between hyperglycemia and IGFBP-2 levels and to elucidate the biological pathways regulated by hyperglycemia that is pertinent to cancer risk and progression. The study will also educate comparison studies in cancer specific samples. This novel recall-by-genotype design is efficient, maximising statistical power, and enables the collection of extremely precise phenotypic data that is impractical to collect in a larger sample.

Funding Source
Cancer research UK

G-246 - Commercial Crude Extract Of Curcuma Longa Regulates WNT-_-Catenin Activity In HEPG2 Cells

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Introduction: Deregulation of Wnt/β-catenin signaling plays an important role in development of several types of cancer, including hepatocellular carcinoma. Curcumin, the major constituent of Curcuma longa has been shown to modulate the activation of Wnt/β-catenin pathway and diminishes methylation levels of extracellular Wnt antagonists. Likewise, the complete spice (curcuma) displayed hepatoprotective effects, however there are few studies performed with curcuma complete extract in liver cancer.

Purpose: To determine the effect of a commercial crude extract of Curcuma longa in the sub-cellular localization and transcriptional activity of β-catenin in HepG2 cells.

Methods: Curcuma extract was obtained by dissolving a commercial curcuma powder in dimethyl sulfoxide (DMSO). On a daily basis, HepG2 cell line was treated with a non-cytotoxic dose of 250 µg/ml of curcuma extract or 0.25% of DMSO. After 96 hours of treatment, cells were fixed and stained with a primary antibody against β-catenin (BD Transduction Laboratories), Alexa fluor 488 (Life Technologies) as secondary antibody and then counterstained with Hoescht (Life Technologies); subsequently, the sub-cellular localization of β-catenin was evaluated by confocal microscopy. In order to determine β-catenin transcriptional activity, TOPFLASH and FOPFLASH plasmids (Upstate Biotechnology), containing wild-type and mutant TCF binding sites, respectively, were transfected to HepG2 cells to quantify the luciferase activities.

Results: Cells exposed to curcuma extract exhibited low nuclear and cytoplasmic levels of β-catenin in comparison with untreated cells. In addition, curcuma treatment reduced significantly the transcriptional activity of the Wnt/β-catenin pathway.

Conclusion: The results showed here suggest that crude extract of curcuma could regulate Wnt/β-catenin signaling pathway, even in HepG2 cells that has a regulatory domain deletion in one allele of *CTNNB1* gene. These observations need further investigation to reveal the mechanisms involved in β-catenin regulation by complete extracts of Curcuma longa.

Founding source: ITM grant number P10242

G-247 - Folate And DNA Methylation Patterns Within The Breast Cancer EPIC Study

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Purpose: Experimental evidence supports a mechanistic basis for the effect of specific nutrients on breast cancer (BC) development. Among these, there is increasing evidence showing that folate is a relevant candidate for modulation of the epigenome. However, the epidemiological evidence linking nutrition, epigenome and BC development is poorly documented. We aimed to assess the relationship between biomarkers of folate intake and DNA methylation patterns in the European Prospective Investigation into Cancer and nutrition (EPIC) study.

Methods: 451 BC cases and as many matched controls were analysed as part of a nested case-control study on BC within the EPIC cohort. Genome-wide DNA profiling in white blood cells was measured among cancer free women on about 450,000 CpG sites. Beta regression adjusted for laboratory variables (e.g batch) were conducted for each CpG site to determine methylation patterns related to blood folate level. Models were also adjusted for alcohol consumption and age at recruitment, menopausal status, level of different lymphocyte subtypes and BC status. False discovery rate (FDR) was used to control for multiple-testing.

Results: Folate blood levels (median: 12.9 hmol/L, range: 1.2-75.2 hmol/L) were significantly associated with methylation levels in 8 CpG sites after FDR correction. For 7 of these CpGs a high level of folate was associated with an increased methylation level while one CpG was inversely associated. Most of these CpG sites (7) were located in island regions on the chromosome and one in an open sea region. DNA methylation levels in these sites were not correlated (maximum correlation of 0.51).

Conclusions: A list of 8 CpG sites having a methylation level significantly influenced by the blood folate level was identified. Folate can either increase or decrease the level of methylation in these CpG sites.

Funding sources: Institut National du Cancer, Fondation de France and World Cancer Research Fund International

G-248 - ESR1 Overexpression Is Associated With Recurrence On Stage I Endometrioid Endometrial Carcinoma

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Purposes: Endometrial cancer is classified into two subtypes of tumors with different clinicopathological features and prognosis. Endometriod endometrial carcinoma (EEC) is the most frequent subtype. Most of these tumors are diagnosed in early stages and have a favorable prognosis, but some may present an unexpected recurrence, with limited responsiveness to treatment. As prognosis is based solely on clinicopathological features, this study was designed to analyze the EEC global gene expression profile in stage I cases which presented relapse comparing to non-recurrent cases.

Methods: DNA microarray platform was applied in tumor samples of 10 stage I EEC cases, from which 5 presented relapse and 5 didn't. An enrichment analysis of differentially expressed genes (DEG) and a transcriptional factor network assessment were performed in recurrent cases, where one overexpressed factor was identified. Therefore, a quantitative PCR (RT-qPCR) of its encoded gene was performed with a larger number of formalin-fixed paraffin-embedded (FFPE) samples of stage I EEC (n=64): 22 recurrent and 42 not recurrent (n=42) cases.

Results: The estrogen receptor, encoded by ESR1, presented overexpressed in recurrence. ESR1 expression was 4.3-fold higher in relapse cases compared to no recurrence cases in DNA microarray analysis (n=10). Assessment of ESR1 expression by RT-qPCR showed 4.29-fold higher expression in recurrent tumors. ROC curve demonstrated 81.4% of specificity and 65.9% of sensitivity, with 87% of accuracy. Univariate analysis showed a significant association between high expression of ESR1 and worse prognosis in disease-free survival (p = 0.001) and overall survival rates (p = 0.013), increasing the risk of relapse in 5.48 fold and the risk of death in 4.188-fold. In multivariate analysis, high expression of ESR1 was reported as independent prognosis variable for both disease-free survival (p=0.003) and overall survival (p=0.023).

Conclusion: ESR1 overexpression is associated with worse prognosis in stage I EEC.

Funding: CNPq, FAPERJ, CAPES, MS

G-249 - GREB1 Protein Expression Is Associated With Low Recurrence Risk On Stage I Endometrioid Endometrial Carcinoma

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Purposes: Endometriod endometrial carcinoma (EEC) is usually diagnosed in early stages and has a favorable prognosis. However, some cases may present unexpected relapse with poor responsiveness to treatment. A previous DNA microarray assessment was performed with stage I EEC tumors, comparing gene expression profile of recurrent and non-recurrent cases. GREB1 (Growth Regulation by Estrogen in Breast Cancer 1) overexpression showed significant association with relapse. Therefore, the purpose of this study was to evaluate GREB1 protein expression on stage I EEC regarding recurrence status.

Methods: Clinicopathological features of 107 stage I EEC cases were collected, from which 35 presented recurrence and 72 had no relapse. GREB1 protein expression was assessed by immunohistochemistry (IHC) with the primary rabbit polyclonal antibody against GREB1 (N-13) (Santa Cruz Biotechnology, Inc®). The staining score evaluation was performed by two independent pathologists. Protein expression was considered positive when nuclear staining was greater than 10% and its results were compared to relapse status and other clinicopathological data. The chance of recurrence was calculated by Odds Ratio (OR).

Results: IHC revealed that GREB1 expression was found positive on 54 (50.5%) of 107 cases. Regarding non-recurrence group (n=72), it was positive in 42 (58.3%) cases; in 35 cases that presented relapse, it was positive in 12 (34.3%) (p=0.0196). No variables showed a significant association with GREB1 positive expression. However, women with low grade tumors had a higher chance of 2.7-fold to present positive GREB1 expression (p = 0.044). Crude and adjusted by age OR were calculated and both showed GREB1 positive expression conferred a protection association: positive GREB1 tumors provide 63% lower risk of relapse ocurrence comparing to negative tumors (OR = 0.37; p = 0.021).

Conclusion: positive GREB1 protein expression is associated with low recurrence risk on stage I EEC.
Funding: CNPq, FAPERJ, CAPES, MS.

G-250 - Analyses Of MSI Status Frequency, MSI-Target Genes Mutation Profile, And Association With Genetic Ancestry In A Large Series Of Brazilian Colorectal Cancer Patients

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Colorectal cancer (CRC) is the fourth in incidence and in mortality worldwide. Chromosome instability, microsatellite instability (MSI) and CIMP are important in its pathogenesis. MSI is less common and is frequently related with HNPCC Syndrome. In Brazil, the MSI frequency and clinical impact is unexplored. Furthermore, it has been reported that ancestry can influence cancer behavior. In this study we aimed to assess the MSI status frequency in series of 1018 CRC, to analyze the a panel of 25 MSI target-genes, and to determine the molecular ancestry. The MSI evaluation was performed using 5 mononucleotide markers. The MSI-positive tumors were assessed for 25 MSI target-genes by fragment analyses, which were further analyzed for MLH1 promoter methylation and BRAF V600 mutation status. The molecular ancestry was evaluated using 46 ancestry-informative markers (AIMs). We observed that 10.5% (107/1018) of cases exhibited a MSI-H phenotype. The study of MSI target-genes in these 107 cases showed distinct mutations frequencies, with the highest mutated genes been ATM, EGFR, and HSP110 and the lowest ones BLM, WISP3 and TRBP2. In the MSI-H with loss MLH1 expression cases, the frequency of MLH1 promoter methylation was 72% and the frequency of BRAF V600 mutation was 43%. We showed that the ancestry average for all cases was 74% for European component, 12% for African, 7% for Native Americans and 7% for East Asian, and no statistical difference was observed between MSS, MSI-L and MSI-H groups. Concluding, we showed that MSI frequencies in Brazilian CRC are in agreement with literature. We identify altered MSI target-genes with potential clinical impact. Methylation was main cause of MLH1 alteration and almost half of MSI-H with MLH1 negative cases were BRAF V600 mutated. Finally, the MSI status in Brazilian CRC is not associated with the distinct ancestry background of patients

G-251 - RASSF1A And DOK1 Promoters Methylation Levels In Hepatic Tissues With And Without Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death worldwide. Liver cirrhosis promoted by chronic hepatitis C virus (HCV) and chronic hepatitis B virus (HBV) infections are the major risk factors for developing HCC. Hypermethylation of gene promoter regions is the main epigenetic silencing mechanism and has been associated with the development of HCC. Ras association domain family 1 isoform A (RASSF1A) and downstream of tyrosine kinase 1 (DOK1) are tumor suppressor genes whose inactivation has been reported in patients with HCC development. The aim of this study is to determine whether occurrence of aberrant methylation of RASSF1A and DOK1 is associated with the progression of liver disease and HCC in Brazilian patients. Methylation levels were measured by bisulfite pyrosequencing of DNA extracted from formalin-fixed, paraffin-embedded liver tissues. A total of 41 liver samples were analyzed. Of these, 20 were HCC, 9 cirrhotic and 12 normal tissues. In each sample, the percentage of methylation was determined for six RASSF1A and five DOK1 promoter CpG islands. A statistically significant difference ($p< 0.001$) was observed between HCC and non-HCC tissues for both genes. Mean percents of methylation in RASSF1A and DOK1 were as follows: 59.1% and 56% for HCC, 26.1% and 19.6% for cirrhotic, and 16.2% and 12% for normal tissues, respectively. In addition, hypermethylation for RASSF1A and DOK1 was found in 29% and 43% of the cirrhotic tissues, respectively, and in 88% of the HCC tissues for both genes. Our results suggest that methylation levels are related to the stage of the liver disease, being lower in normal, intermediate in cirrhotic, and higher in HCC tissues. This study will help to elucidate epigenetic changes associated to HCC that can be used as molecular markers for liver cancer prognosis, diagnosis and treatment.
Financial support: CNPq, FAPERJ and FIOCRUZ.

G-252 - Analysis Of GSTM1, GSTT1, MDM2 And p53 Polymorphisms And Hepatitis C Virus Genetic Variability In Brazilian Patients With And Without Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death worldwide. Liver cirrhosis promoted by chronic hepatitis C virus (HCV) infection is the major risk factor for developing HCC in Brazil, accounting for over 50% of cases. The development of HCV-induced HCC is a multistep process affected by both genetic and virological factors. The aim of this study is to analyze the association of genetic polymorphisms in GSTM1 and GSTT1 (null genotypes), p53 (Pro72Arg), and MDM2 (SNP309 T/G) genes, as well as the occurrence of the R70Q core mutation in HCV genotype 1b strains, with the severity of liver disease in Brazilian patients. The genetic polymorphisms for each gene were detected by PCR-RFLP, and HCV genotypes were determined by core region nucleotide sequencing followed by phylogenetic analysis. At this moment, 145 HCV positive patients (44 with HCC, 63 with cirrhosis, and 38 with chronic hepatitis) were analyzed. The proportion of null genotype for GSTT1 was higher among patients with HCC (22.7%) or cirrhosis (22.2%) than chronic hepatitis (7.9%). The occurrence of both null genotypes for GSTM1 and GSTT1 was 11.4%, 4.8% and 2.6% in patients with HCC, cirrhosis and chronic hepatitis, respectively. Simultaneous occurrence of MDM2 G/G and p53 Pro/Pro genotypes was only observed among HCC patients (n=2, 5,7%). Furthermore, the HCV 1b-R70Q mutation was found in 6 (46.2%) and 9 (56.3%) patients with HCC and cirrhosis, respectively, but in only one (9.1%) of those with chronic hepatitis. These preliminary results showed that the highest frequencies of GSTM1 plus GSTT1 null genotypes, MDM2 G/G plus p53 Pro/Pro genotypes, as well as HCV 1b-R70Q mutation, were found in patients with advanced liver disease. Genetic and virological factors may be predictors of disease progression and useful for the early HCC detection in HCV chronic patients.
Financial support: CNPq, FAPERJ and FIOCRUZ.

G-253 - Genome-Wide Gene-Smoking Interaction Analysis Identified Signals At RFTN1 And ZC3H11A Gene In Lung Cancer Carcinogenesis

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Purpose: Genome-wide association studies have identified interactions between tobacco smoking and genes on chromosome 15q25.1 and 6q that increase risk of lung cancer. However the identified interactions are still limited because of small effect size and samples size. In this study, we conducted a gene-smoking interaction analysis in a GWAS of lung cancer in Caucasian population to identify latent genes interacting with smoking status.
Methods: We performed the analysis in a three-stage design. In stage I and II, we evaluated all pair-wise (502933) gene-smoking interaction analysis in 1,149 subjects (641 cases and 508 controls) and 2,152 (1082 cases and 1070 controls) using a logistic regression model with adjustment for first three principal components. We then validated the signals at two candidate genes in 30,427 samples (16912 cases and 13513 controls). We also combined all the samples and reported an overall effect. By adopting the same strategy, we also evaluated the gene-smoking interactions in patients with lung adenocarcinoma.
Results: We identified two SNPs, chr3_16408247_A_T, and chr3_16409729_A_G, in RFTN1 gene on chromosome 3 that interacted with ever & never smoking status (chr3_16408247_A_T : p-value=1.67x10-3, 1.70x10-4 and 2.92x10-4 for stage I-III, combined p-value=3.83x10-7; and chr3_16409729_A_G p-value=1.53x10-3, 1.12x10-4, 8.68x10-5 for stage I-III, combined p-value=5.31x10-8). When restricted to lung adenocarcinoma, we identified six SNPs in ZC3H11A gene on chromosome 1 interacted with smoking status. The SNP with strongest signal has p-value=1.53x10-3, 1.12x10-4, 8.68x10-5 for stage I-III, and 5.31x10-8 , OR=1.5 in combined analysis.
Conclusions: An synergetic gene-smoking interaction were observed at RFTN1 and ZC3H11A genes in lung cancer carcinogenesis. The two interactions identified in this study may help explain the missing heritability in lung susceptibility. This study also indicated the existence of latent gene-environment interactions in lung cancer development and provided strong evidence for further evaluation of gene-smoking interactions.
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G-254 - Genetic Alterations In Gliosarcoma And Giant Cell Glioblastoma

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Purpose
The majority of glioblastomas develop rapidly with a short clinical history (primary glioblastoma IDH wild-type), whereas secondary glioblastomas progress from diffuse astrocytoma or anaplastic astrocytoma. *IDH* mutations are the genetic hallmark of secondary glioblastomas. Gliosarcomas and giant cell glioblastomas are rare histological glioblastoma variants, which usually develop rapidly. Clinically, they are considered variants of primary glioblastoma, but genetic data are still scant. The objectives of the present study were to further genetically characterize these glioblastoma variants.
Methods
Sanger sequencing was performed for the *IDH1/2* mutations and *TERT* promoter mutations in 36 gliosarcomas and 19 giant cell glioblastomas. Quantitative PCR was performed to assess LOH 1p, 19q, and 10q in 17 gliosarcomas and 12 giant cell glioblastomas. The Illumina Infinium HumanMethylation450 (450k) array was used for 5 gliosarcomas, and chromosomal copy-number profiling was generated using DNA methylation data. ATRX immunohistochemistry was performed on 17 gliosaromas and on 16 giant cell glioblastomas.
Results
IDH1/2 mutations were absent in all 36 gliosarcomas and in 18/19 giant cell glioblastomas analyzed, indicating that they are histological variants of primary glioblastoma. Furthermore, LOH 10q (88%) and TERT promoter mutations (83%) were frequent in gliosarcomas. Copy-number profiling using the 450k methylome array revealed CDKN2A homozygous deletion (3 cases), trisomy chromosome 7 (2 cases), and monosomy chromosome 10 (2 cases). Giant cell glioblastomas had LOH 10q in 50% and LOH 19q in 42% of cases. ATRX loss was detected immunohistochemically in 19% of giant cell glioblastomas, but absent in 17 gliosarcomas.
Conclusions
These and previous results suggest that gliosarcomas are a variant of, and genetically similar to, primary glioblastomas, except for a lack of *EGFR* amplification, while giant cell glioblastomas occupy a hybrid position between primary and secondary glioblastomas.
Funding sources
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G-255 - The Methylome Landscape Of Cholangiocarcinoma: Crosstalk With Chromatin Regulation And Cancer Driver Mutations

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Cholangiocarcinoma (CCA), a malignancy of the biliary epithelium, exhibits incidence rates that vary widely between geographic regions, reflecting potentially different underlying etiologies. For example, CCA is endemic to Thailand and neighboring regions with high prevalence of liver fluke infections but shows recent incidence increases elsewhere. Exome-sequencing recently identified mutation signatures specific to liver fluke- versus non-fluke-related CCA. However, the epigenomic landscape of CCA is poorly characterized. Using HM27 array and next-generation sequencing (RRBS), we recently identified differentially methylated CpGs associated with specific target genes (mainly Homeobox) of the Polycomb Repressor Complexes (PRCs), which are required for long term epigenetic silencing of chromatin through histone methylation. Homeobox genes that were hypermethylated in gene body regions were highly expressed in CCA tumor tissues and cell lines compared to normal counterparts. Homeobox gene expression also correlated with chromatin status, which was less condensed in CCA cells, as evident by the absence of PRC-mediated repressive histone methylation marks, relative to normal biliary cells. This further supports a role for PRCs in CCA development, as suggested by the methylome-wide analysis. The strongest differences in DNA methylation and expression between tumor and normal cells were evident in HoxA3 and HoxB7. Knock-down of HoxB7 selectively decreased the proliferation of CCA tumor but not normal biliary cells; whereas, HoxA3 knock-down had an inverse effect, highlighting a potential causal role for HoxB7 in CCA tumorigenesis. This study represents the largest epigenome-wide analysis of CCA using cutting-edge technology and can identify epigenetic markers of CCA risk which are being integrated with data on exposure factors and mutation profiles currently under investigation. Moreover, coupled to CCA in vitro models, this work enables a better understanding of the mechanistic insights of this disease, which involves an intricate interplay between DNA methylation, mutation and chromatin regulation. [Acknowledgement: IARC Postdoctoral Fellowship-Marie-Curie-Actions-People-COFUND].

G-255-1 - BRAF V600E Mutation As Initiating Event In The Causation Of Rat Gliomas Following Postnatal Exposure Of N-Ethyl-N-Nitrosourea (ENU)

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Purpose
A single dose of *N*-ethyl-*N*-nitrosourea (ENU) during late prenatal or early postnatal development induces a high incidence of malignant schwannomas and gliomas in rats. While T:A -> A:T mutations in the transmembrane domain of the *neu* (*c-erbB-2*) gene are the driver mutations in ENU-induced malignant schwannomas, the molecular basis of ENU-induced gliomas was unknown. The objectives of this study were to identify driver mutations in ENU-induced rat gliomas.
Methods
We performed whole genome sequencing of gliomas that developed in 3 BDIV and 2 BDIX rats exposed to a single dose of ENU (80 mg / kg body weight) on postnatal day one. Somatic mutations in gliomas were obtained by direct comparison with normal DNA from the same strain of rats. Bioinformatics were carried out to identify common somatic alterations. Candidate alterations were validated by Sanger sequencing and further screened for in ENU-induced gliomas in 33 BDIV and 12 BDIX rats. Immunohistochemistry was carried out in 10 rat gliomas with *Braf* V600E mutation.
Results
T:A -> A:T and T:A -> C:G mutations, which are typical for ENU-induced mutagenesis, were predominant (41-55% of all somatic single nucleotide mutations). Braf V600E (A -> T) mutations were detected in all 5 rat gliomas in bioinformatic analysis, and were validated by Sanger sequencing. Further screening revealed that 33 gliomas in BDIV rats and 12 gliomas in BDIX rats all carried a *Braf* V600E mutation, while peritumoral brain tissue of either strain (n=16) had the wild-type sequence. Immunohistochemistry showed cytoplasmic expression of BRAF V600E in gliomas.
Conclusions
Braf V600E mutations, which are present in several human neoplasms, are the initiating event in the development of rat gliomas caused by a single dose of ENU.
Funding sources
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H-256 - HNdb: An Integrated Database Of Gene And Protein Information On Head And Neck Squamous Cell Carcinoma

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The total amount of scientific literature has grown rapidly in recent years. Specifically in the field of cancer, the number of citations is enormous. This makes it difficult, if not impossible, to manually retrieve relevant information on the mechanisms that govern tumor behavior or the neoplastic process. Furthermore, cancer is a complex disease or, more accurately, a set of diseases. The heterogeneity that permeates many tumors is particularly evident in head and neck (HN) cancer, one of the most common types of cancer worldwide. In the present study, we present a head and neck squamous cell carcinoma database (HNdb) that provides a unified and comprehensive resource for information on the genes involved in this disease, including data on gene products and literature citations. Different literature searches of MEDLINE abstracts were performed using specific Medical Subject Headings (MeSH terms) for oral, oropharyngeal, hypopharyngeal and laryngeal squamous cell carcinomas. A curated gene-to-publication assignment yielded a total of 1,370 genes related to HN cancer. The diversity of results allowed identifying novel and mostly unexplored gene associations, revealing, for example, that processes linked to response to steroid hormone stimulus are significantly enriched in genes related to HN carcinomas. Thus, our database expands the possibilities for gene networks investigation, providing potential hypothesis to be tested.

H-257 - TP53 Variations In Human Cancers: New Lessons From The IARC TP53 Database And Genomics Data

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Purpose
Mutations in the TP53 gene are among the most frequent somatic events in cancer. The IARC TP53 database (http://p53.iarc.fr/) compiles occurrence and phenotype data on TP53 germline and somatic variations linked to human cancer. The database is a popular resource appreciated for the quality and scope of its data and actively used worldwide. The deluge of data from cancer genomic studies generates new data on TP53 variations and attracts a growing number of database users for the interpretation of TP53 variants. Here, we present the current contents and functionalities of the IARC TP53 database and perform a systematic analysis of data extracted from the IARC database and from genomic data repositories.

Methods
Mutation frequency data were extracted from the IARC TP53 database (Sanger sequencing studies) and from TCGA and ICGC data portals (next generation sequencing - NGS - studies). Mutation distributions by protein location and by cancer types were computed and plotted using R software.

Results
The IARC TP53 Database provides a broad scope of data on TP53 gene variations that can be queried with an advanced search interface. The available data on somatic mutations are more extensive than what is currently available in the genomic repositories, with larger number of TP53 mutations and more cancer types covered. However, the higher sensitivity and more complete screening achieved by NGS highlighted some overlooked facts about TP53 mutations, such as the presence of a significant number of mutations occurring outside the DNA-binding domain in certain cancer types. We also provide a list of variants that should be considered as neutral frequent variations and a list of cell-lines with their updated TP53 status.

Conclusions
The data presented will help users to efficiently use this resource and will provide an update of current knowledge on TP53 variations in human cancer.

Funding sources
IARC

H-258 - LoLoPicker ñ An Improved Method Of Detecting Low-Fraction Variants From Cancer

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The detection of tumor-only mutations remains challenging. One of the major complexities is that low-fraction variants (LFVs) are commonly observed in tumor samples, owing to normal-tissue contamination and cancer heterogeneity. Failing to remove unknown errors can significantly affect the specificity of variant calling, especially in calling variants at low-fraction, since most of the random or systematic errors are not frequent. The situation is even worse in calling LFVs from formalin fixed paraffin embedded (FFPE) samples, since error rates in these samples are much higher than high-quality samples.

WES has emerged as a promising tool to discover disease-causing genes. For many basic research or clinical laboratories, the number of samples being sequenced has increased dramatically. Some laboratories build their in-house database to enable them filtering out false-positive calls that are specific to similar protocols, instruments and environmental factors. Such database provides an opportunity to precisely estimate site-specific error rates from control samples, and gives the advantage to increase the sensitivity of calling LFVs on sites with lower error rates, and reduce false positives on sites with high error rates.

No existing software is sufficient to call variants on the whole-exome level, with high sensitivity and low false-positive rate. Here we present LoLoPicker, a tool dedicated to call LFVs from WES data using tumor and its matched normal tissue, plus a user-defined panel of control samples. We observed superior performance of LoLoPicker in comparison with MuTect and VarScan2. While LoLoPicker maintains highest sensitivity among other programs, the specificity of LoLoPicker is significantly improved. Our approach is particularly suited for FFPE samples, since FFPE-specific errors can be identified from a panel of FFPE controls. This tool will open doors for studying targeted therapy and drug resistance.

This algorithm is implemented in Python language and the package is released at https://github.com/jcarrotzhang/LoLoPicker.

H-259 - A Literature And Database Mining Pipeline To Systematically Identify And Curate Renal Cancer Risk Factors

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Introduction

Renal cancer is the twelfth most common cancer in the world, with over 328,000 incidence cases in 2012. A range of risk factors for renal cancer have been identified in observational epidemiology; ranging from diabetes to elevated urinary arsenic levels. However, the causal or confounded nature of these observational associations requires further investigation. Mendelian randomization is an approach to robustly evaluate causality using genetic variants associated with hypothesised risk factors of interest which are not susceptible to confounding or reverse causation. We used a literature and database mining pipeline to systematically identify and curate renal cancer risk factors and their associated genetic proxies in order to appraise their causal nature.

Methods and Results

Literature outlining hypothesised renal cancer risk factors were collated from the PubMed database and organised by prevalence using the statistical programme R (Version 3.0.1) in conjunction with the bibliographic extraction package 'RISmed'. Of an initial 2296 literature results, 232 papers remained, outlining 205 hypothesised risk factors. Genetic variants associated with these risk factors were then assessed by comparison against ‘traits’ in the form of Experimental Factor Ontologies (EFOs) curated by the GWAS Catalog. After matching literature-reported risk factors to EFOs, the strength of these genetic proxies was assessed using a P-value threshold of 5e-8. Each trait was also classified into a primary or secondary analysis, taking into account the variance explained by each trait. A total of 37 risk factors with robust genetic instruments remained to undergo genetic correlation and Mendelian randomization analyses.

Discussion

Many risk factors associated with renal cancer can be proxied by common genetic variants. Further steps are being taken to appraise the magnitude of the association between these genetic variants and renal cancer in a large GWAS, which may ultimately be used to establish whether they are causal in influencing disease onset.

H-260 - Effects Of Dibenzoylmethane Structural Analogues On The Alternative Recombination Pathway For Telomere Lengthening

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Purpose - Cancer cells can bypass the crisis either through telomerase reactivation or through an alternative recombination pathway for telomere lengthening (ALT). Our previous study showed that topoisomerase III (TOP3) is required for type II survivors in yeast and the ALT pathway in human cancer cells. We also reported that dibenzoylmethane (DBM) displays multiple actions toward a carcinogenesis process. In this report, we identified several structural similar DBM derivatives by computer simulated screen to look for TOP3 inhibitor. We evaluated these potential inhibitors in blocking the ALT formation pathway.
Methods - Using various telomeric assays, the ability of telomere recombination in topoisomerase deficient cells was evaluated in yeast and in human. Recombinant human topoisomerase proteins were purified and DNA relaxation assay was also performed.
Results –We use homology modeling to predict the structural of hTop3a, and the screen by molecular docking showed three potential hTop3a inhibitors, which are also the DBM structural analogues. ALT-associated PML bodies (APBs) formation assay revealed one of the potential inhibitors could decrease APB foci formation. Treated with high drug concentration, the enzyme activity of recombinant hTop3a could be inhibited, and the growth of ALT cells was also decreased when concentration increased.
Conclusions –In this report, the molecular docking model was used to predict the potential human TOP3 inhibitors. The results indicated that this screened inhibitor might be a potential anti-tumor drug in blocking the ALT formation pathway.
Funding source - Ministry of Science & Technology of Taiwan.

H-261 - Young Normal Thyrocytes Show A Delayed DNA Repair Kinetics After Irradiation, Not Associated With A Transcriptional Deregulation Of DNA Repair Genes

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Purpose: Ionizing radiation (IR) is the most well-known risk factor for papillary thyroid cancer (PTC), especially during childhood, mainly due to the gradual loss of DNA repair genes and the accumulation of DNA damage. Recent molecular characterization of PTC revealed alterations of DNA methylation in the promoter of several DNA repair genes. Thus, aberrant methylation of DNA might be a plausible mechanism for the inactivation of suppressor genes in radiation-induced thyroid tumors. Herein, we investigated the association among promoter methylation and expression of DNA repair genes and DNA damage in normal thyrocytes after irradiation. **Methods:** Thyroid cell lines derived from normal 3-week and 3-months old mice, FRTL5 and PCCL3, were exposed to single 1-10 Gy X-rays doses for 1-48 h or five cycles of 5 Gy with 72 h intervals. The following parameters were evaluated: cell viability (MTT), cell cycle (propidium iodide/citometer), DNA double-strand breaks (western blot and immunofluorescence of γH2AX and 53BP-1), promoter methylation (pyrosequencing), gene expression (real-time PCR) and senescence (morphology and β-galactosidase activity). **Results:** IR promoted: 1) G2/M arrest, more pronounced in young thyrocytes; 2) a rapid γH2AX accumulation (1h) and an earlier DNA damage resolution in adult thyrocytes, with γH2AX and 53BP1 colocalization in DNA damage sites, 3) biphasic promoter methylation profile of DNA repair genes (Atm, Brca1, Rad50, Lig4, Xrcc4, Xrcc6, Xrcc1) in 5-15% of the cells, with no impact on gene expression. This phenomenon was totally abolished after G0/G1 synchronization with TSH deprivation; 4) senescence when cells were chronically exposed to doses ≥ 15 Gy. **Conclusions:** Young thyrocytes seem to be more sensitive to deleterious effects of IR. Aberrant methylation of DNA repair genes might not be the mechanism involved in the delay of DNA repair kinetics observed in normal young thyrocytes after IR exposure. Funding source: Ministério da Saúde, CAPES, FAPERJ and CNPQ.

H-262 - Exploring The Role Of TLR9 In Contributing To Both Cellular And Immune Surveillance During Breast Cancer

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Breast cancer (BC) is the first cancer in females worldwide; from which 500,000 women die each year. Evading the immune system and cell cycle control are two key events associated with cancer development. The activation of Toll Like Receptor 9 (TLR9) (an innate immune sensor mainly expressed on pDCs) leads to the huge production of type I interferon; a critical mediator involved in tumor immunosurveillance and rejection. TLR9 has been reported to be downregulated in several viral induced tumour cells. In addition, TLR9 responses from tumour associated plasmacytoid dendritic cells (TapDCs) are impaired in ovarian cancer. Based on these results, we hypothesized that TLR9 may contribute to both cellular and immuno-surveillance within the BC. Therefore, we will explore the regulation and decipher the mechanisms of TLR9 dysfunction in mammary carcinoma cells and TApDCs.
Using different tumoral cell lines and an in vitro model of cell senescence, we are currently investigating the role of TLR9 in cell cycle regulation. In parallel, we are generating tools to perform cell cycle analysis and analyze the expression and the role of putative endogenous TLR9 ligands within breast TME.
Overall, this project will allow a comprehensive view of the cellular and immune networks mediated by TLR9 in BC and allow a rational design of innovative therapeutic strategies. The ultimate expected outcome is an improved medical management of the patients from diagnosis to cure.
This study is funded by INCA and is a collaboration between 3 teams, Hasan U. (CIRI), Caux C. (CRCL) and Tredan O. (CLB).

H-263 - Regulation Of ID1 Following Chemotherapy In GBM Is Dependent On Src/TGF-_ Signaling Pathway

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The inhibitor of DNA binding (ID) family of proteins are present at high levels in stem and progenitor cells. They are known to control the timing of cell fate determination and differentiation in stem and progenitor cells during normal development and adult fate specification. ID genes are frequently disregulated in many types of cancers. ID1 has been implicated as a key regulator of cell phenotype in Glioblastoma multiforme (GBM).

In this study, we aimed to investigate the role of ID1 as a mediator of GBM chemo-resistance. Immunoprecipitation (IP) of ID1 protein complex showed ID1 protein is stabilized by de-ubiquitination as a result of TMZ treatment. We further analyzed ID1 protein stability by using the Cycloheximide chase assay to determine its half-life. Thereafter we developed a glioblastoma stem cell line expressing ID1 with a Flag-tag. IP of ID1-Flag protein complex followed by mass spectrometry demonstrated a decrease in the E3 ubiquitin-protein ligase TRIM21 to undetectable levels as a result of TMZ treatment. Furthermore, we identified the proto-oncogene tyrosine-protein kinase Src as a TMZ-induced binding partner of ID1. Western blot analysis along with IP of Src protein complex resulted in correlation of ID1/Src with pSmad2/3 (TGF-β signaling pathway marker) and Smad4 protiens. Using the TGF-β inhibitor LY-36497 and BMP inhibitor Noggin, we determined that the interaction of ID1 with Src, pSmad2/3 and pSmad 1/5, is dependent on activation of the TGF-β signaling pathway.

Together, our results suggest that impaired ubiquitination and stabilization induces ID1 to partner with Src and elements of the TGF-β signaling pathway upon TMZ treatment. This interaction promotes tumor cell proliferation and cell self-renewal, and drives tumor recurrence. We propose that promoting ID1 degradation will provide therapeutic potential for GBM patients.

H-264 - ID1 Is A Pro-Survival Gene Responsible For Glioblastoma Initiation And Tumor Growth

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Glioblastoma multiform (GBM) is one of the most aggressive primary brain tumors. Progress in the treatment of GBM over the last few decades has remained marginal and GBM is still universally fatal with short survival times after initial diagnosis. Temozolomide (TMZ) was the last drug to bring a significant improvement of survival for patients with GBM. Resistance to TMZ is largely due to glioblastoma stem cells (GSC) population.

Transcription regulatory protein, inhibitor of DNA Binding 1 (ID1), has been implicated as a key regulator in GSC. Studies have shown an increase in ID1 expression in a variety of solid tumors. Up-regulation of ID1 correlates with both poor prognosis and chemo resistance. In our study, we investigated the role of ID1 in response to TMZ chemotherapy in GSCs.

We were able to show that ID1 protein expression is up-regulated in response to TMZ in GCS cell lines. We found a majority of GSCs are resistant to TMZ and are able continue proliferating post-TMZ treatment. The next step was to use an effective method for investigating ID1 loss of function and its influence on tumorogensis. Here we utilized CRISPR/Cas9-mediated somatic gene disruption. We established a knockout of ID1 in immortalized GSC cell line U251. Post-TMZ treatment, ID1-/U251 cells displayed significantly lower instance of relapse in cell growth. This result indicated in-vitro ID1 acts as a pro-survival protein in GBM post chemotherapy.

We then exploited this finding by injecting ID1-/-U251 cells along with a luciferase reporter into a mouse xenograft model which resulted in a very substantial delay in tumor formation compared to control, thereby leading to extended survival times. Hence suggesting ID1 is a key factor responsible for GBM initiation and tumor growth. Combined our results provide a rationale for ID1 inhibition as a synergistic therapeutic approach along with chemotherapy against GBM.

H-265 - Modulating DNA Repair Pathways In The Treatment Of Malignant Brain Tumours

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Purpose: Current methods to treat glioblastoma multiforme (GBM) are highly invasive, lead to poor quality-of-life and an abysmal patient survival rate thus making GBMs one of the most difficult-to-treat and deadliest form of all primary CNS malignancies. The targeted use of Topoisomerase-1 (Top1) poisons/inhibitors to sensitize or augment tumour cell killing is a long-standing and powerful tool in cancer therapy. A number of trials utilizing Top1 inhibitors to manage GBM have shown promise.

We have uncovered a novel functional requirement for ATM (Mutated in Ataxia Telangiectasia) in resolving oxidative DNA breaks and Topoisomerase 1-DNA covalent complexes (Top1cc), a DNA-protein intermediate that can generate DNA breaks upon collision with the transcriptional machinery or DNA replication forks. These data have identified Top1cc as the first specific endogenous pathogenic neural DNA lesion associated with loss of ATM and heritable pediatric neurodegenerative disease. Furthermore, biochemical and genetic studies identified collaboration of ATM and TDP1 (Tyrosyl-DNA Phosphodiesterase 1) in the resolution of Top1cc during neurodevelopment.

Methods: We hypothesize that co-inhibition of ATM and TDP1 will sensitize brain tumours to Top1-dependent chemotherapy by augmenting Top1cc levels and anti-tumour success. Genetic and biochemical methods to co-inhibit ATM and TDP1 and improve the efficacy of Top1 poisons include cell-based DNA damage repair and viability assays and *in vivo* brain tumour regression assays using mouse xenograft models.

Results: We have found that brain tumour cell killing via Top1-dependent inhibition is greatly enhanced through an ATM and TDP1 co-inhibition strategy. We are presently validating these results *in vivo.*

Conclusions: ATM and TDP1 co-inhibition represents an effective two-pronged approach to chemoradiosensitize CNS tumours. As TDP1 antagonizes Top1cc formation and efficacy of Top1 poisons such as the camptothecin (CPT) cohort of drugs, my findings will improve existing Top1-mediated anti-cancer strategies by enhancing tumour cell killing while reducing clinical doses and patient side-effects.

H-266 - Exploration Of Esophageal Cancer Etiology Using Comprehensive DNA Adduct Analysis (DNA Adductome Analysis)

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China has the highest incidence and mortality rate of esophageal cancer in the world. Ci Xian, one of the high-risk areas in China, demonstrates a much higher incidence when compared with other urban areas in China. To address the etiology of esophageal cancer in Ci Xian, we carried out a comprehensive DNA adduct analysis (DNA adductome) using surgical specimens collected from esophageal cancer patients living in high- and low-risk areas. The results of principal component analysis showed that several DNA adducts were present in tissues among patients in the high-risk area. By referring to the DNA adducts database, N^2-(3,4,5,6-tetrahydro-2*H*-pyran-2-yl)deoxyguanosine (THP-dG), which was derived from *N*-nitrosopiperidine (NPIP), emerged as a major DNA adduct. In order to confirm the DNA adduct diagnosed as being highly correlated to the high-risk area, we synthesized authentic 15N-THP-dG and analyzed it by quantitative LC-MS/MS apparatus. A peak corresponding to THP-dG, eluted at the same position of authentic 15N-THP-dG, was observed in the surgical specimens collected from the high-risk area. Based on the whole exome/genome analyses of esophageal cancer patients living in the high-risk area and *Salmonella* strains exposed to NPIP with metabolic activation systems, G:C to A:T transition was predominant in both human and bacteria samples. Furthermore, the carcinogenicity of NPIP has been investigated using F344 male rats, and esophageal tumors were observed at a high incidence.
We are now analyzing the THP-dG levels using biological samples collected from subjects residing in both high- and low-risk areas. Moreover, mutational profiles of esophageal tumors in the rats fed NPIP are also being investigated.

H-267 - Exposome-Explorer: A Database On Biomarkers Of Exposure For Cancer Risk Factors

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Purpose: Biomarkers can be used to directly assess environmental exposures to cancer risk factors from biological samples. The identification and selection of the most relevant exposure biomarkers for epidemiological studies is complex and many parameters must be taken into consideration. The corresponding information is scattered in hundreds of scientific publications and often heterogenous in nature. We present here Exposome-Explorer, a new database and web application specifically designed for the collection, organization and retrieval of information on biomarkers of exposure to lifestyle and environmental risk factors measured in epidemiological or biomonitoring studies.

Methods: Highly detailed information on biomarkers of dietary and pollution exposure measured in population studies was systematically collected from peer-reviewed publications. It includes a description of the populations and subjects in each study, samples analyzed, methods used for biomarker analyses, concentrations in biospecimens, correlations with external exposure measurements and biological reproducibilities over time. The database and the web interface to insert, validate and retrieve data were developed in Ruby on Rails.

Results: Data was manually extracted from the scientific literature and inserted in Exposome-Explorer using the annotation interface. The content of almost 500 publications has already been analyzed and 8,850 concentration values in blood, urine and other biospecimens for 492 dietary and pollutant biomarkers were extracted. Exposome-Explorer also contains over 8,000 correlations values between dietary biomarker levels and food intake in various populations. Additionally, 539 intraclass correlation coefficients (ICC) values for biological reproducibility of dietary and pollutant biomarkers over time were also compiled. The new web interface allows making all types of queries to retrieve and analyse the data.

Conclusions: Exposome-Explorer is the first existing database dedicated to biomarkers of exposure to environmental factors. It should be very useful to define panels of exposure biomarkers for epidemiological studies on cancer.

Funding sources: European Commission FP7, NutriTech and Exposomics projects.

H-268 - Impact Of Chronic Multi-Mycotoxin Exposure In Europe On Cancer Incidence: A Basis To Develop Future Public Health Strategies

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Mycotoxins are fungal toxins, estimated by the Food and Agricultural Organization (FAO) to contaminate 25% of the world's most frequently consumed foods and feeds. Several fungi may co-occur on crops, resulting in co-occurrence of multiple mycotoxins. Given the ubiquity of many fungi worldwide, an urgent need exists for a coordinated international response to the problem of dietary mycotoxins.

In terms of chronic toxicity, mycotoxins are estimated to be the most hazardous food contaminants. The International Agency for Research on Cancer (IARC) identifies aflatoxins B1, G1, and M1 as sufficiently evident carcinogens, while other mycotoxins are possibly or probably carcinogenic (e.g. ochratoxin A and fumonisins).

Consumed with food, mycotoxins most commonly affect the liver, where they are metabolized, though not always inactivated. Further down the gastro-intestinal tract, mycotoxins and their active metabolites may interact with colon cancer cells.

Utilizing the European Food Safety Authority (EFSA) database of mycotoxin occurrences in foods, together with the European Prospective Investigation into Cancer and Nutrition (EPIC) study data on food consumption, the applicant will estimate dietary mycotoxin exposures in 23 regional European populations, associating chronic multi-mycotoxin exposure with carcinogenesis.

Preliminary analyses of combined data from EFSA and the European Food Consumption Validation (EFCOVAL) Project reported unexpectedly high exposures, some above upper tolerance levels (unpublished data). This dataset will have been validated through UHPLC-MS/MS quantification of mycotoxin 'exposure biomarkers' in blood and urine, by the time of this conference.

Ultimately, the applicant will determine how chronic multi-mycotoxin exposure influences carcinogenic incidence in Europe. Environmental mutagenic factors will be statistically controlled, to elucidate clear relationships between specific multi-mycotoxin profiles and relative cancer risk.

This is the first large-scale cohort study investigating the effect of multi-mycotoxin intakes on hepatocellular and colorectal cancers. The resulting mycotoxin databases will be instrumental for further characterizing the health effects of real exposure.

H-269 - Genome-Wide Association Study Of Lung Adenocarcinoma And Relationship With Tumor EGFR Mutations Among Never-Smoking Women In Asia, And Comparison With Findings In Western Populations

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Among never-smokers, rates of lung cancer in Asian women are among the highest in the world. We have previously shown that indoor use of coal for home heating and cooking is causally associated with risk of lung cancer among women in China. To provide further insight into the environmental and genetic etiology of lung cancer among never-smoking females in Asia, we formed the Female Lung Cancer Consortium in Asia (FLCCA) including study centers in Mainland China, Hong Kong, Taiwan, South Korea, Japan, and Singapore and conducted a multistage GWAS and meta-analysis of 10,780 cases of lung adenocarcinoma and 10,938 controls. We identified nine independent signals associated with risk of adenocarcinoma overall and a tenth signal (rs3817963, BTNL2) associated with risk of adenocarcinoma among cases with tumors that contained EGFR mutations. In addition, rs9387478 (ROS1-DCBLD1) and rs2179920 (HLA-DPB1) showed stronger effects in EGFR-positive compared to EGFR-negative cases. Comparison of the overall associations with findings in Western populations reported to date revealed that the majority of signals in our studies among Asians were distinct from those reported for Western populations. We also found evidence of gene-environment interactions between two GWAS findings and use of coal for indoor cooking and heating. Our results suggest that both environmental and distinct genetic variants may contribute to the excess of lung cancer among never-smoking women in this region.

I-270 - Rapid Hygienic Evaluation Of Environmental Genotoxic Carcinogens

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Purpose: The aim of the work was to determine the principal possibility early immunological, pathomorphological and genotoxic changes in the organism for assessment the chemicals carcinogenicity.
Methods: The experiment was performed on white random-bred male mice. It included 2 series of the investigations: application of benz(a)pyrene on skin in doses (10.5μg; 2.1μg; 0.21μg); peroral administration of benz(a)pyrene and phenol (single dose - 0.1 mg). Genotoxic changes in skin and forestomach were assessed with the help of micronuclear test.
Results: Regardless of routes of administration carcinogen we determined an increase frequency of micronuclei cells and suppression of T-link of immune system during the first month. In the period between the 1t and the 3d months we observed a stabilization of the number of micronuclei cells and deepening of immunosuppression at the expense of the suppression of humoral chain of the immunity. Repeat increasing of genotoxic effects were found also in later periods of experiment, which is not dependent on the dose of carcinogen, but was associated with induced morphological manifestations of different carcinogenesis stages in target organs.

Conclusion: Revealed differences in the effect of carcinogen and toxic substances, parallel development and unidirection relative to carcinogenesis of the changes of the indices of mutagenic effect and immunologic reactions and also a presence of the reliable correlative link between them in early period (during 1 month) only under exposure of benz(a)pyrene doses which induced the tumors of skin and forestomach is an evidence of a possibility of the use of the complex of these indices as an early criteria of the carcinogenicity of genotoxic chemicasl.

Funding source: The obtained data became a basis for the development of methodic scheme of accelerated testing of the chemical substances for assessment carcinogenicity and hygienic setting of genotoxic carcinogens.

I-271 - Epigenetic Alterations Induced By Genotoxic Occupational And Environmental Human Chemical Carcinogens: A Systematic Literature Review

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Accumulating evidence suggests that epigenetic alterations play an important role in chemically-induced carcinogenesis. Although changes to the epigenome and genome may be equally important in carcinogenicity, the genotoxicity of chemical agents and exposure-related transcriptomic responses have been more thoroughly studied and characterized. To gain a better understanding of the body of evidence of epigenetic alterations, and their potential association with genotoxic endpoints, we conducted a systematic review of published studies that reported epigenetic alterations associated with exposure to genotoxic environmental and/or occupational hazards. Specifically, we searched for reports of epigenetic alterations in studies of one or more of the 31 agents and occupations that are listed in the International Agency for the Research on Cancer (IARC) monographs volume 100F, one component of an extensive re-evaluation of data on known human carcinogens. Of the 31 agents and occupations, 28 have strong evidence of a genotoxic mechanism of carcinogenesis, and we narrowed our literature review to those. We identified a total of 156 studies that evaluated one or more epigenetic alterations in 12 of the 28 included agents and occupations (1,3-butadiene, 4-aminobiphenyl, aflatoxins, benzene, benzidine, benzo[a]pyrene, coke production, formaldehyde, occupational exposure as a painter, sulfur mustard, and vinyl chloride). Aberrant DNA methylation represented the most commonly studied epigenetic feature, followed by changes in the expression of non-coding RNAs, and finally histone modifications (totaling 85, 59, and 25 studies, respectively). For 3 carcinogens (benzo[a]pyrene, aflatoxins and benzene), 10 or more studies reporting epigenetic endpoints were identified. However, epigenetic studies were sparse for the remaining 9 carcinogens; for 4 agents, only 1 or 2 published reports were identified. While further research is needed to better identify carcinogenesis-associated epigenetic perturbations for many potential carcinogens, published reports on specific epigenetic endpoints can be systematically identified and increasingly incorporated in current cancer hazard assessments.

I-272 - Benzene As A Cause Of Hematological Cancers: A Recurring Example Of The Importance Of Mechanistic Understanding And Animal Studies

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IARC can be justly proud of decision processes that combine human, animal, and mechanistic information into carcinogen classification. Benzene provides an example of persistent problems. The original identification of benzene as a known cause of acute myelogenous leukemia (AML) was inappropriately delayed until the 1977 cohort study of Infante et al. (IARC 29, 1982) This occurred decades after causality was accepted by clinicians, which was based upon the collected cases of benzene-associated AML among workers around the world and in different occupations; AML occurring often among those with benzene-induced aplastic anemia; and that similarly to ionizing radiation, a known leukemogen, benzene produced chromosomal abnormalities. Authoritative bodies refused to accept the epidemiologic evidence from Turkey or Italy of statistically significant 2 and 20 fold increases in risk because of the absence of well- defined cohorts despite far greater direct information about the cases comprising the numerator of the relative risk calculations. Infante has since shown that death certificates underestimated cases in his cohort study. Unfortunately, the same overdependence on cohort epidemiology was evident in 2009 when IARC again accorded sufficient evidence for benzene as a cause of AML (100F) but not non-Hodgkins lymphomas (NHL). Epidemiologically there were positive and negative studies, but the animal and mechanistic information for NHLs was far superior to that for AML in 1982. Lymphatic cells are now recognized as deriving from the same stem cell mutated in AML; benzene affects multiple hematopoietic precursor chromosomal sites; genotoxicity is readily observable in circulating lymphocytes; and benzene–exposed animals develop NHLs. Listing additional cancers caused by an already known human carcinogen relates directly to cancer prevention. Designation of causality increases the litigation success of affected individuals which affects purveyors of carcinogens. Further, incorporating the additional cancers into risk estimations can increase regulatory priority for the carcinogen.

I-273 - Impact Of Hepatitis B Virus On Natural Killer Cell Activity

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Natural killer (NK) cells play a crucial role in the immunosurveillance of cancers and in the early control of viral infections. However, in the context of chronic infections, e.g HCV or HIV infections, **a state of NK cell tolerance or exhaustion** has been reported. IL-15 induced-mTOR activation is essential for NK cell activation and acquisition of effector functions. In addition, the immunosuppressive cytokine TGF-b can impede NK cell control of metastatic development and disrupts mTOR activation by IL-15 (unpublished results). **We therefore hypothesized that NK cell exhaustion might result from mTOR pathway deregulation caused by viruses.**

Using the oncovirus Hepatitis B virus (HBV) as liver chronic infection model, we studied the regulation of IL-15 and TGF-β. Both peripheral (blood) and local (liver) crosstalk between macrophages and NK cells were investigated. Kupffer Cells (KC), (i.e specialized liver macrophages) transcriptome was also characterized in this context.
Our data show that IL-15 levels dropped in human KC as well as in monocytes exposed to HBV at a viral genome equivalent of 1000 while TGF-β1 levels increased. This was further confirmed at the protein level. Moreover, by co-cultured experiments with monocytes, we observed that **HBV can inhibit IL-15 signaling** as read out by pS6 (mTOR activation marker) and impaired NK cells functionality (read out: Granzyme B/perforin).

In conclusion, we highlighted a putative mechanism by which HBV could alter innate NK cell response. The virus may increase TGF-b1 secretion that has immune-modulatory properties and down regulate IL-15 expression and signaling leading to the impairment of NK cells activity. **This process might participate to NK cells exhaustion during chronic infection.** Further studies focusing on the mechanistic used by HBV are required. Such knowledge may have important clinical implications to develop novel immunotherapeutic approaches.

This study was supported by La Ligue contre le Cancer and l'ANRS.

I-274 - Study Of Novel Aziridine-Based Brutonís Tyrosine Kinase Inhibitor In Mantle Cell Lymphoma

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Mantle cell lymphoma (MCL) is an aggressive B-cell non-Hodgkin's lymphoma showing hyperactive, autonomously growing neoplastic B cells with extended tumor cell survival. Bruton's tyrosine kinase (BTK), a crucial kinase enzyme in the B-cell antigen receptor (BCR) signaling pathway was emerged as a novel target of MCL therapy. A novel BTK- targeting inhibitor JuSt-23F, which belongs to the class of aziridine-based compound, was prepared. JuSt-23F possessed BTK catalytic activity in vitro with the IC50 value 37,3 μM. As a model for inhibitor testing we have used two mantle cell lymphoma cell lines Mino and Maver-1. WST-8 cytotoxicity assay was explored to determine cytotoxicity and IC50 values were calculated as 32 μM and 37 μM for Mino and Maver-1, respectively. Annexin V-FITC method revealed JuSt-23F - mediated apoptosis selectively in B-lymphoma, but not T lymphoma cells. We detected phosphorylation of p65/RelA on Serine 536 (pNF-kB) in whole Jurkat (T lymphoma), Mino and Maver-1 cells treated with JuSt-23F or untreated after stimulation with tumor necrosis factor alpha (TNF-a). As a result, downregulation of pNF-kB was determined in a dose- depending manner ($P < 0.001$) in TNF-α-induced Mino and Maver-1 cells: 1,6 folds inhibition of pNF-kB in Mino cells and 2,3 folds in Maver-1 cells. We also demonstrated JuSt-23F for mediated inhibition of phosphorylation of the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in mantle lymphoma stimulated by phorbol-12-myristate-13-acetate (PMA). Thus, JuSt-23F exerts its activity through targeting of the downstream BTK signaling cascade via NF-kB and ERK1/2 pathways downregulation. Our findings propose a novel aziridine-based BTK inhibitor JuSt-23F as an attractive potential agent for mantle cell lymphoma treatment. We are planning to develop new derivatives with more efficient inhibition of BTK catalytic activity and downstream signaling pathways.

I-275 - The Role Of B Cells And TLR9 Deregulation By Hepatitis B Virus During Innate Immune Response

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Chronic HBV infection affects more than 240 million people worldwide and is a major risk factor for developing cancer in which 10-30% of cases will progress towards liver cirrhosis and hepatocellular carcinoma. Infection outcome relies on the immune system maturity. TLR9 is a sensor of viral and bacterial DNA motifs and activates pDCs and B cells to generate effective immune responses against infection. Evidently, B cells play a major role in mediating humoral immune responses to clear the infection.
We have previously reported that TLR9 transcription was deregulated by HBV in pDCs. Moreover, we observed the loss of TLR9 expression in PBMCs, particularly B cells, which were derived from chronic HBV patients.
In this study, we aimed to determine if TLR9 expression and function is affected by HBV in human B cells. We also investigated the mechanism by which HBV can deregulate TLR9 pathway and which viral component is responsible for its suppression. TLR7 expression was also assessed as a control. Finally we corroborated the in vitro results using patients with chronic hepatitis B.
We found that HBV decreases TLR9 expression, at both mRNA and protein levels, in all B cells subsets and that TLR9 function, such as proliferation and pro-inflammatory cytokines secretion were abrogated in the presence of HBV; however Ig secretion was not affected. These results were confirmed, in CHB patients with variations between the different patients groups. Furthermore, we observed that HBV can downregulate TLR9 on a transcriptional level by deregulating its promoter. Moreover, we found that this downregulation is mediated by CRE/CREB pathway and that HBsAg participated majorly in this mechanism.
The effect of HBV on TLR9 activity in B cells should give insights into oncoviral immune escape strategies providing knowledge that will be essential to develop novel immunotherapeutic approaches.
This study was funded by ANRS.

I-276 - Innovative In-Vitro Systems For Genome-Wide Modeling Of Mutational Spectra Of Human Cancer Risk Agents

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Purpose
Covalent interaction of carcinogenic compounds with DNA (adduct formation) and other DNA-altering factors can produce characteristic mutation patterns. Thus, identification of mutational signatures of chemical compounds in human tumors provides insights on cancer etiology. Given the complexity of human exposures, it remains a challenging task to extract individual mutational signatures attributable to particular agents. To address this question, we developed robust *in-vitro* models allowing for individual exposures to be tested in a controlled experimental setting.

Methods
Here we present two experimental cell systems that take advantage of selective barrier bypass, clonal expansion and immortalization upon carcinogen exposure: primary mouse embryonic fibroblasts (MEF) and HepaRG human liver cell line. MEFs have been successfully used in the past to reveal mutational effects of known carcinogens on the TP53 sequence. In our models, we investigate exome-wide mutational profiles. A list of tested chemical agents has been defined in collaboration with the IARC Monographs Section, and by extensive semi-automated data mining to prioritize compounds with evidence for mutagenicity, DNA adducts and epidemiological studies.

Results
Primary MEF cultures were exposed to the potential carcinogens acrylamide (Group 2A) and ochratoxin A (Group 2B), whereas HepaRG cells were treated with aristolochic acid I (Group 1). Upon treatment, MEFs underwent senescence followed by senescence bypass leading to immortalized clones which were subject to sequencing and mutational signature analysis. Meta-analysis with *in-vivo* mutational spectra in rodent tumor collection of the US National Toxicology Program and with public human cancer genomics data will be performed to ensure high-confidence identification and cross-validation of the determined mutational signatures.

Conclusions
This simple and powerful experimental strategy can facilitate the interpretation of mutation fingerprints identified in human tumors, elucidate cancer etiology, and ultimately support IARC's carcinogen classification by providing mechanistic evidence.

Funding sources
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I-277 - Analysis Of Size-Dependent Carcinogenic Potential Of Multiwalled Carbon Nanotubes

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MWNT-7, a kind of the various types of multi-wall carbon nanotubes (MWCNTs) has the potential to induce mesothelioma by an intrascrotal or intraperitoneal administration in rats and mice. And a recently reported chronic two-year inhalation study indicated that the MWNT-7 induced lung cancer in rats. To investigated carcinogenic potential of other types of MWCNT, we exposed seven different MWCNTs to rat by single intraperitoneal administration and the rats were then housed for 52 weeks. The potentials of the cytokines induction by macrophage cell of THP-1 were examined for the MWCNTs. At the end of the observation period, four of the seven different MWCNTs induced mesothelioma in all rats of each administration group. The remaining three MWCNTs caused low incidence (0-7.7%) of mesothelioma. The relative carcinogenic potency seems to be depending on the ratios of longer (more than 5 μm) fiber numbers. The potency of the production of inflammatory cytokines (ex. IL-1β) in the THP-1 cells also mainly depended on the ratio of longer fibers numbers and correlated with the potency of the mesothelioma induction. However, in some types of MWCNTs, the cytokines induction potency was not correlated with the mesothelioma induction potency. We previously reported that the longer type (7.6 ± 4.5 μm) of high-temperature calcined fullerene nanowhiskers (HTCFNW) exhibited robust IL-1β production. However, at the preliminary study, the HTCFNW did not induce mesothelioma by single intraperitoneal administration in mice. In conclusion, bio-persistency for long-term and sample preparation methods at in vitro study may be an important factor to assess the carcinogenic potency by MWCNTs exposure, in addition to the ratio of long fiber numbers. This study was supported in part by Health and Labour Sciences Research Grants (H24-Kagaku-Shitei-009, H27-Kagaku-Shitei-004) from Ministry of Health, Labour and Welfare, Japan.

I-278 - Different Mutation Processes Affect HBV Genome In Peruvian Patients With Hepatocellular Carcinoma

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Purpose
In Peru, Hepatocellular carcinoma (HCC) is characterized by an unusual bimodal distribution for age with a first peak of incidence around 20-25 yo. Although, some hitherto unidentified risk factors are suspected to be involved in the patho-physiology of the disease, hepatitis B virus (HBV), found in almost 80% of cases, is known to play here a prominent role.

Methods
We characterized HBV at the molecular level in 64 pairs of HCC and matching non-tumor liver tissues from Peruvian patients.

Results
All viral strains were belonging to F1b subtype, endemic to this region of South America. A striking feature was the extremely low viral loads observed both in tumor and non-tumor tissues (1 viral copy for 100 cell genomes), a situation in contradiction with most observations that consider high HBV loads as the key-risk factor for early HCC. The comparison of HBV DNA mutation spectra in young (n=34) and older (n=19) patients was performed on different region of HBV genome (PreS-S, HBx, HBe-HBc, ≈1500 nucleotides/isolate) and revealed significant differences. Whereas HBV from young patients were mostly mutated on HBe-HBc gene (mean=24 vs. 12%, P=0.004), those from older ones were altered mostly in HBx. Furthermore, HBV DNA in young patients was displaying significantly higher rates of mutation at TT di-nucleotides (27 vs. 15% of total mutation number, p=0.002).

Conclusion
This situation suggests that liver tissue in young patients is the siege of a specific mutational process that contributes to virus restriction. Whether it is contributing or not in liver tumorigenesis is currently under investigation.

Funding sources
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I-279 - Biomarkers Of Chemoradiotherapy Response In Rectal Carcinomas

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Purpose: The large scale gene expression analysis was performed in rectal carcinoma (ReCa) from patients that undergo neoadjuvant radio- or radiochemotherapy (nCRT) aiming to identify biomarkers of pathological complete response (pCR).
Methods: The transcriptome analyses (GeneChip® Human Transcriptome Array 2.0, Affymetrix, USA) were performed in tumor biopsies from 29 patients with ReCa: 21 with pathological incomplete response (pIR) and 8 with complete response (pCR). Data were normalized and analyzed (Transcriptome Analysis Console 3.0, Affymetrix) (ANOVA $p<0.05$) according to the manufacturer´s recommendations.
Results: The data comparison between pIR and pCR cases resulted in 193 genes differentially expressed; 179 of them showed lower expression levels in pCR patients. Among the genes downexpressed in pCR, 15 are related to histone modification (HIST1H4A, HIST1H4B, HIST1H4C, HIST1H4D, HIST1H4E, HIST1H4F, HIST1H4H, HIST1H4I, HIST1H4J, HIST1H4K, HIST1H4L, HIST4H4, HIST2H3A, HIST2H3C, and HIST2H3D), suggesting the involvement of epigenetic alterations in the nCRT response.
Conclusions: Lower expression levels of these particular histones could result in a less tightly bound to DNA and thus making the chromatin more accessible to radio and chemotherapy. Patients with pCR have better prognosis than those with residual disease. These patients could be spared of a highly morbid surgery if the response to nCRT were accurately identified before the procedure.
Financial Support: INCiTO (FAPESP 2008/57887 and CNPq 573589/08-9) and FAPESP (2014/06323-9)

I-280 - Perinatal DDT Exposure Shortens The Latency Of Spontaneous Mammary Tumorigenesis In Mice

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Purpose. The contribution of exposure to dichlorodiphenyltrichloroethane (DDT) to breast cancer risk is controversial. The recent report by the International Agency for Research on Cancer (IARC) Monograph 113 Working Group concluded that “no clear association exists between breast cancer and DDT or DDE measured in samples of blood or adipose taken in adulthood; however, the possible importance of early-life exposure to DDT remains unresolved.”
Methods. We hypothesized that perinatal DDT exposure would result in shortened latency of spontaneous mammary tumorigenesis and increased incidence of lung metastasis. To test this hypothesis, C57BL/6J female mice, bred with B6.FVB-Tg(MMTV-PyVT)634Mul/LellJ male mice, were administered DDT from gestational day 11.5 to postnatal day 5 to achieve maternal serum levels within the upper range of the human cohort study that found a positive association between prenatal DDT exposure and breast cancer risk. We evaluated mammary lesion onset, growth and pulmonary metastasis in the transgenic heterozygotes. We also aimed to study possible mechanisms for DDT increasing mammary cancer risk including features of puberty development and the metabolic syndrome.
Results. Perinatal DDT exposure significantly shortened latency of spontaneous mammary tumorigenesis and was associated with a statistically insignificant doubling of the number of central pulmonary metastases per mouse. Prior to the development of mammary lesions, mice with perinatal DDT exposure had delayed pubertal maturation of mammary glands and elevated fasting blood glucose.
Conclusions. These studies in mice support the finding in humans that perinatal DDT exposure is associated with an increased risk of mammary tumors. Further, the data suggest that disrupted puberty and metabolism may contribute to the early incidence of mammary tumors in mice with perinatal DDT exposure. Our findings call for future research to further evaluate the effects and mechanisms of perinatal DDT exposure on breast tumorigenesis.
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J-281 - Kaempferol Blocks Angiogenesis Through The Suppression Of VEGF-C and HIF-1_ and Prevent Proliferation Through G1 Cell Cycle Arrest In Hepatocellular Carcinoma

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Several pre-clinical studies have shown that Kaempferol has anticancer and anti-inflammatory effect. However, the exact mechanism of anticancer effect of Kaempferol has not been studied. Hence, the effect of Kaempferol on cell cycle and angiogenesis in Hepatocellular carcinoma (HCC) has been investigated. Initially, Kaempferol was tested for its cytotoxicity against Hep3B cells by MTT assay. The effect of Kaempferol on the cell cycle progression was evaluated by flow cytometry. The effects of Kaempferol on the expression of G0/G1 cell cycle regulatory genes were examined. The in vivo model of CAM assay was used to clarify the effect of Kaempferol on liver tumor angiogenesis. Besides, to validate the effect of Kaempferol on tumor angiogenesis, VEGF-C and HIF-1α gene expression were analyzed by RT-PCR. To analyze a possible effect of Kaempferol on migration of Hep3B cell, we analyzed wound closure assays.
Treatment of Hep3B cells with 40 μM (IC50) Kaempferol resulted in the accumulation of cells in the G1 phase when compared to untreated cells. Kaempferol inhibits cell proliferation through G1 cell cycle arrest by activation of P53 gene expression and inhibiting the expression of cyclin D1 and their complex genes of CDK4 and CDK6 in HCC cells. Upon dissection of the CAM of a 12- day old chick embryo, low angiogenic activity in CAM was observed in control. However, high angiogenic activity was found in Hep3B treated. Moreover, Kaempferol also decreases the expression of angiogenic factors VEGF-C and HIF-1α. The untreated cells closed the wound within 6 hrs, whereas the Kaempferol treated cells does not healed/closed over the same period. In conclusion, Kaempferol decrease the angiogenesis activity through the suppression of VEGF-C and HIF-1α and prevent proliferation through G1 cell cycle arrest by inhibiting the expression of cyclin D1 and their complex genes of CDK4 and CDK6 in HCC cells.

J-282 - New Possibilities In Colorectal Cancer Diagnosing: Application Of The Optical Methods For Studying Red Blood Cells And Blood Plasma

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The aim of this work was to assess the potential of the optical methods for studying erythrocytes (Er) and blood plasma (BP) for verification of colorectal cancer (CRC).
Methods: A total of 48 persons (50+9 years old) with CRC in T1-2 stage (20 patients) and in terminal stages T3-4 (28 patients) were examined. The controls consisted of 20 healthy people. Er parameters were investigated by terahertz spectroscopy (THzS), dielectrophoresis. The optical properties of BP were studied by ellipsometry, Raman, NMR spectroscopy. The reaction of the monoclonal antibodies with Tumor Type M2-Pyruvate Kinase (Tu M2-PK) in BP of CRC patients was studied by ProteOn XPR36 (BioRad).
Results: THzS revealed a more intensive lowering of amplitude transmission levels of Er suspensions at all frequencies in the range from the controls to T3-4 ($p<0,001$-$0,05$), which correlated with low capacitance ($r=0,76$, $p<0,02$), Er membrane dipole moment ($r=0,62$, $p<0,01$), low Er deformability ($r=0,71$, $p<0,001$). The increasing the refractive index in combination with a reduction in BP film thickness as weighting CRC stage has been established ($p<0,01$-$0,05$). Using 1HNMR analysis, chemometrics, a differentiation pattern was obtained between the metabolites in the plasma of CRC patients and normal ($p<0,0001$).The main pathways were bile acid, vitamin B6 biosynthesis, synthesis and degradation of ketone bodies. The areas of peaks (1005-1520 cm-1) in Raman spectra were significantly lower in patients with CRC compared with healthy ones ($p<0,001$-$0,04$), correlating with the stage of the process ($r =-0,85$, $p<0,001$) and effectiveness of anti-tumor therapy ($r=0,92$, $p<0,01$). Tu M2-PK plasma levels in CRC terminal stages was above significantly than those in the T1-2($p<0,0001$-$0,02$), correlating with the presence of metastases ($r=0,76$,$p<0,01$), treatment efficiency ($r=-0,82$,$p<0,012$). Specificity of method, obtained in the analysis of the controls, was 93%.
Conclusion. Optical methods for studying Er and blood plasma should be considered as promising for colorectal cancer diagnosing.

J-283 - Physical Activity And Activity Energy Expenditure Are Inversely Correlated With Serum Metabolites Of The Metabolic Syndrome, Body Mass Index And Central Obesity

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Modifiable lifestyle factors, including physical activity and activity energy expenditure (AEE), may attenuate unfavorable health effects of obesity, including components of the metabolic syndrome (MetS) and chronic diseases such as cancer, although the underlying mechanisms are not clear. In this study we sought to investigate whether the metabolic profiles of MetS and adiposity assessed by BMI and central obesity are inversely correlated with physical activity and AEE. We studied 47 women and 35 men, aged 30-60 years, using doubly labeled water to derive AEE and physical activity level and the Sedentary Time and Activity Reporting Questionnaire (STAR-Q) to determine time spent in moderate and vigorous physical activity. Proton nuclear magnetic resonance spectroscopy was used for serum metabolomics analysis. Serine and glycine were found in lower concentrations in participants with more MetS components and greater adiposity. In contrast, serine and glycine concentrations were higher with higher levels of physical activity and AEE in those with and without MetS components. Pathway analysis suggested that the lower serine and glycine concentrations could be a consequence of serine entering sphingolipid metabolism. In conclusion, this exploratory study suggests that the metabolic profiles of MetS and adiposity, and serine and glycine in particular, may be inversely associated with physical activity and AEE. It also provides a potential mechanistic link between obesity and obesity-related diseases. Although promising, future studies need to assess the results relevance to the prevention of obesity-related diseases including cancer.

J-284 - Modulation Of Molecular Markers By Polymeric Black Tea Polyphenols (PBPs) In Tobacco Carcinogen Induced Lung Carcinogenesis In A/J Mice

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Purpose: Chemoprevention with phytochemicals is an evolving approach in cancer management. We evaluated chemopreventive-efficacy (anti-initiation and anti-promotion) of predominant polyphenols in black tea, polymeric black tea polyphenols (PBPs) in experimental lung carcinogenesis.

Methods: Pretreatment of black tea derived PBPs (0.75,1.5,3%) were employed to study the dose-related anti-initiation effects (expression and activity of XMEs) on B(a)P induced lung carcinogenesis in A/J mice using western blotting and BPDE-DNA adducts using immunohistochemical staining. Anti-promotion mechanism of 1.5% PBPs on B(a)P and NNK induced lung lesions was investigated by decrease in macroscopic and microscopic lung tumor incidence and/or multiplicity and/or delay in the latency period. Inflammation, cell proliferation and apoptosis markers along with signaling kinases like p38, Akt and their phosphorylated forms were studied using immunoblotting and immunohistochemical staining at 4^{th},10^{th} and18^{th} week post-carcinogen treatment.

Results: Pretreatment with 1.5 and 3% black tea derived PBPs showed significant down-regulation in carcinogen induced expression and activity of isoforms of phase I (CYP1A1 and 1A2) and up-regulation in phase II (GST mu, pi and alpha) enzymes with decrease in BPDE-DNA adducts; Administration of PBPs decreased the macroscopic and microscopic lung tumor multiplicity significantly. Although, tumor incidence and latency period remains unaffected, histopathological evaluation of lung at 6, 10 and 18 weeks post-carcinogen treatment decreased tumor multiplicity which correlated with different molecular markers. Along with anti-inflammatory action (reduced Cox-2), PBPs down-regulated proliferation (diminished PCNA and Bcl-2) and enhanced apoptosis (increased Bax) potentially through p38 and Akt phosphorylation.

Conclusions: Chemoprevention by PBPs through modulation of xenobiotic metabolizing enzymes (anti-initiation) and inhibition of carcinogen induced inflammation, cellular proliferation and induction of apoptosis possibly via modulation of signaling kinases (anti-promotion). Evaluation of such compounds in multiple organs will further help in monitoring the chemopreventive clinical trials.

Funding: Authors thank TMC and DAE for providing fellowship to RH and supporting the project.

J-285 - Altered Expression Of Tumor-Suppressor And Oncogenic MicroRNAs May Predict Response To Paclitaxel Therapy In Breast Cancer

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Purpose: MicroRNAs (miRNAs) are small non-coding RNAs which have been interested in tumorigenesis and could play tumor-supressive or oncogenic roles, based on their target genes. In this study, expression of four tumor-suppressor and oncogenic microRNAs and their target genes in HER2-positive (BT-474 and SKBR-3) and HER2-negative (MCF-7 and MDA-MB-231) breast cancer cell lines was investigated before and after treatment with Paclitaxel. Methods: Expression level of miRNAs was investigated using quantitative real-time PCR. Results: Expression of both let-7a and miR-205 as tumor suppressors were significantly increased in HER2 over-expressing cell line BT-474 (26.4 fold, p=0.0009 and 7.2 fold, p=0.00013, respectively). In contrary, HER2 negative cell lines, MCF-7 and MDA-MB-231, showed significant decreased expression of both let-7a (30.3 fold, p<0.0001 and 13.5 fold, p<0.0001, respectively) and miR-205 (20 fold, and 18.1 fold, p<0.0001 respectively). Controversially, SKBR-3 revealed mild decreased expression of both let-7a (1.3 fold) and mir-205 (1.3 fold). For important oncomirs, expression level of both miR-21 and miR-203 were increased in HER2-positive cell lines BT-474 (17.66 fold, p=0.002 and 2.09 fold, p=0.06, respectively) and SKBR3 (2.42 fold, p=0.008 and 2.07 fold, p=0.0002, respectively). HER2-negative cell lines, MCF-7 and MDA-MB-231 showed decreased expression of both miR-21 (0.02 fold, and 0.3 fold, respectively) and miR-203 (0.09 fold, and 0.006 fold, respectively). Conclusions: Increased and decreased levels of tumor-suppressor miRNAs were more prominent than oncomirs in BT-474 HER2-positive cell line and HER2-negative cell lines, respectively. This could partially explain different response of HER2-positive and –negative and also better response of HER2-positive breast cancers to paclitaxel therapy. On the other hand, differential expression of miRNAs could be useful biomarkers for response to therapy. However, more studies with broad spectrum of cell lines and patient samples, and also for different miRNAs need for better conclusion.
Funding source: Immunology research center, Tabriz University of Medical Sciences

J-286 - Disregulation Of MicroRNA Expression In Triple Negative Breast Cancer

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PURPOSE: Triple-negative breast cancer (TNBC) represent the most common malignancy in women with aggressive behavior pattern, limited treatment options and poor prognosis. Difficulties in therapy TNBC result from a lack of well-characterized molecular profile. There is increasing evidence that epigenetic factors such as microRNAs (miRNAs) are significantly engaged in the development of TNBC. Expression of microRNAs can serve as a potential biomarkers important for diagnostic, prediction and prognostic in TNBC. The aim of our study was to examine expression of selected miRNAs in TNBC and to assess the relationship between miRNA expression and clinical features.
METHODS: Expression level of 19 selected microRNAs were analyzed by Real Time PCR in breast tissues of 11 TNBC patients. We evaluated the relations between the miRNAs expression level and lymph node status and age.
RESULTS: We found that in TNBC tissues expression of miR-190a, miR-136-5p and miR-126-5p was significantly reduced, whereas miR-135b-5p and miR-182-5p was significantly increased compared with normal breast tissues. However, there was no association between the miRNAs expression level and lymph node status and age.
CONCLUSIONS: miRNAs expression is deregulated in TNBC. However, clinical implication of miRNAs expression need to be elucidate on a larger population.
FUNDING SOURCE: This study was supported by the grant of the National Center of Science, Poland, 2011/01/B/NZ4/03345

J-287 - Circulating Inflammatory Markers And Risk Of Differentiated Thyroid Carcinoma In EPIC

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Purpose
This work is part of the ongoing project to study the aetiology of differentiated thyroid carcinomas (TC) within the European Prospective Investigation into Cancer and nutrition (EPIC) cohort and establish the fraction of possible overdiagnosis in different countries using cancer registry data. Previous results showed direct associations of TC risk with obesity, total energy intake, low consumption of polyunsaturated fatty acids, low alcohol intake. For biomarkers, we found positive associations with circulating concentrations of thyroglobulin and insulin-like growth factor and a negative association with thyroid stimulating hormone. In women, little associations were observed with reproductive history and female hormone use. To further understand the association between overweight and obesity (a state of chronic inflammation) with TC risk, we have set up a study to investigate the relationship between the risk of differentiated TC in men and women and the concentrations of leptin, adiponectin, C-reactive protein, interleukin(IL)-6, IFN-γ, IL-10 and TNF-α.
Methods
A case-control study has been nested within EPIC. Among subjects with a blood sample, 483 first primary incident differentiated TC cases have been identified (404 women and 79 men) and matched on pertinent variables to two (women), or three (men) controls chosen among cancer-free cohort participants by incidence density sampling. Biomarkers are currently being measured on serum samples using previously validated, highly sensitive commercially available immunoassays. Relative risk of differentiated TC by levels of each biomarker will be estimated using conditional logistic regression.
Results
Analyses are ongoing and will be completed in May. Preliminary results will be presented at the meeting.
Conclusions
The proposed study is the first prospective study conducted on inflammation, cytokines and differentiated TC risk, and will provide insights on mechanisms relating overweight and obesity to TC risk. It may inform strategies for the prevention and control of the disease.
Funding: Institut National du Cancer

J-288 - Associations Between Serum Lipids And Breast Cancer Incidence And Survival In The Prospective E3N-EPIC Cohort Study

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Purpose
Several mechanistic studies support a role of cholesterol or its metabolites in breast cancer etiology, but inconsistent associations have been observed in epidemiological studies. Moreover, in observational studies, possible reverse causation must be accounted for using a prospective design. Our aims were to study, in the E3N-EPIC cohort, the associations between pre-diagnostic serum lipid levels (total cholesterol (TC), High-density lipoprotein cholesterol (HDLC), Low-density lipoprotein cholesterol (LDLC), triglycerides (TG)) and breast cancer risk and survival.

Methods
Analyses were performed on 486 cases (diagnosed between 1994 and 2005 and free of cancer at blood collection) and 816 matched controls (matching criteria: date of blood collection, age and menopausal status at blood collection, center) included in a case-control study nested in the French prospective E3N-EPIC cohort. Odds Ratios (OR) and 95% confidence intervals were estimated using conditional logistic regression. Risks of recurrence were estimated in cases using Cox proportional hazards model. Models were adjusted for lifestyle risk factors and mutually adjusted on lipids level. Survival analyses were additionally adjusted for tumor characteristics.

Results
Overall, no association was observed between any of the biomarkers and breast cancer risk (TC: ORT3vsT1=0.94, IC 95%=0.69-1.29; HDLC: ORT3vsT1=1.02, IC 95%=0.61-1.71; LDLC: ORT3vsT1=1.03, IC 95%=0.64-1.65; TG: ORT3vsT1=0.79, IC 95%=0.57-1.11). A significant interaction was observed between triglycerides and alcohol consumption (Pinteraction=0.03, alcohol consumption <10g/day: ORT3vsT1=1.06, IC 95%=0.77-1.45; alcohol consumption >10g/day: ORT3vsT1=0.61, IC 95%=0.40-0.93). No association was observed with invasive disease-free survival in breast cancer cases.

Conclusions
These results suggest an absence of association between blood lipids and breast cancer risk and survival.

Funding source
Mathilde His was supported by a PhD fellowship from the French League against Cancer. The E3N study receives financial support from the French League against Cancer, the Mutuelle Générale de l'Education Nationale, the Gustave Roussy Institute, and the National Institute of Health and Medical Research.

J-289 - Circulating Leptin, Adiponectin, And Breast Density In Premenopausal Mexican Women: The Mexican Teachersí Cohort

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Purpose
Leptin and adiponectin are adipocytokines produced by the adipose tissue. Mammographic density (MD) is the strongest predictor of breast cancer (BC), and is highly influenced by adiposity. How MD directly influences BC risk is still unknown, especially in premenopausal women, where adiposity seems to be protective for BC. The aim of the present study was to explore the association between circulating leptin, adiponectin, and their ratio, with mammographic density in Mexican pre-menopausal women who are part of the large Mexican Teachers' Cohort (MTC), a cohort of over 100,000 teachers recruited in 2006-2008 in 12 Mexican states.

Methods
A subsample of 2,084 women from the MTC participated in a clinical evaluation (anthropometric measurements, a mammogram, collection of biological specimens). Of them, 574 premenopausal women were randomly selected for this study, proportionally to size sampling from four MD strata. A single radiologist performed MD in all regions, taking cranio-caudal views on each breast. Leptin and adiponectin concentrations were measured in serum by immunoassays. Multivariate regression analyses were performed to compare means of MD by quartiles of leptin, adiponectin and their ratio.

Results
After adjustment for BMI, high leptin levels were significantly associated with lower percentage MD compared to low leptin levels (31.02% vs 43.38%, first vs fourth quartile, ptrend<0.0001). No significant association was observed between adiponectin concentrations and MD. The leptin/adiponectin ratio was significantly associated with a lower percentage MD, although this association lost significance after adjustment for BMI.

Conclusions
Low percentage MD is associated with high leptin concentrations, suggesting that the inverse association observed between BMI and BC in premenopausal women might be mediated by leptin, but not adiponectin.

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American Institute for Cancer Research, CONACyT (Consejo Nacional de Ciencia y Tecnología, Mexico), the Ministry of Health of Mexico, AVON, Banorte

J-290 - Circulating Levels Of Copper And Zinc And Risk Of Hepatobiliary Cancer Development

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Purpose: Copper (Cu) and zinc (Zn) are essential trace elements and co-factors of many enzymatic reactions, including those involved in redox processes. Both elements may also play a role in the pathogenesis of cirrhotic complications and liver cancer development. The aim of the study was to assess pre-diagnostic circulating levels of Cu and Zn in relation to development of hepatocellular carcinoma (HCC) and cancers of the gallbladder and biliary tract (GBTC).

Methods: A nested case-control study was conducted within the EPIC cohort. Serum Zn and Cu levels were measured by total reflection X-ray fluorescence in cancer cases (HCC n=109; GBTC n=97) and their matched controls (1:1). Multivariable odds ratios and 95% confidence intervals (OR; 95% CI) were used to estimate cancer risk associations, comparing highest versus lowest tertiles.

Results: For HCC, an inverse risk association was noted (OR=0.33; 95% CI: 0.11-1.00), while Cu was not significantly associated (OR=1.23; 95% CI:0.44-3.47). For GBTC, no significant risk associations were observed (Zn OR=1.45; 0.48-4.37, Cu OR=1.35; 0.53-3.43).

Conclusions: Zn may have a protective role against HCC development, perhaps due to its antioxidant or hepato-protective properties.

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J-291 - Biomarkers For Diagnosis Of Malignant Pleural Mesothelioma

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Aims. To determine the diagnostic performance of two plasma-biomarkers –mesothelin and calretinin – for the diagnosis of MPM, and set their cut off points in the population studied.
Methods. We carried out a case–control study of MPM in 652 insured by the Mexican Institute of Social Security, all Valley of Mexico residents, with 163 incident cases and 489 controls. Plasmatic levels of the biomarkers were measured in all participants by immunoassay sandwich-ELISA technique. Cases were confirmed through immunohistopathological examination. ROC curve analyses, and cut off points were established according to maximum sensitivity and specificity for each biomarker. Unconditional logistic regression models were built to calculate the probability of each biomarker to determine a case of MPM.
Results. Mesothelin AUC was 0.92 (CI;0.87-0.97) with the cut-off point at 0.84 nmol/L (sensitivity of 90.6%; specificity of 80.2%). The AUC of calretinin was 0.85 (CI;0.79-0.91) with the cut-off point at 0.23 ng/mL (sensitivity 83.7%; specificity 70%). The an unconditional logistic regression model was built, with each biomarker based on the cut off points; when mesothelin are >0.84 nmol/L, the OR=12.4 (CI; 5.3-28.5); when calretinin are >0.23ng/mL, the OR=9.4 (CI; 4.4-20.2) and occupational exposure the OR=3.9 (1.4-9.7) and adjusting for age.
Conclusions. Our study provides evidence supporting the mesothelin and calretinin in plasma, can support the diagnosis of MPM. However, further studies to develop a panel of biomarkers are still needed.
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J-292 - AHRR (cg05575921) Hypomethylation Marks Smoking Behavior, Morbidity And Mortality

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Background
Self-reported smoking produces underestimated disease risk estimates. Smoking affects DNA methylation, in particular the cg05575921 site in the *AHRR* gene. We tested the hypothesis that *AHRR* cg05575921 hypomethylation is associated with smoking behavior, risk of smoking related morbidity, and mortality.
Methods
From the Copenhagen City Heart Study representing the Danish general population, we studied 9234 individuals. Using bisulphite treated leukocyte DNA, *AHRR* (cg05575921) DNA methylation was measured. Genotype for rs1051730 (*CHRN3A*) was used to evaluate smoking heaviness and methylation. Participants were followed for up to 22 years for events of chronic obstructive pulmonary disease (COPD), lung cancer, and all-cause mortality. Six-year lung cancer risk was calculated according to the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial ($PLCO_{M2012}$).
Results
AHRR (cg05575921) hypomethylation was associated with smoking status, daily and cumulative smoking, and time since smoking cessation (all p-values<$3*10^{-49}$), and the smoking-related *CHRN3A* genotype (p=0.003, trend test). The multifactorially adjusted hazard ratios for the lowest versus highest methylation quintiles were 2.91(95% confidence interval, 2.23-3.80) for COPD, 4.87(2.31-10.3) for lung cancer, and 1.67(1.48-1.88) for all-cause mortality. Finally, among 2576 high-risk smokers eligible for lung cancer screening by CT, the observed cumulative incidences of lung cancer after 6 years for individuals in the lowest and highest methylation quintiles were 3.7% and 0.0% (p=$2*10^{-7}$), whereas the predicted $PLCO_{M2012}$ 6-year risks were similar (4.3% and 4.4%, p=0.77).
Conclusion
AHRR (cg05575921) hypomethylation is a marker of past and current smoking behavior and provides potentially clinical relevant risk predictions of future smoking related morbidity and mortality.

J-293 - C-Reactive Protein And Risk Of Lung Cancer: A Pooled Analysis Of 20 Prospective Cohorts

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Background: Inflammation may have an important role in the etiology of lung cancer, and several studies have reported that C-reactive protein (CRP) is associated with risk of lung cancer. To clarify this association, we conducted a pooled analysis of CRP and lung cancer risk using data from 20 prospective cohort studies.

Methods: Within the NCI Cohort Consortium, we designed a prospective nested case-control study. Controls were selected from appropriate risk sets and were matched to cases on smoking status, sex, and age at blood draw. This analysis included 5,299 case-control pairs nested within 20 cohorts. Rate ratios (RR) and their 95% confidence intervals associated with a doubling in concentration of CRP were estimated using conditional logistic regression models.

Results: Overall, higher circulating CRP was associated with an increased risk of lung cancer (RR 1.05, 95% CI [1.03, 1.08]). This association varied strongly by smoking status (p-heterogeneity < 0.01), being similar for current (1.09 [1.05, 1.13]) and former smokers (1.09 [1.04, 1.14]), but not for never smokers (0.95 [0.91, 1.00]). The association was strongest for cancers diagnosed less than 2 years after blood draw (1.21 [1.13, 1.29], p-heterogeneity < 0.01), and weakened as time between blood draw and diagnosis increased. The association was similar across all histological subtypes, with the exception of adenocarcinoma for which we observed no association.

Conclusions: CRP is associated with risk of lung cancer. The fact that the association is restricted to ever-smokers, and is most prominent for cancers diagnosed in the first 2 years of follow-up, strongly suggests that CRP is not a causal risk factor, but rather a distal marker of disease.

J-294 - Parthenolide Induces Autophagy In Cervical Cancer Through The Modulation Of Autophagy Dependant Signaling PI3K/AKT Pathways

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Purpose: Autophagy is a major degradative cellular process that involves the delivery of cytoplasmic cargo into lysosomes leading to the formation of autophagosomes. It prevents the spread of cancer by promoting the death of cancerous cells. In the present work, the parthenolide induced autophagy in cervical cancer HeLa cell line was investigated.
Methods: MTT assay was performed to evaluate the cytotoxicity of parthenolide and to determine its IC 50 value. The auto fluorescent agent Monodansylcadaverine (MDC) was used as a marker to detect the autophagosome in HeLa cells. After 24hrs treatment with parthenolide, the cell morphology was examined and visualized using fluorescent microscopy.
Results: The parthenolide treated cells exhibited green color. MTT assay showed a dramatic loss of viability of cancer cells treated with varying concentrations of parthenolide (0, 2, 4, 6, 8 and 10 μM). Parthenolide (IC50 = 6μM) significantly inhibited the anti-apoptotic Bcl-2 gene expression and simultaneously up regulated the proapoptotic gene Bax and Caspase-3 expressions. Furthermore, Parthenolide induced autophagy in cervical cancer cells through the formation of autophagosomes by activating PTEN gene expression. In addition, it inhibited PI3K/AKT signaling pathways through the expression of autophagy related genes viz. Atg-5, Beclin-1 via suppressing mTOR gene, which is a key regulator of autophagy and apoptosis.
Conclusion: Parthenolide can exert anticancer effects by activating autophagy and by inducing apoptosis in HeLa cells through the upregulation of PTEN gene and inhibition of PI3K/AKT signaling. Our results suggest that parthenolide may have potential activity against cervical cancer cells.

J-295 - Metabolic Profiles Of Plasma Samples From Patients With Colorectal Cancer, Colorectal Adenomas, And Controls

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Purpose: Metabolomics is a promising high-throughput approach to define metabolic biomarkers associated with cancer and to help provide insight into the role of metabolism in carcinogenesis or responses to disease treatment. The primary objective of this colorectal cancer (CRC) patient study is to locate plasma metabolic biomarkers distinguishing three patient groups (cancers, adenomas, and disease-free) to inform CRC screening strategies. Secondary objectives are to: (1) Associate a metabolic profile with colorectal neoplasia pathology or location, and (2) Examine the metabolic profile of the cancers with regard to clinical outcome (i.e., do particular metabolic profiles associate with disease prognosis or treatment response?).
Methods: One hundred forty five metabolites were measured in 390 plasma samples from sample cohorts from Ireland and the Czech Republic using the AbsoluteIDQ® p180 kit (Biocrates, Innsbruck, Austria) and a Q-trap 5500 mass-spectrometer (AB-Sciex, Framingham, MA). The Irish study includes 27 CRC patients, 133 with advanced adenomas or polyps, and 57 controls (normal after colonoscopy). The Czech group comprises 126 CRC patients and 47 blood-donor controls of a similar age range. The different concentrations and ratios of metabolites will be analysed as continuous and categorical variables. Correlations of metabolite levels will be represented by heat maps among cases (CRC or adenoma) and controls, and differences in levels between cases and controls will be estimated by t-tests and ANOVA. Logistic regression models will be used to estimates odds ratios for significant difference between disease state. Differences by batch, cancer stage, treatment responses and survival outcomes, sex, country, cases and controls will also be assessed.
Results & Conclusions: As we are still finishing the final sample runs and analysing our results, the findings will be presented at the meeting.

Funding: Sample collections were funded by AZV 15-27580A (Czech Ministry of Health) and the Meath Foundation grant 2008-2010 (Dublin, Ireland).

J-296 - The Impact Of Short-Term Exposure To Disinfection By-Products On The Metabolome ñ A Metabolome-Wide Association Study

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Purpose
Exposure to disinfection by-products (DBPs), found in drinking water and swimming pools, has been associated with adverse health outcomes such as bladder cancer and impaired respiratory health. The underlying biological mechanisms are still unknown and therefore the aim of this study was to investigate the impact of DBPs on the metabolome.

Methods
We used data from the experimental PISCINA-II study, which was performed in an indoor chlorinated pool where 60 volunteers (18-40y non-smokers) swam for 40 minutes. Questionnaires about lifestyle factors and physical activity were completed, heart rate was monitored, and exhaled breath and blood samples were collected before and 2 hours after swimming. Exposure to DBPs was assessed using measurements of chloroform, bromodichloromethane, dibromochloromethane and bromoform in exhaled breath and pool water. Untargeted metabolomics of plasma samples was conducted using a UHPLC-QTOF mass spectrometer operated in ESI positive mode. PLS-DA was performed and the association between DBP-exposure and levels of metabolites was analysed using confounder adjusted linear mixed models (FWER 5%).

Results
All exposures were significantly higher after the experiment. PLS-DA suggested that samples obtained before swimming can be distinguished from samples obtained after swimming. Linear mixed models showed an association between chloroform, bromoform and total trihalomethanes concentrations measured in exhaled breath and levels of 15, 1, and 3 metabolites, respectively. For exposures measured in pool water, additional associations were found for bromodichloromethane and the brominated species.

Conclusions
After annotation of the metabolites, our work will provide insights into metabolic changes induced by DBP exposure, shedding light on biological pathways affected by these exposures, and in-turn impacting future risk of adverse health outcomes.

Funding source
EXPOsOMICS project

J-297 - Pre-Diagnostic Targeted Metabolomic Profile Of Hepatocellular Carcinoma Risk In A Nested Case-Control Study Within EPIC Cohort

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Purpose: Hepatocellular carcinoma (HCC) is highly malignant with increasing incidence rates in Western countries. We aimed to identify metabolite alterations associated with HCC development in the EPIC cohort.
Methods: In a nested case-control study with 147 HCC cases matched to 1 control each, 141 metabolites were measured in prospectively collected sera using Biocrates AbsoluteIDQ p180Kit. Metabolite levels were log-transformed and standardized, and odds ratios and 95% confidence intervals were calculated with multivariable conditional logistic regression. Bonferroni correction for multiple testing was applied. In order to identify the most consistently predictive metabolites, we subsequently applied and compared four additional methods for variable selection: (i) PCA; (ii) variable importance in projection in PLSDA; (iii) stepwise selection in logistic regression and (iv) elastic net analysis. Receiver operating characteristic (ROC) curves were constructed to estimate discriminatory accuracy of the metabolites that appeared as significant in at least 4 methods.
Results: Bonferroni correction showed significant HCC risk associations for 31 metabolites: 3 amino acids (glutamine, glutamate and tyrosine), 20 glycerophospholipids (8 lyso phosphatidylcholin(PC): c16:0, c17:0, c18:0, c18:1, c18:2, c20:3, c20:4, c28:1; 8 diacyl PC: c28:1, c32:3, c34:4, c36:4, c36:6, c38:5, c28:6, c42:5; 4 acyl-alkyl PC: c30:2, c36:1, c38:0, c40:1), 4 sphingomyelins (c16:1, c18:0, c18:1, c20:2) and 4 hydroxysphingomyelins (c14:1, c16:1, c22:1, c22:2). In all 5 statistical analyses glutamate, diacyl PC c42:5, lysoPCs c17:0 and c20:4 appeared as predictors of HCC development, while PC diacyl c32:3 and acyl-alkyl c38:0 and sphingomyelin c18:1 appeared in 4 out of 5 analyses. Based on ROC, discriminatory power of these 7 metabolites was 89%.
Conclusions: Our findings indicate that metabolic alterations, especially those related to glycerophospholipids and glutamate metabolism, are involved in HCC development. To identify additional novel metabolic pathways in HCC development, we are currently conducting an untargeted metabolomic analysis of the same samples.
Funding source:French National Cancer Institute

J-298 - Quantification Of Temporal Fractions Of The Human Exposome Using Differential Stable Isotope Coding Technique Coupled With High Resolution Mass Spectrometry

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The exposome conceptually represents the totality of individual' environmental exposures and how these exposures relate to biological responses leading to disease development. An individual's exposome is highly variable and dynamic throughout the lifetime; thus its measurement is challenging. Luckily, owing to advanced technologies available to date, the ability to accurately measure different (temporal) fractions of the human exposome has begun to develop. Here, we describe a metabolomic approach developed for the semi-quantification of fractions of the exposome containing a large suite of biomarkers of exposure to dietary and environmental chemicals such as phenols, polyclyclic aromatic hydrocarbons, pesticides, parabens, and phthalates. We employed differential stable isotope coding technique, based on the use of 13C/12C-dansyl chloride and 13C/12C p-dimethylaminophenacyl reagents, to permit compounds containing phenol and amine, or carboxylic acid groups to be uniformly detected using ultra-high resolution mass spectrometry (Hybrid Quadrupole Orbitrap Mass Spectrometer and Quadrupole Time-of-Flight Mass Spectrometer). This approach combines a highly sensitive broad scan detection of hundreds of compounds with the reliable estimation of their presence in biospecimens. In addition, stable isotope coding significantly reduces intrinsic matrix effects, and generally improves sensitivity of the measurements. Exploratory analysis of pooled urine samples revealed detection of 3,5,6-trichloro-2-pyridinol (a metabolite of chlorpyrifos and chlorpyrifos-methyl), bisphenol a, naphthols, and dietary phenols commonly found in trace amounts in urine of different populations. This could, therefore, warrant further use of this approach in large prospective epidemiological studies linking human exposures to cancer risk.

J-299 - Use Of Targeted Metabolomics In The Relationship Between Healthy Lifestyle Index And Hepatocellular Carcinoma In The EPIC Study

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Purpose: Metabolomics has the potential to disclose pathological processes leading to a better understanding of disease development. The “meeting-in-the-middle” principle is particularly suitable to explore such data, as it may reveal exposure-specific biomarkers that are predictive of morbid conditions. Using this concept, components of a healthy lifestyle index (HLI) were explored with respect to serum metabolites in a nested case-control study on hepatocellular carcinoma (HCC) within the EPIC cohort.

Methods: Using 147 HCC cases and 147 matched controls, Partial Least Squares (PLS) analysis related 7 HLI variables (“predictors”, including diet, body mass index (BMI), physical activity, lifetime alcohol consumption, smoking, diabetes and hepatitis) to 132 metabolites (“responses”), acquired using standard targeted metabolite profiling protocols (BiocratesKit). A series of multiple PLS was further applied using each HLI variable separately. All resulting PLS scores were related to HCC risk in conditional logistic regression models.

Results: One overall PLS factor was retained. Its HLI component was associated with low levels of lifetime alcohol, BMI, smoking and diabetes and high levels of physical activity. Its metabolic counterpart was positively related to sphingolipids C14:1, C16:1, C22:2, and negatively with glutamate, hexoses, and glycerophospolipids C32:0, C32:1. Both components displayed a decreased HCC risk with odds ratios (OR) equal to 0.46 (95% CI: 0.43-0.95, P = 0.03) and 0.81 (0.72-0.91, P<0.001) for a 1 SD change in the components’ scores. Specific metabolic signatures of BMI, smoking and lifetime alcohol were found to be statistically significantly associated with an increased HCC risk, with OR=1.35 (1.12-1.62, P<0.01), 1.31 (1.13-1.51, P<0.001) and 1.47 (1.03-1.27, P=0.01), respectively.

Conclusions: In a setting with targeted metabolomics, this study explored relations between metabolites, lifestyle variables and HCC risk, using an integrative approach to maximize the informative potential of high-throughput data with respect to cancer risk.

Funding: INCA, EDISS Lyon.

J-300 - Untargeted Metabolomics For The Discovery Of Plasma Biomarkers Of Coffee Intake In The EPIC Cohort

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Purpose
The consumption of coffee has been consistently associated with lower risk of cancers of the liver, endometrium and skin, as well as overall mortality. However, epidemiological studies of coffee and health typically rely on a non-specific measure of total coffee intake obtained from dietary questionnaires. It is unknown whether heterogeneity in this complex dietary component impacts these associations. The aim of this study was to use untargeted metabolomics to discover new plasma biomarkers of diverse coffee intakes in free-living subjects that may be used as an alternative or complement to questionnaire-based methods.

Methods
Firstly, 76 coffee brew samples were analysed by high resolution mass spectrometry coupled to liquid-chromatography (LC-MS) to identify prominent coffee compounds and evaluate differences between their profiles by species, production and preparation type. Secondly, plasma samples from 475 participants of the European Prospective Investigation into Nutrition and Cancer (EPIC) were also profiled. These subjects were from France, Germany, Italy and Greece and reported habitual coffee intake using a food frequency questionnaire. Mass spectral features whose intensities were correlated with reported coffee intake were identified using a multinomial regression, adjusting for country, sex, smoking status and alcohol consumption.

Results
A number of plasma metabolites correlated with high coffee consumption were identified using knowledge of coffee compounds gained by analysis of the 76 coffee brews and mining of open-source web databases. These characteristic signals included alkaloids, polyphenols, diterpenes, amino acids and aldehyde and ketone flavour compounds. Many of these are highly specific to coffee.

Conclusions
These biomarkers will be subsequently validated and used individually or in combination to aid coffee intake estimation in future cohort studies and to further clarify the role of coffee in cancer prevention.

Funding source
National Cancer Institute, Bethesda, USA.

J-301 - The Effect Of Quercetin And Doxorubicin Combination In Inhibiting Resistance In MCF-7 Cell

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PURPOSE. This purpose of this study to investigate the effect of quercetin and doxorubicin combination in inhibiting the development of resistance in MCF-7 cell.
METHODS. Doxorubicin-resistant MCF-7 cell were developed from the parent MCF-7 cell by giving doxorubicin concentration below the IC50 value of parental MCF-7 cell, twice a week for a period of 25 days. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) citotoxicity assay and flowcytometry assay were performed to investigate P-glycoprotein level as a marker of doxorubicin resistance developed in MCF-7. The inhibitory effect of resistance was evaluated via exposured MCF-7 cells to 75 nM doxorubicin and 750 nM quercetin combination in the same manner with resistance induction. MTT citotoxicity assay and flowcytometry assay were performed to investigate the degree of resistance and inhibition of resistance development.
RESULTS. Exposure of MCF-7 cells to 75 nM doxorubicin reduce the sensitivity of the cancer cells and enhance P-glycoprotein level. This effect was statistically-significant (95% CI;$p<0,05$). The combination of 750 nM quercetin and 75 nM doxorubicin (MCF-7 cells/dox75q750) significantly increase sensitivity of MCF-7 cell to doxorubicin ($p<0,05$) and decrease in P-gp expression ($p> 0,05$).
CONCLUSIONS. The combination of quercetin and doxorubicin have potency to inhibit the development of doxorubicin-acquired resistance MCF-7 cell by increasing cell sensitivity and reducing P-gp expression level.
KEYWORDS. MCF-7 cell line, Resistance, Quercetin, Doxorubicin, P-gp
FUNDING SOURCE. This study was financed partly by HPEQ (Health Professional Education Quality Project)-Dikti through Faculty of Medicine-UII who had provided scholarship.

J-302 - Differential Isotope Labelling Of 38 Dietary Polyphenols To Measure Exposure To Dietary Polyphenols In Epidemiological Studies

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Purpose: A large number of studies support a role of polyphenols in the prevention of chronic diseases such as cardiovascular diseases, diabetes or cancers, however epidemiological evidence is still limited. Robust methods are needed to reliably assess exposure to a large variety of dietary polyphenols which can be easily applied to epidemiological studies.
Methods: We report here the development of a method to quantify dietary polyphenols in urine and in plasma, based on differential ^{12}C-/^{13}C-isotope labelling of polyphenols through derivatization with isotopic dansyl chloride reagents and on the analysis of the labelled polyphenols by tandem mass spectrometry. Urine or plasma samples are first hydrolysed with a β-glucuronidase/sulfatase enzyme mixture and the resulting polyphenol aglycones extracted twice with ethyl acetate. Samples containing the polyphenols tagged with ^{13}C-dansyl groups are mixed with a reference urine or plasma sample containing polyphenols tagged with ^{12}C-dansyl groups and analyzed by tandem mass spectrometry. Polyphenol concentrations are estimated through the calculation of ratios of labelled over non-labelled polyphenols
Results: The method was successfully applied to the measurement of 38 different polyphenols, either native compounds representative of the main classes and subclasses found in the diet, or metabolites formed by the microbiota or human tissues. It was applied to the analysis of 475 urine samples of the European Prospective Investigation on Cancer and nutrition (EPIC) cross-sectional study, and 1170 plasma samples of a case-control study on colorectal cancer nested in EPIC.
Conclusions: The method provides a simple and robust mean for measuring polyphenols in urine and in plasma and overcomes the need of having expensive labelled standards for each compound.

Funding sources: Institut National du Cancer (INCa 2011-105) and Wereld Kanker Onderzoek Fonds (WCRF NL 2012/604).

J-303 - Higher Plasma Levels Of Lyso-PC 18:0 Are Related To A Lower Risk Of Common Cancers In A Prospective Metabolomics Study

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Purpose: First metabolomics studies have indicated that metabolic fingerprints from accessible tissues might be useful to better understand etiological links between metabolism and cancer. However, there is still a lack of prospective metabolomics studies on pre-diagnostic metabolic alterations and cancer risk.

Methods: Associations between pre-diagnostic levels of 120 circulating metabolites (acylcarnitines, amino acids, biogenic amines, phosphatidylcholines, sphingolipids, and hexoses) and the risks of breast, prostate, and colorectal cancer were evaluated by Cox regression analyses using data of a case-cohort sample from the EPIC-Heidelberg study including 835 incident cancer cases.

Results: The median follow-up duration was 8.2 years among non-cases and 6.5 years among incident cases of cancer. Higher levels of lyso-phosphatidylcholines (LysoPCs), and especially LysoPC a C18:0 were consistently related to lower risks of breast, prostate and colorectal cancer, independent of background factors. In contrast, higher levels of phosphatidylcholine PC ae C30:0 were associated with increased cancer risk. There was no heterogeneity in the observed associations by lag time between blood draw and cancer diagnosis.

Conclusion: Shifts in blood lipid composition precede the manifestation of common malignancies several years prior to diagnosis. Considering the consistency of the present results across three cancer types the observed alterations point to a global metabolic shift in phosphatidylcholine metabolism that may drive tumorigenesis.

Funding source: The present metabolomics project was supported by the Helmholtz Association (Portfolio Theme “Metabolic Dysfunction”). The EPIC-Heidelberg study was further supported by the German Federal Ministry of Education and Research (BMBF) (Grant number 01ER0809).

J-304 - Metabolic Profile And Prostate Cancer Risk In EPIC

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Purpose
The aetiology of prostate cancer is largely unknown. Elevated circulating insulin-like growth factor I (IGF-I) remains the only established and potentially modifiable risk factor. Protein intake may be positively associated with risk, and diets high in protein can increase circulating IGF-I. Metabolomics may help to clarify the mechanisms underlying these associations and may identify novel risk factors for prostate cancer. For example, dietary amino acids may affect cancer risk through effects on the synthesis of IGF-I and/or by stimulation of the mTOR pathway, which integrates signals from nutrients and growth factors and is an important mediator of cancer progression. We aimed to prospectively investigate the association between pre-diagnostic metabolic profile in plasma and prostate cancer risk.

Methods
A case-control study has been nested within the EPIC cohort, with 2000 cases of prostate cancer and 2000 matched controls. Concentrations of 145 metabolites (acylcarnitines, amino acids, biogenic amines, glycerophospholipids, hexose and sphingolipids) are being measured at IARC in prediagnostic plasma samples using the BIOCRATES AbsoluteIDQ p180 Kit, a targeted metabolomic assay. Relative risks for prostate cancer in relation to concentrations of individual metabolites and metabolic profiles will be estimated using conditional logistic regression.

Results
Assays from a total of 1000 case-control pairs will be completed by March and these data will be presented at the meeting.

Conclusions
This study will provide prospective data on the relationships between plasma metabolites and prostate cancer risk, and will advance our understanding of the relationships between diet, circulating hormones and risk for the disease, as well as the underlying mechanisms. The identification of potentially modifiable metabolic profiles associated with risk, and of correlated dietary and hormonal factors, may inform the future design of effective public health policies aimed at prostate cancer prevention.

Funding: Cancer Research UK, World Cancer Research Fund

J-305 - A Robust Workflow And Quality Control Procedure To Analyze The Human Metabolome By High-Resolution Mass Spectrometry In Epidemiological Studies

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Purpose: Blood and urine samples contain thousands of metabolites that can be analyzed in prospective epidemiological studies by high resolution mass spectrometry (MS) to provide new information on disease risk factors and on mechanisms leading to cancer. A major challenge to apply these analytical methods to cancer epidemiology has been the control of the technical variability associated with sample processing and MS analysis to make possible the statistical comparison of levels of thousands metabolites in several hundred subjects. Unlike in quantitative analysis, calibration standards for the metabolites specific cannot be employed, and thus drifts in the instrument performance over time may compromise data quality.

Methods: Plasma/serum samples (20-30 µL) were prepared by protein precipitation in well plates and analysed by high resolution MS (Agilent 6550 Q-TOF) coupled with UHPLC. Two orthogonal chromatographic methods were used (HILIC, RP) with electrospray ionization in both positive and negative polarities. Data-dependent MS/MS spectra were acquired from a pool of study samples as part of the analytical batch. Data preprocessing was performed using Agilent feature extraction workflow. Rigorous quality control (QC) was employed by monitoring of selected metabolites in QC samples.

Results: Sub-15 minute analysis time and straightforward sample preparation enabled throughput of 500 samples per week. Representative QC results for a batch of 404 plasma samples showed 2900 features with CV<20% in QCs (n=36), with CV% for 10 known compounds 5.9-15.8% without loss in overall signal intensity along the whole batch. The workflow has been successfully used for cross-sectional, nested case-control, and nutritional intervention studies with preliminary results presented.

Conclusions: An untargeted metabolomic workflow for epidemiological investigations is presented that enables fast analysis of large sets of samples without commonly observed analytical drifts, with a robust QC procedure for in-depth assessment of the data quality.

Funding source: IARC Postdoctoral Fellowship, EU-FP7 Cofund, Eurocan.

J-306 - An Evaluation Of The Inter-Laboratory Reproducibility Of A Targeted Metabolomics Platform For Analysis Of Human Serum And Plasma

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A critical question facing metabolomic research is whether data obtained from different centres can be effectively compared and combined, enhancing the statistical power and returnon investment of metabolomics studies. One important part of addressing this question is the assessment of the inter-laboratory precision (reproducibility) of the analytical protocols used.
Several test materials, including the NIST reference human plasma (SRM 1950), were distributed to six laboratories and independently analysed using the AbsoluteIDQTM p180 Kit (Biocrates Life Sciences AG). This LC-MS/MS platform allows the targeted analysis of amino acids, biogenic amines, acylcarnitines, sphingolipids and glycerophospholipids.

After excluding 12 metabolites (of 189) not consistently detected in all laboratories, a high degree of analytical precision was observed across for metabolites measured quantitatively. Normalisation of measurements to the profile of a standard reference material obtained in each laboratory run significantly improved the interlaboratory precision of the lipid profile measured. After normalisation, the majority (typically ~75%) of metabolites in each test material exhibited an interlaboratory coefficient of variance (CV) of <10%. Approximately 90% of metabolites exhibited an interlaboratory coefficient of variance (CV) of <20%. Ongoing analysis will also assess the impact of highly lipidic samples and varying anticoagulant on precision, as well as the accuracy of measurement of specific quantified metabolites. This is the first interlaboratory assessment of this metabolomics platform, providing critical information for users to interpret these data appropriately.

J-307 - Hypoxic Cancer Secretome Induces A Proliferative Phenotype In Adjacent Cells

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Over the past years, it has become evident that cancer initiation and progression depends on several components of the tumor microenvironment, including inflammatory and immune cells, fibroblasts, endothelial cells, adipocytes, and extracellular matrix. These components of the tumor microenvironment and the neoplastic cells interact with each other providing pro and antitumor signals. The present study aimed to analyze tumor-microenvironment interactions and their effects on the secretome of cancer cells. For this purpose, two cell lines from head and neck carcinomas were cultured in hypoxia conditions. The medium conditioned by these cells (secretome 1) and their control cells were used to grow untreated normal human fibroblasts from oral cavity. The peptides from these fibroblasts and their secretome (secretome 2) were analyzed by LTQ Orbitrap Velos mass spectrometer coupled to the nanoACQUITY Ultra Performance liquid chromatography system. For protein identification, the data were searched using MASCOT v.2.0. The results were loaded in Scaffold Q+ and quantitative data were compared using Student's t-test. Differences in expression were considered significant if the probability of error was $p<0.05$. Proteomics analysis of fibroblasts and their secretome allowed identification of 45 and 19 differentially expressed proteins, respectively. Most proteins of secretome 2 have been related to extracellular matrix organization, and others are involved in cell proliferation and migration, MAPK cascade, fibroblast growth factor receptor signaling pathway and response to hypoxia. Similarly, cellular proteins with a high expression levels in fibroblasts have been associated with response to hypoxia and to oxidative stress, differentiation, growth, proliferation, inflammation, angiogenesis, invasion, metastasis, extracellular matrix organization and negative regulation of apoptotic process. Our results suggest that signals derived from cancer cells in response to hypoxia drive the protein expression of adjacent cells. Financial support: FAPESP, CNPq.

J-308 - Discovery Of Novel Biomarkers Of Whole Grain Rye In A Dietary Intervention Study Through Metabolomics

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Purpose: Intake of dietary fiber, in particular cereal fiber, is associated with a reduced risk of colorectal cancer. However, the role of subtypes of cereals is unclear and accurate measurement of the intake of specific whole grains is difficult with traditional dietary assessment methods. Our aim was to employ untargeted metabolomics to find molecular biomarkers of intake for whole grain rye, a significant source of dietary fiber in the Nordic countries.

Methods: Fifteen free-living subjects completed an intervention with a 4-week run-in and two 4-week test periods in cross-over design. White wheat bread (WW, 3% fiber) was consumed during the run-in, followed by whole grain rye bread (WGR) and white wheat bread enriched with bioprocessed rye bran (WW+BRB) (both 10% fiber). Fasting plasma samples were collected after each period and analyzed by high resolution mass spectrometry coupled with an UHPLC system. Data preprocessing was performed using Agilent feature finding workflow and the discriminant features were found using univariate differential analysis.

Results: After WGR period, 22 compounds showed significantly increased plasma concentration when compared to WW period ($q \leq 0.1$, fold change ≥ 1.5). After WW+BRB period, mean concentrations of all the 22 compounds were significantly higher or comparable to the WGR period. Eleven compounds could be identified, including 2-aminophenolsulphate and several conjugated alkylresorcinols such as 5-nonadecyl-1,3-benzenediol. For three alkylresorcinols, both sulphate and glucuronide conjugates were observed.

Conclusions: We found 2-aminophenol sulphate and metabolites of alkylresorcinols as potential biomarkers for wholegrain rye intake. Bioprocessed rye bran yielded similar results confirming bran as the main source for these compounds. Validation of these markers in population studies is needed together with similar studies to find biomarkers for other sources of cereal fiber.

Funding source: IARC Postdoctoral Fellowship, EU-FP7 Cofund, Eurocan.

J-309 - Functional Study Of KLK8 In Head And Neck Carcinoma

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Head and neck squamous cell carcinoma (HNSCC) is one of the most common cancers in the world. The median overall survival for patients with recurrent or metastatic lesions is low, despite recent advances in therapeutic techniques. The understanding of the molecular pathways involved in the initiation and progression of these tumors is therefore important not only for understanding their biology, but also for the development of effective therapeutic approaches. In our previous studies, the kallikrein 8 gene (KLK8) was observed differentially expressed in laryngeal carcinomas, suggesting its potential as a tumor marker. Kallikreins participate in proteolytic pathways that contribute to normal physiology and pathological conditions, modulating cell proliferation and survival and regulating angiogenesis, cell migration and invasion. The objective of the present study was to investigate the participation of the kallikrein 8 in the HNSCC development. The specific objectives included (a) to analyze the expression pattern of KLK8 and its most abundant variant in HNSCC, (b) to evaluate the effect of ectopic expression of KLK8 on HNSCC secretome, using proteomic and metabolomic approaches, and (c) to develop molecular homology modeling of protein KLK8. The results of gene expression analysis showed that the variant 1 of KLK8 has significantly reduced levels in HNSCC, unlike the other five variants. Its ectopic expression resulted in changes of cell morphology, increased proliferation, viability and migratory capacity, but no alterations in invasiveness. The data from cells with ectopic expression of KLK8 revealed small differences in their proteomes compared to control cells. Otherwise, these cells exhibited changes in their glycolytic pattern and in the effect of their secretome on the metabolism of other cells. For the first time, differences in expression of KLK8 variants and the effects of their ectopic expression were evaluated in HNSCC cells. Financial support: FAPESP, CNPq.

J-310 - Development Of Ultrasensitive Liposome-Quantum Dot Based Optical Nanobiosensor For Detection Of Cancer Cells Without Target Amplification

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Purpose: The detection of tumor cells in early stages is crucial for diagnosis, prevention, and treatment of cancer. In present study, we developed a novel strategy to amplify fluorescence signal for highly sensitive optical detection of cancer cells regarding telomerase activity using liposomes encapsulated with Cadmium Telluride (CdTe) quantum dots (QDs).
Methods:In this strategy, the telomerase extracted from HeLa cells, elangated the biotinylated telomerase substrate (TS) probe; then, the probe was immobilized on streptavidine coated microplate wells. Next, hybridization of immobilized TS probe with biotinilated capture probe was carried out. Aftre that, biotinilated liposomes were attached to capture probe through streptavidin. In final step, liposomes were disrupted by Triton X-100 and the fluorescence activity of released QDs was measured.
Results:The results showed that proposed nanobiosensor could be applied to determine telomerase activity from equivalent down to 10 HeLa cells without the polymerase chain reaction (PCR) amplification of telomerase extension products.
Conclusions:Offered methodis not only convenient and sensitive,but also has a simple operating protocol and wide dynamic range.The platform, might be further applied for the detection of viral reverse transcriptase enzymes and various biological targets with a combination of different probes and aptamers.
Funding source: Funded by Tabriz University of Medical Sciences

J-311 - Dendrosomal Curcumin Nanoformulation Modulate Apoptosis-Related Genes And Protein Expression In Hepatocarcinoma Cell Lines: Possible Anti Proliferative Effects

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Purpose: The side-effects observed in conventional therapies have made them unpromising in curing Hepatocellular carcinoma; therefore, developing novel treatments can be an overwhelming significance. One of such novel agents is curcumin which can induce apoptosis in various cancerous cells, however, its poor solubility is restricted its application. To overcome this issue, this paper employed dendrosomal nanocurcumin was employed to in prevent hepatocarcinoma in both RNA and protein levels.
Methods: Hepatocarcinoma cells, p53 wild-type HepG2 and p53 mutant Huh7, were treated with dendrosomal nanocurcumin and investigated for toxicity study using MTT assay. Cell cycle distribution and apoptosis were analyzed using Flow-cytometry and Annexin-V-FLUOS/PI staining. Real-time PCR and Western blot were employed to analyze p53, BAX, Bcl-2, p21 and Noxa in dendrosomal nanocurcumin-treated cells.
Results: dendrosomal nanocurcumin inhibited the growth in the form of time-dependent manner, while the carrier alone was not toxic to the cell. Flow-cytometry data showed the constant concentration of 20μM dendrosomal nanocurcumin during the time significantly increases cell population in SubG1 phase. Annexin-V-PI test showed curcumin-induced apoptosis was enhanced in Huh7 as well as HepG2, compared to untreated cells. Followed by treatment, mRNA expression of p21, BAX, and Noxa increased, while the expression of Bcl-2 decreased, and unlike HepG2, Huh7 showed down-regulation of p53.
Conclusions: In summary, dendrosomal nanocurcumin-treated hepatocellular carcinoma cells undergo apoptosis by changing the expression of genes involved in the apoptosis and proliferation processes. These findings suggest that dendrosomal nanocurcumin, as a plant-originated therapeutic agent, could be applied in cancer treatment.

J-312 - Metabolic Profiling Of Plasma: Potential In Oral Cancer Diagnosis And Prognostic

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Introduction and Purpose: Oral squamous cell carcinoma (OSCC), the most common type of oral cancer, arises from the mucosal lining of the oral cavity and oropharynx, and accounts for more than 300,000 new cases worldwide annually. Despite intense research and recent advances in diagnosis and therapy, the five-year survival rate (about 50%) for this disease has not significantly changed over the past two decades. The objective of the present study was to investigate differentially expressed metabolites in plasma from patiens with oral cancer that can serve as potential biomarkers for prognosis and monitoring of OSCC.
Experimental description: Targeted metabolite analysis was carried out on 30 plasma samples from patients with OSCC and 12 controls for the quantitation of amino acids, biogenic amines, acylcarnitines, hexose, and lipids. The assay was based on phenylisothiocyanate-derivatization followed by flow injection analysis tandem mass spectrometry (FIA-MS/MS) and liquid chromatography LC-MS/MS. The normalized data were processed using MetaboAnalyst software for statistical analysis.
Results and Discussion: Significant differences in the concentration of 25 metabolites were observed between plasma from OSCC patients and controls. Similarly, the rate of free carnitine/phosphatidylcholine was able to discriminate patients at different stages of OSCC and isoleucine/methionine levels significantly were correlated with node metastasis. The results also showed that urea and citrulline/arginine cycles are involved in oral tumorigenesis and that increased glutaminolysis occurs during tumor progression. In conclusion, we could demonstrate that non-invasive metabolite analysis of plasma has a potential role in improving early diagnosis and prognosis of OSCC.
Financial Support: FAPESP, CNPq.

J-313 - MicroRNAs In Blood As Biomarker Of Pleural Malignant Mesothelioma

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Purpose: Malignant Pleural Mesothelioma (MPM) is an aggressive cancer refractory to current therapies caused almost exclusively by asbestos. New specific diagnostic markers for early MPM diagnosis are needed. MiRNAs are single stranded noncoding that post-transcriptionally regulate gene expression by triggering mRNA cleavage or repressing translation. Changes in the expression of miRNAs have been implicated in several diseases and cancers, including MPM. miRNAs are stable molecules that can be easily investigated in different specimens (e.g. blood), and used as a disease biomarker. Our aim was to determine if a specific miRNA signature in plasma may help to discriminate between malignant pleural mesothelioma patients (MPM) and healthy subjects with a Past Asbestos Exposure (PAE).
Methods: We investigated a group of 23 MPM patients and 19 healthy subjects with Past Asbestos Exposure (PAE). In this study population we screened 754 miRNAs in blood by TaqMan™ OpenArray® Human MiRNA Panel. Than we selected for validation, in the same groups of subjects, the top-23 differential miRNAs. RNU48 was used as endogenous control. We used multiple linear and logistic regression models adjusted for age, sex, BMI, and smoking habits to compare miRNAs profiling between MPM and PAE subjects.
Results: After miRNA screening, we identified 29 differential miRNAs in plasma. Among the top 23 differential miRNAs, 19 were validated by Real time PCR and were able to discriminate between MPM and PEA subjects. In receiver operating characteristic (ROC) curve analysis, the three best miRNAs were miR-103 (area under curve, AUC=0.82), miR-98 (AUC=0.82) and miR-744 (AUC=0.81).
Conclusions: The identified signature was useful for MPM diagnosis. Further studies are needed to verify if they can be of help for early MPM diagnosis and/or to detect high risk groups.
Funding source: Lombardy Region; Ministry of Health and INAIL; Associazione Italiana per la Ricerca sul Cancro.

J-314 - Evaluation Of Molecular Alterations In Esophageal Squamous Cell Carcinoma Using RNA Sequencing (RNA-seq)

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Esophageal cancer is the eighth most frequent cancer type and the sixth most lethal worldwide. There are two main histological types of this disease, but the most frequent is esophageal squamous cell carcinoma (ESCC). ESCC represents a challenge regarding its diagnosis and treatment. The 5-year survival for this cancer is less than 10%, mainly due to late diagnosis. Characterizing the molecular alterations present in ESCC can help identifying possible targets for diagnosis and treatment improval. Thus, this study aimed to analyze the gene expression and mutational profiles, and the presence of gene fusions by RNA sequencing in 14 ESCC samples and matched non-malignant mucosa. When comparing ESCC and adjacent mucosa 6,698 genes were classified as differentially expressed. The enrichment analysis using KEGG database revealed pathways mainly related to inflammation and others linked to cancer. The thorough analysis of Pathways in Cancer led to the observation of an enrichment of the WNT signaling pathway in which three members had impact on overall survival (WNT16, WNT7B and FZD6). WNT7B overexpression and impact on prognosis were validated in an independent cohort. The mutational analysis revealed that TP53 is the most frequently mutated gene in ESCC with a frequency of around 80%, both in the training and validation cohorts. The evaluation of gene fusions revealed 21 events in seven tumors with no common alterations among samples. The presence of gene fusions was not associated with any clinic-pathological characteristic , but samples with this profile showed an increased expression of ATR. Our data suggests a role for the WNT-signaling pathway in ESCC progression and proposes new prognostic factors. Also, we show for the first time such a high frequency of TP53 mutations in Brazilian samples. Finally, the gene fusion phenomena seems to be a consequence and not a cause of ESCC development.

J-315 - Metabolite Profiling For Cancer Stem Cells In Malignant Gliomas Revealed That Protoporphyrin-IX Is A Biomarker For Tumor-Propagating Cells And In _-Aminolevulinic Acid-Mediated Photodynamic/Radiosensitizing Therapy

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Tumor heterogeneity of high-grade gliomas (HGGs) is recognized in 3 major subtypes based on core gene signatures: mesenchymeal, proneural and classical. Among them, HGGs profiled in the mesenchymeal subtype tend to show worse prognosis than others. Recently, also as for glioma stem cells, genome-wide transcriptional analysis identified two mutually exclusive subtypes of glioma stem cells (GSCs) with distinct dysregulated signaling and metabolic pathways; mesenchymal GSCs (MES-GSCs) and proneural GSCs (PN-GSCs). Similar to HGGs with a MES signature, MES-GSCs display more aggressive phenotypes and are markedly resistant to radiation as compared with PN-GSCs, consistent with the relative radiation resistance of MES-GBM.

In the present study, we used 5 human GSC lines established from 3 MES-HGGs and 2 PN-HGGs. Metabolome analysis for these GSCs using liquid chromatography-tandem mass spectrometry (LC-MS/MS) revealed that the glycolytic pathway and porphyrin biosynthesis were significantly activated in MES-GSCs compared to PN-GSCs. Furthermore, exogenous administration of δ-aminolevurinic acid (ALA), the first metabolite in the porphyrin synthesis pathway, significantly increased the endogenous production of protoporphyrin-IX (PpIX), a heme precursor porphyrin with photosensitizing and radiosensitizing activities, in MES-GSCs than PN-GSCs. To reflect those difference, ALA/PpIX-mediated photodynamic and radio-sensitizing therapies were significantly more effective in MES-GSCs than in PN-GSCs both *in vitro* and *in vivo*. Furthermore, when MES-GSCs were sorted by PpIX-fluorescence intensity into three fractions by FACS, MES-GSCs with high intracellular PpIX level showed significantly higher expression of GSC marker genes (nestin, L1CAM, SSEA-1 etc.) and *in vivo* tumor-initiating ability compared to those with low intracellular PpIX. Those results seemed to suggest that PpIX could be a metabolic biomarker to detect and extract cells with high tumor-propagating phenotype among malignant gliomas.

Porphyrin metabolism may therefore represent a metabolic vulnerability in MES-GSCs under photodynamic and radiosensitizing therapies that could in principle be targeted for therapeutic benefit.

J-316 - Soluble B-Cell Activation Marker Of sCD27 And sCD30 And Future Risk Of B-Cell Lymphomas: A Nested Case-Control Study And Meta-Analyses

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Pre-diagnostic serum/plasma concentrations of B-cell activation markers have been associated with future risk of B-cell lymphomas (BCL) in HIV-infected patients and in the general population. Current evidence for the general population is however limited and relies on relatively small numbers of observations, especially for specific histologies. We carried out a nested case-control study, including 218 BCL and 218 matched controls, within two prospective cohorts, to investigate the association between plasma levels of soluble (s)CD27 and sCD30 and future risk of BCL, and main histologic subtypes separately. To expand the evidence further, we performed meta-analyses of the published data on these associations from prospective studies among the general population. Our study revealed a significant relationship between sCD30 concentration and BCL risk (OR=0.86, 1.53, 1.76, for the 2nd-4th quartiles respectively, P-trend=0.01). Similar increased risks were observed for diffuse large B-cell lymphoma and follicular lymphoma. Analyses of sCD27 blood concentrations did not show significant associations with BCL, (OR=0.90, 1.26, 1.65 for the 2nd-4th quartiles, respectively, P-trend=0.17), but significant associations were observed for chronic lymphocytic leukaemia and for the group of ‘other BCL’ subtypes. Our findings involving sCD30 were confirmed within our meta-analyses of five prospective cohorts, while results were more heterogeneous for sCD27 with the exception of CLL which was found consistently in all studies. Data to date suggest that chronic B-cell stimulation might be an important mechanism involved in B-cell lymphomagenesis both in HIV-infected and in the general population.

J-317 - Identification Of Dietary Biomarkers For Meat And Fish Intake Through Metabolomics

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Several biomarkers of meat or fish intake have been proposed but their specificity for different types of meat or fish has seldom been considered. In this work a metabolomic approach was used to identify dietary biomarkers for three different types of meat and fish in a dietary intervention study and in the European Prospective Investigation on Cancer and nutrition (EPIC) cohort study.
24-Hour urine samples were first collected from four groups of subjects (n=10 in each group) after consumption of meals containing three different doses of either chicken, red meat (beef), processed meat (cooked ham) or fish (hake). Urine samples were analysed by high resolution mass spectrometry (MS) coupled with Ultra-High Performance Liquid Chromatography. After correction for multiple testing, 230 MS features were found to be significantly associated with the intake of either one of these four foods and showed a monotonic increase with the dose. The same MS features were analysed in 24-hour urine samples collected in EPIC subjects. Exclusive consumers of one of the same 4 foods (based on 24-hour dietary recalls) were compared to subjects who did not consume any meat or fish during the 24 hours of urine collection (n=10 per group). Sixty-five MS features out of the 230 previously identified were able to distinguish consumers of either of the 3 meats or fish when assessed by Receiver Operating Curve analysis with permutation testing. The identities of 8 of them were finally confirmed based on their mass fragmentation spectra and comparison with authentic standards: anserine, carnosine, acetylcarnitine, propionylcarnitine, 1-methylhistidine, 3-methylhistidine, trimethylamine-N-oxide, and 2-methylbutyroylcarnitine. These 8 biomarkers used alone or in combination, may provide accurate measurements of chicken, red meat, ham and fish intake, and will be further validated in a larger set of EPIC samples.

J-318 - Novel Association Between Omentin And Risk Of Colorectal Cancer: Data From The EPIC-Potsdam Cohort

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Background
Omentin - also known as intelectin-1 or intestinal lactoferrin receptor - is a novel biomarker described to exert metabolic, inflammatory and immune-related properties. Higher omentin concentrations have been particularly associated to inflammatory bowel disease, immune responses, and infection as potentially predisposing factors for the development of colorectal cancer [CRC]. However, population-based studies to evaluate the association of omentin with CRC risk are currently lacking.
Methods
We investigated the association between circulating plasma omentin concentrations and risk of CRC in a case-cohort study comprising 251 incident CRC cases diagnosed over a mean follow-up time of 10.4 years and 2295 cancer-free individuals in the European Prospective Investigation into Cancer and Nutrition (EPIC) - Potsdam. Multivariable-adjusted hazard ratios as a measure of relative risks (RR-s) and 95% confidence intervals (CI-s) were computed using a Prentice modified Cox regression analysis.
Results
In a model adjusted for age, sex, education, dietary and lifestyle factors, body mass index (BMI) and waist circumference, higher omentin concentrations were associated with a higher CRC risk (RR for highest quartile versus the lowest = 2.31, 95% CI: 1.48 – 3.58; Ptrend <0.0001). The association was not altered after additional adjustment for inflammatory and metabolic biomarkers. Furthermore, addition of omentin to the multivariable-adjusted model statistically significantly improved risk assessment of CRC beyond established and suspected risk factors. When the analysis was stratified according to body mass index (BMI) status, the association was retained in participants with a BMI < 30 (RRcontinuously per doubling of omentin concentrations= 2.26; 95% CI: 1.57-3.27), but not in those with BMI ≥ 30 (RRcontinuously per doubling of omentin concentrations= 1.07; 95% CI: 0.63-1.83; Pinteraction= 0.005).
Conclusions
In this prospective cohort study, higher circulating concentrations of omentin were associated with a higher CRC risk, independent of CRC risk factors, adiposity and metabolic biomarkers.

POSTERS

PREVENTION & MORTALITY REDUCTION

PREVENTION & MORTALITY REDUCTION - Challenges in primary prevention

K-319 - Knowledge, Attitudes And Practice Of Cervical Cancer Vaccination Among Young Women Attending A Tertiary Institution In Singapore

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Introduction: To describe the knowledge, attitudes and practices of young women with regards to cervical cancer and Human Papilloma Virus (HPV) vaccination.

Methods: We conducted a descriptive, cross-sectional, questionnaire-based study among female students of a tertiary institute in Singapore.

Results: A total of 258 questionnaires were completed and formed the basis of the analysis. 238 (92.3%) of the total participants were of the age group 15-22 years. 255 (98.8%) participants were unmarried and 243 (94.2%) never had sexual intercourse. Only 25 (9.7%) of the women had undergone vaccination. Amongst the participants that did not receive vaccination, intention to consider vaccination was present in 134 (57.5%) of them and 62% of them cited lack of information as the major barrier. Knowledge regarding cervical cancer and HPV vaccination was also assessed and graded with a maximum score of 14. Knowledge was found to be low with a median score of 7.5. There is a significant association between HPV vaccination uptake and where they first heard about the vaccination. (p=0.007) Vaccinated subjects tended to first hear about it from their relatives and friends (60% vs 25.3%)

Conclusion: There is poor uptake of HPV vaccination amongst Singapore's susceptible youth and poor knowledge regarding HPV and HPV vaccination. Public health education on HPV, cervical cancer and HPV vaccination is still needed and has to be targeted not just at the subjects but also at their family and friends.

Keywords: Primary care, Vaccination, Cervical Cancer

K-320 - Reduction In Melanoma Incidence And Mortality Rates In Younger Western Australians. Are Skin Cancer Prevention Programs Working?

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When it comes to cancer prevention – the real outcomes of our efforts focus on reduction of disease incidence and are not expected for some decades after prevention efforts commence. From exposure to the known carcinogen, the gap between the risk factor exposure (e.g. tobacco smoking or sun exposure) and cancer diagnosis is some decades.
Skin cancer prevention efforts have been in place for almost three decades in Western Australia (WA), with consistent financial investment in sun protection programs at the highest per capita rate of anywhere in the world. Should we now expect to see some impact of the prevention efforts in incidence rates ?
Age standardised melanoma incidence rates continue to rise, albeit with signs of having plateaued, in WA, a population of close to 2.5 million.
Mortality rates seem to have been rising in men and flattened out more recently. Mortality rates have been flat in women for some decades.
A closer analysis of both incidence and mortality rates in WA shows considerable reductions in the younger age groups, specifically among those under the age of 40 years.
While many factors may be at play, data will be presented to support the thesis that skin cancer prevention efforts are likely to be contributing to progress on important skin cancer outcomes. Dominant factors driving these trends will be presented. National data in this context will also be presented.

K-321 - Innovative Integrated Cancer Screening Day: A Wellness Day For Women...By Women

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Purpose
An inter-professional collaboration of public health nurses, family health teams, Ontario Breast Screening program sites, Nurse Practitioners (NPs), and Trent University Nursing students resulted in an innovative primary prevention strategy - The Cancer Screening Day: A Wellness Day for Women, by Women aimed to promote access to Cancer Care Ontario's three screening programs - ColonCancerCheck, the Ontario Breast Screening Program and the Ontario Cervical Screening Program while addressing common barriers to screening.

Methods
A personal invitation was sent to under/never screened women from their health care provider emphasizing the importance of preventative health care. The Wellness day for Women...By Women was designed to reduce barriers to screening, enhance the social context and establish partnership champions. Listening to clients, attending to their needs, providing one on one instruction for the Fecal Occult Blood (FOBT) test and transportation / personal escort service to the breast assessment centre relieved many anxieties.

Results
The success from two previous Wellness Day events lead to the 2015 expansion that inlcuded three of five family health organizations in the Peterborough area. Of the 155 women registered for the day, 145 (94%) participated. Results of the qualitative and quantitative evaluation have identifed partnership facilitators and barriers; strengths and challenges of interprofessional collaboration.

Conclusions
Our champion NP effectively collaborated with peers and partner agencies to support expansion of the screening day event to two additional family health organizations and one additional breast screening site for 2015.The reach for this novel approach to cancer screening is expanding with NPs taking the lead. Under the leadership of our champion NP, Peterborough Primary Health Care Services were successful in receiving Quality Improvement Funding from Cancer Care Ontario, Central East Cancer Prevention and Screening Network to implement the 2015 Wellness Day for Women.

Funding Source
Quality Improvement Program Funding, Cancer Care Ontario,

K-322 - Impact Of An Outright Ban On Commercial Sunbeds In Australia

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On the 1st January 2015, five of six Australian States introduced an outright ban on all commercial artificial tanning sunbeds. The remaining State, Western Australia, introduced similar legislative controls effective from the 1st January 2016.
An outright ban on all commercial artificial tanning sunbeds effectively removes the right of commercial operators to provide any sunbed services to the general public.
The decision by all state governments in Australia to endorse an outright ban was significant by global standards. While well over 20 countries have implemented controls to restrict under 18 access to commercial sunbeds, only Brazil had implemented a similar outright ban in 2009
As result of an outright ban, there was no noticeable increase in the number of advertisements advertising sunbeds to the private market and the strong enforcement checking by government health authorities ensured compliance by commercial operators was very good in respect to their obligations under the new legislation.
The introduction of an outright ban of commercial sunbeds has been a significant success, not only from the point of view that artificial tanning sunbeds, an instrument that is well known to be the primary cause of melanoma has been removed from the commercial sector, but also because any potential adverse health consequences have been largely adverted for future generations.

K-323 - Objective And Subjective Risk Assessment: A Challenge To Breast Cancer Prevention

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Purpose: One challenge facing primary cancer prevention is individuals' understanding of their cancer risk, and what they can do to reduce their risk. This study investigated breast cancer risk using objective and subjective risk measures.

Methods: Participants were 395 women ≥ 35 years old who self-referred to a breast cancer prevention educational program. They completed three breast cancer risk measures: the National Cancer Institute's Gail Risk Score (includes personal and reproductive medical history, breast cancer in first degree relatives, 5-year breast cancer risk); Siteman Cancer Center's "Your Disease Risk" (includes lifestyle risk behaviours, reproductive and medical history, 4-level risk); and perceived lifetime breast cancer risk (self-rated percent 0-100). Convergence among the risk measures was calculated.

Results: 30% of women were "high risk," based on Gail, and 41% "above average" or "much above average" on Siteman; 70% were "low risk" on Gail and 52% on Siteman. While scores on the two instruments were significantly correlated, there was considerable non-convergence: 53% of women at low Gail risk were also low risk on Siteman; and 62% of women at high Gail risk were "above average" or "much above average" on Siteman. Overall self-perceived risk was 31%. Self-perceived risk in the high Gail group varied positively and linearly according to Siteman score (p

Conclusions: Results indicate that different risk assessment tools provide varying summary risk estimates. Subjective breast cancer risk is almost three-fold population incidence. Subjective risk perceptions in women who have lower biological risk do not reflect the increased risks of lifestyle factors. To achieve primary breast cancer prevention, more attention is needed to understand what women know about risks and how risk perception affects risk reduction.

Funding: Canadian Breast Cancer Foundation British Columbia Yukon

K-324 - Social Representations Of Breast Cancer And Its Social Reality In Two Health Higher Education Institutions In Mexico And Colombia 2015

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Pourpuse.Identify social representations of the concept of breast cancer in two health institutions in Guadalajara, Mexico and Pereira, Colombia, in order to contribute to the implementation of educational programs.Method.Qualitative design of cognitive anthropology with a structural approach on social representations. The data were collected between June-September 2015 through free listings and paired comparison questionnaires besides frequency analysis, association and antagonism between cognemes represented by an analysis and creation of a graph .84 people participated among which 41 men and 43 women. The sample was based on Romney and Weller's assumption of cultural consensus.The selection was of the proactive type.The participants volunteered were guaranteed data confidentiality and anonymity. We analyzed free listings, computed frequencies to identify the 10 words most mentioned. After applying the paired comparison technique, we calculated the distance index that evaluates the similarity and antagonism or exclusion relationship. both countries were analyzed separately per sex and a comparison was made at the end.Results.The average age of men and women participating in Mexico was of 37.5 and 40.5.In Colombia, 36.7 and 29.5. In both countries, the women as well as men were related mainly with negative aspects. The word associated more frequently was "death". Positive representations were also found in women of both countries,the greater amount was found in Colombian women. Negative categories such as pain 16%, death13% and fear 3 and 5% appeared in women of both countries. Conclusion. This analysis could respond to a series of constructs according to the experience of breast cancer, the knowledge obtained and the information contained in prevention programs. There could be factors associated to the lack of data, constructs given the fear of the disease. It is important to culturally modify those constructs to obtain better results in planning educational programs and to modify the perspective on this public health problem.

K-325 - Using Tobacco Control Tactics To Tackle Obesity: The LiveLighter Campaign In Western Australia Focuses On Mass Communication And Policy Reform To Reduce Obesity

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Purpose
Obesity is the most important cancer risk factor among non-smokers and action on obesity is urgently required.

Methods
Cancer Council Western Australia (WA) has partnered with National Heart Foundation (WA) on LiveLighter. The campaign was established in 2012 and draws heavily on Australian tobacco control strategies, including the use of graphic imagery to illustrate the health consequences of obesity. The campaign is well funded and features paid and unpaid mass media, and policy advocacy efforts to influence behavioural choices and promote public policies favourable to reducing obesity.

Results
LiveLighter promotes a range of nutrition and physical activity messages with a recent focus on sugary drinks. Independent campaign evaluation data demonstrates that:

- Awareness of LiveLighter is higher in the target audiences (overweight people and parents)
- The focused sugary drinks phase had the most cut-through with unprompted awareness of television advertisements of 55% (c.f. 33% for phase 1 “toxic fat” and 45% for phase 3 “all advertisements”)
- The campaign minimises adverse consequences
    - Negative perceptions of overweight people did not increase
    - Intentions to lose weight among healthy weight respondents did not increase (slightly decreased)

The campaign has adopted three policy areas for focussed advocacy:

- Adoption of mandatory kilojoule labelling in takeaway food outlets in WA
- Meaningful restrictions on marketing of junk food to children
- Increased tax on sugar sweetened beverages.These policies have been enforced in at least one jurisdiction world-wide.

Conclusions
A long-term commitment to communication and policy efforts will be required to successfully tackle the international rise in obesity. The LiveLighter campaign and creative materials have been adopted by four jurisdictions around Australia and in New York. The campaign serves as an action oriented example of leading edge efforts to address obesity.

Funding source
Western Australian Government, Department of Health

K-326 - Occupational Medicine And Cancer Prevention: A Model Of Good Practice

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-Purpose: Experience gained by Post-graduate School in Occupational Medicine on cancer prevention in everyday workers' health surveillance activities (as suggested by several guidelines and by WHO) and on further ways to share information about cancer.
-Methods: Health data collection during doctor's visits based on the International Classification of Diseases (ICD) and on "Diagnostic criteria for diseases" estabilished and endorsed by the School.
Data collection and frequent updates on overweight and obesity, smoking habit, alcohol consumption, eating habits and physical activity in each worker's medical record.
Sharing information about cancer prevention on the website "Updating Medicina del Lavoro", UMdL (updatingmdl.wordpress.com), a self-managed platform certified for health information based on the voluntary efforts provided by resident physicians and young occupational physicians from the University of Siena.
-Results: Yearly summary of the health data about 3,500 workers from University Hospital of Siena and University of Siena allows to conduct interventions focused on most common risk factors and participation in group physical activities.
The UMdL website provides authorized Italian translations of IARC Press Release (starting from the n.224 on February 2014), is involved in the World Cancer Day campaigns each February 4th, shares information about occupational carcinogens (like asbestos, silica, chemotherapeutic agents handling, …), and about prevention of infection-related cancers. The website counts 12,000 visits and 6,000 visitors until now.
-Conclusions: Primary prevention is a cornerstone of good occupational medicine practice.
Based on principles of quality and comparability the collection and the analysis of data from doctor's visits and the correct use of a website for sharing information seem to be useful tools for cancer prevention in working populations.
-Funding source: No external funding source

K-327 - Association Of Breast Cancer Risk In Traditional Chinese Medicine Use In Endometriosis Patients: A Nationwide Population-Based Cohort Study

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Purpose: Use the National Health Insurance Research Database (NHIRD) for cohort study to evaluate the breast cancer risk in endometriosis patient with Traditional Chinese Medicine.
Methods: We used Longitudinal Health Insurance Database (LHID) to construct the study. The LHID was a sub-database of the National Health Insurance Research Database (NHIRD) which was involved the claims data from Taiwan National Health Insurance program (Taiwan NHI). This study wanted to clarify the effect of TCM treatment for breast cancer risk in endometriosis patient. We selected the new onset endometriosis patient (ICD-9-CM 617) during from 2001 to 2009. The main outcome of the research was the developing breast cancer (ICD-9-CM 174). We terminated the follow-up when the patient withdrawn the insurance, breast cancer occurrence, or until December 31, 2011. TCM group means use TCM treatment after new onset endometriosis diagnosis, and TCM non-users group means patients did not use TCM treatment after endometriosis diagnosis.
Results: The breast cancer incidence density for the patients with TCM visited one year ago before endometriosis diagnosis did not increase significantly (HR = 1.20, 95% CI = 0.77-1.86). The one-year post-operative TCM users group had a 2.30-fold increased risk of developing breast cancer than the TCM non-users group (HR = 2.30, 95% CI = 1.22-4.32).
Conclusions: According to this study, association of breast cancer risk and TCM use in endometriosis patients definitely depends on the timing of TCM intervention before or after new onset diagnosis.
Funding source: This study is supported in part by Taiwan Ministry of Health and Welfare Clinical Trial and Research Center of Excellence (MOHW104-TDU-B-212-113002), China Medical University Hospital, Academia Sinica Taiwan Biobank Stroke Biosignature Project (BM104010092), NRPB Stroke Clinical Trial Consortium (MOST 103-2325-B-039 -006), Tseng-Lien Lin Foundation, Taichung, Taiwan, Taiwan Brain Disease Foundation, Taipei, Taiwan, and Katsuzo and Kiyo Aoshima Memorial Funds, Japan.

K-328 - Preventing Exposures To Occupational And Environmental Carcinogens: Case Studies From CAREX Canadaís Knowledge Translation Programme

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Purpose:
CAREX Canada is a national surveillance system that estimates the number of Canadians exposed to known or suspected carcinogens in workplace and community environments. Inspired by a project developed by the Finnish Institute of Health, CAREX Canada uses carcinogen classifications from IARC's monographs programme to inform priorities for the Canadian setting. The challenge of our current mandate is to translate CAREX Canada's surveillance resources in order to support those looking to better understand – and help reduce or eliminate – exposures to carcinogens across Canada.

Methods:
The approach we've taken to addressing this challenge is to work closely with research, policy, and program specialists to mobilize our estimates of exposure based on needs as well as opportunities for action. Through these relationships, CAREX Canada has informed priorities, supported action, and enhanced capacity; the associated activities included developing tools to explore our estimates, packaging our information in various ways (i.e. by industry, occupation, jurisdiction, exposure pathway, cancer site), and offering training and knowledge sharing workshops.

Results:
The results of this work are a series of case studies of uptake and action. Three of these will be highlighted here: 1) informing exposure reduction priorities at a provincial workers' compensation board and helping to monitor emerging issues such as exposure to antineoplastic drugs; 2) supporting action by providing the exposure evidence required for several not-for-profit organizations to pursue radon policy initiatives; and 3) enhancing capacity among First Nations groups to assess and address community concerns such as exposures in traditional foods and drinking water.

Conclusions:
This presentation will discuss the knowledge translation strategies and outcomes of these case studies, including lessons learned and opportunities for future work.

Funding:
CAREX Canada is funded by the Canadian Partnership Against Cancer, with grants for First Nations knowledge translation from the Canadian Institutes for Health Research.

K-329 - Home-Based Carersí General Cancer Knowledge: A Case Study Of One Rural Village In Vhembe District, South Africa

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This paper assessed the general cancer knowledge amongst home-based carers of a selected rural village in Vhembe district, South Africa. The study adopted a qualitative descriptive design collecting data fromeight members of a selected home based care group between 30 to 45 years who were conveniently recruited and
interviewed using unstructured interview guide. Permission to enter the village was obtained from the local chief.
Informed consent was obtained from individual participants. Participants' rights to anonymity and privacy were
observed. Data was analysed through content analysis. The results revealed that though the majority of participants
knew the importance of screening for cancer, their cancer knowledge was inadequate. This paper concluded that
home-based carers of the selected rural village possess inadequate general knowledge of cancer; and recommendedthat nationally collaborated projects regarding cancer training be intensified amongst rural home based care workers.
KEYWORDS Cancer. Knowledge. Home-based Carer. Rural. Village

K-330 - Dietary Habits And Head And Neck Cancer: Preliminary Results Of A Multicentric Case Control Study In Brazil ñ Interchange Project

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INTRODUCTION In Brazil, it has been estimated 22,930 cancer cases of mouth, larynx and oropharynx for the year of 2014 for both sexes, being 11,280 new cases of oral cavity cancer in men and 4,010 in women and, 6.870 of larynx cancer in men and 770 in women (INCA, 2014).
Observational studies have shown a protective effect with the consumption of fruits and vegetables, whereas others do not (PAVIA, 2006; MARCHIONI, 2007; FREEDMAN, 2008; TOLEDO, 2010; Marchioni, 2011). In Brazil there was reduced risk of oral cancer when vegetable consumption was 3-7 servings per week (MARCHIONi, 2007). Therefore to analyse lifestyle and eating habits in patients with head and neck cancer and their controls can bring new informartion about risk factors for head and neck cancer . OBJECTIVES To analyze data collected on lifestyle, eating habits in case control study Interchange (IARC) in three Brazilian capitals: Goiânia, São Paulo and Vitória. associated head and neck cancer risk. METHODS InterCHANGE is a multicentric cases and controls project , on head and neck cancer coordinated by IARC (http://interchangedb.iarc.fr/). interchange aims is about survival and risk factors for cancer of oral cavity, oropharynx and larynx. RESULTS 745 cases and 580 controls were included in the analysis. Males accounted 541 and females 147. wiht proportion male.female of 3,6 :1 male/female, average age of the cases in the 3 cities was 58 years, average weight for cases were 66kg in goiania,61 kg and 75kg in Sao Paulo The consume of vegetables by citiy was 41% in Goiania, 67% in Sao Paulo and 56% in vitoria.More detailled analysis is on going
CONCLUSIONS .Dietary habits in cases of oral cavity,oropharyn and larynx cancer in e cities of Brasil has heterogenous pattern of weight at diagnosis and dietary eating habits .

K-331 - Establishing National CARcinogen EXposure (CAREX) Programs In Latin America And The Caribbean: Achievements And Future Directions

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Purpose: Cancer is the second-leading cause of death in Latin America and the Caribbean (LAC). Exposure to workplace carcinogens is an important factor, yet there are sparse data about the numbers and types of LAC workers exposed. The objective of this project was to build capacity for developing CARcinogen EXposure (CAREX) projects in LAC.

Methods: The CAREX method, originally developed in the European Union for estimating exposure to occupational carcinogens, has been used and modified in multiple Central American countries and Canada. The approach generally involves combining labour force data with estimates of the proportions of workers exposed to priority carcinogens in each country. A two-day workshop involving over 20 participants from Canada and 12 LAC countries was held as a forum for discussing methodological approaches, issues unique to LAC, and research opportunities.

Results: CAREX programs in LAC have been established in Costa Rica, Nicaragua, Panama, Guyana and Colombia, with projects currently in progress in Peru, and Chile. Central American CAREX projects included exposure estimates by sex for approximately 30-35 carcinogens that incorporated levels of uncertainty. Both informal and formal workers were covered in exposure estimates, although estimates for these populations are challenging in most countries. In general, agents with the greatest prevalence of exposure in all industries included solar radiation, environmental tobacco smoke, crystalline silica, and pesticides. Stakeholder consultations were held in Peru to identify priority carcinogens. Proportion of exposure values from other CAREX projects were considered for the Peruvian context.

Conclusions: This project demonstrated that the CAREX methodology can be readily adapted to different countries, economies, and priority carcinogens. Exposure estimates generated from CAREX projects are integral for informing primary prevention activities and improving estimates of the global occupational cancer burden.

Funding source: Canadian International Development Research Centre; Pan American Health Organization; National Cancer Institute of Colombia

K-332 - Cancer Mortality Projections In South Korea Up To 2030

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Prediction of the cancer mortality is important to estimate the needs of the cancer related services and to prevent the cancer. Despite the short-term estimations of the cancer incidence and mortality were conducted up to 2015 in South Korea, long-term future projections of the cancer mortality has not been conducted. Therefore, our objective is to estimate the future cancer mortality by cancer sites up to 2030 in South Korea. The specially programmed software, the Nordpred, is used to estimate the cancer mortality. The cancer death data from 1983 to 2012 and the population projection data from 1983 to 2032 are from Korean National Statistics Office. The age-standardized rates with the world standard population of the all cancer deaths are estimated to decline from 2008-2012 to 2028-2032 (men: -39.8%, women: -33.1%). However, the crude rates are predicted to rise (men: 29.8%, women: 24.4%) and the overall number of the cancer deaths are also estimated to increase (men: 35.5%, women: 32.3%). Several cancer deaths are projected to increase (lung, liver & gallbladder, colon & rectum, pancreas and leukemia in both sex, prostate in men, breast and ovary in women), Whereas other cancer deaths are expected to decrease (stomach, esophagus and larynx in both sex, cervix in women). The largest contribution on increasing cancer deaths is due to aging of population in Korea. It is urgently need to set up the nationwide strategy for primary prevention, early detection and early treatment to cope with the rapidly increasing cancer due to population aging.

K-333 - The Burden Of Occupational Cancer In Korea

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1. Objectives: The aim of this study was to produce an estimate of the current burden of occupational cancer for Korea.
2. Methods: The carcinogenic agents or exposure circumstances were identified for each cancer as those classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogens. Estimates of relative risks of occupational carcinogens for each cancer are obtained from a search of the literatures from Asian studies for an occupational cancer. Meta analysis was done to estimate the occupational risk among the Asian literatures. Estimation of the proportion of the population exposed to each carcinogen was calculated, after thenthe Attributable Fraction(%) for each cancer for the target year i.e. 2007 was calculated.
3. Results: In Korea, 67112 deaths (42521 men and 24591 women) from cancer and 155771 incidences (82121 men and 73650) women) for cancer reported by Statistics Korea and National Cancer Center in 2007. For carcinogen with "strong plus suggestive" evidence of carcinogenicity in humans, the overall occupational attributable fraction (AF) for the cancer deaths in 2007 in Korea was estimated to be 11.62% in men and 3.25% in women with an overall estimate of 9.27% for men plus women. Estimated numbers of deaths attributable to occupation were 4943 for men and 798 for women giving a total of 6224. The proportion of cancer incidences in 2007 attributable to occupation was estimated to be 7.72% in men and 1.49% in women with an overall estimate of 5.13% for men plus women. Estimated numbers of incidences attributable to occupation were 6341 for men and 1099 for women giving a total of 7991.
4. Discussions: This study suggests that the numbers of deaths and incidences due to past high occupational exposures will continue to be substantial in the near future, particularly asbestos-related cancers.

K-334 - Challenges In The Primary Prevention Of Ovarian Cancer: The Tubal Origin Hypothesis

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Purpose
Several organisations have recently recommended prophylactic opportunistic bilateral salpingectomy, with ovarian conservation, to reduce ovarian cancer risk. This recommendation is based on molecular and histological studies suggesting a tubal origin of high-grade serous ovarian cancer, together with epidemiological evidence of reduced ovarian cancer risk following tubal sterilization.
Methods
Using Cox regression models, we estimated relative risks (RRs) of different histotypes of ovarian and of other cancers amongst women with versus without tubal sterilization in a large prospective study of UK women, adjusted for potential confounders.
Results
In 1,278,783 women without previous cancer, 8,035 ovarian cancers accrued during 13.8 years' follow-up. Tubal sterilization was associated with a reduction in overall risk of ovarian cancer (RR=0.80, 95% CI: 0.76-0.85). Risk varied significantly by ovarian cancer histotype (heterogeneity: $p<0.001$); for the most common serous tumours, risks were significantly lower ($p=0.01$) for high-grade (RR=0.80, 0.70-0.91; n=1,682) than low-grade tumours (RR=1.12, 0.89-1.42; n=447); risks were halved for endometrioid (RR=0.45, 0.34-0.59; n=590) and clear cell tumours (RR=0.55, 0.39-0.77; n=401); mucinous tumour risk was not reduced (RR=0.99, 0.84-1.18; n=836). Tubal sterilization was also associated with significant reductions for peritoneal (RR=0.81, 0.66-0.98; n=730) and fallopian tube cancers (RR=0.60, 0.37-0.96; n=168).
Conclusions
Our results confirm that tubal sterilization is associated with a reduced risk of certain ovarian cancer histotypes, and of peritoneal and fallopian tube cancers, consistent with hypotheses that many of these have shared origins in the fallopian tube. Opportunistic prophylactic salpingectomy may reduce ovarian cancer risk, but is an untested primary prevention strategy.
Funding source
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L-335 - Provision Of Breast Cancer Care And Survival In Germany ñ Results From A Population-Based High Resolution Study From Saarland

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Provision of breast cancer care and survival in Germany – results from a population-based high resolution study from Saarland

Purpose:Studies on the implementation of Clinical Practice Guidelines (CPG) and its effect on breast cancer (BRC) survival on a population-level are scant. This study provides data on the usage of BRC treatment, the extent of adherence to CPG and, as novelty, survival of BRC patients according to major recommended treatment options.

Methods: Data from the Saarland Cancer Registry including women diagnosed with invasive BRC without distant metastasis and follow up in 2000-2009 were used. Provision of treatment according to CPG is presented by age, BRC type, and over time. Period analysis was used to derive estimates of 5-year relative survival (RS) and the effect of non-adherence to CPG on relative excess risk of death (RER).

Results: The study revealed increasing guideline adherence, with high levels already seen for local treatment (e.g. 67% of the patients in 2008/09 received breast conserving surgery), and substantial progress over time with regard to sentinel node dissection (SND) and adjuvant systemic treatment (e.g. SND and chemotherapy was provided to 62% of all patients and 79% of the patients with N+ or hormone receptor negative BRC in 2008/09, respectively). It further demonstrated increased cancer related mortality among patients without guideline compliant cancer treatment (e.g. patients with N+ and hormone receptor negative BRC without chemotherapy had a 5-year RS of 29% compared to 54% for patients receiving chemotherapy (RER: 2.89, 95% CI: 1.46–5.71)).

Conclusions: This study provides data on the implementation of CPG in Germany, extends available survival data of BRC patients and may provide evidence of increased cancer related excess mortality, if BRC patients do not receive guideline compatible treatment.

Funding source: None

L-336 - Effectiveness Of Three Strategies For The Management Of ASC-US Cytology In Healthcare Services Of Medellin, Colombia: Study Design Of A Pragmatic Randomized Trial (ASCUS-COL Trial) And Partial Results

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Purpose. To compare, under routine clinical conditions, three triage strategies in women with ASC-US cytology to reduce untreated CIN2/3+ at 2-years (effectiveness) and minimize healthcare utilization (efficiency). The strategies are: immediate colposcopy (IC-arm), repeat conventional cytology at 6/12 months (RC-arm) and HPV testing (HPV-arm).

Methods. Between 2011 and 2014, 20-69 years-old women from three healthcare management organizations (HMOs) in Medellin, Colombia, were enrolled, randomized in equal proportions and referred for routine colposcopy (IC-arm: everyone, RC-arm: if >=ASC-US and HPV-arm: if hrHPV+). All procedures, except HC2-HPV (QIAGEN©), were performed by HMOs. Women were scheduled to attend visits at 12 and 24 months (exit visit). Healthcare utilization data (number of cytologies, colposcopies and histologies) were retrieved from HMOs. Proportion ratios were used to compare healthcare utilization (relative utilization, RU) and rates of CIN2/3+ (relative risks, RR) identified by HMOs. Partial results within 15 months since the ASC-US index are presented under intention-to-treat principle.

Results. 2,661 women were randomized (IC-arm=882, RC-arm=890, HPV-arm=889). Twenty-seven percent in RC-arm had >=ASC-US and 41% in HPV-arm were hrHPV+. Compared to RC-arm, cytology utilization was similar in the IC-arm (RU=0.77, 95%CI 0.53-1.13) and lower in the HPV-arm (RU=0.64, 95%CI 0.58-0.69). Compared to IC-arm, colposcopy and histology utilization was lower in RC-arm (RU-colposcopy=0.44, 95%CI 0.41-0.48 and RU-histology=0.50, 95%CI 0.44-0.56) and HPV-arm (RU-colposcopy=0.58, 95%CI 0.54-0.62 and RU-histology=0.60, 95%CI 0.54-0.67). Although non-significant, the RRs of having a CIN2/3+ diagnosis suggest that RC-arm and HPV-arm identified 60-70% more cases than IC-arm (RR=1.6, 95%CI 0.8-3.0 and RR=1.7, 95%CI 0.9-3.2, respectively).

Conclusions. In these routine conditions, the follow-up of women with ASC-US cytology with repeat cytology or hrHPV testing identified same number of CIN2/3+ cases but with less colposcopy and histology utilization than immediate colposcopy.

Funding source. Fundación Pedro Nel Cardona, Estrategia Sostenibilidad, 2013-2014 -Universidad de Antioquia (CPT-9889-1208), COLCIENCIAS (1115-459-21657).

L-337 - Mobile Reporting And Evaluation Of Symptoms Among Cancer Patients

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Purpose. Cancer is the third leading cause of morbidity in the Philippines and under-treatment of symptoms persists. Patient feedback on treatment effectiveness, compliance and engagement in self-care are critical. Telehealth applications influence patient engagement in self-care, improve health behavior and outcomes, likely by enhancing autonomy, competence, and relatedness in health care practices (self-determination theory). We previously documented the prevalence of mobile phone use and acceptability and readiness for a web-based patient-reported outcomes monitoring system among our cancer patients. We now set out to develop a mobile system for symptom reporting and evaluation among cancer patients.
Methods. The literature was surveyed for validated symptom tools available in English and Filipino. A focused-group discussion (two oncologists, two pain specialists and an international symptom researcher/collaborator) was conducted to assess face validity and elect an instrument. Application interface and system design was developed in collaboration with local information technology consultants over several iterations until beta testing revealed a satisfactory design.
Results. The Edmonton Symptom Assessment Scale (ESAS) was elected due to its validity, ease of administration and prevalent use in local research and clinical settings. A mobile symptom monitoring system (the *Internet-based Computerized Patient Assessment System, iComPASS*) was developed and functions satisfactorily on beta testing. The application allows patients to report symptom severity and pain location, view prescriptions and receive notifications from their physicians.
Conclusions. The iComPASS is a beta-tested, functional mobile application. It will be subjected to user-acceptability testing prior to implementation and integration into institutional care pathways. A clinical trial will be conducted to determine its impact and define maintenance and scale-up issues.
Funding Source. Cancer Conquer Foundation

L-338 - Development And Validation Of The Web-Based Patient-Reported Outcomes Capture System ñ Needs, Acceptance And Readiness Assessment (WPROCS ñ NARA) Questionnaires

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Purpose: Web-based patient-reported outcomes capture systems improve efficacy of symptom monitoring and management and may overcome barriers to long-term monitoring and care among adult cancer patients. We developed an instrument to explore perspectives and attitudes for such a remote capture system among Filipino adult cancer patients.
Methods: The study was consisted of 3 parts: (1) development of questionnaire through literature review of applicable instruments and relevant studies; (2) face and content validation through modified Delphi technique examination of relevant stakeholders (ie. oncologists, oncology nurse, information technology consultants, and biostatistician) and questionnaire administration to 20 cancer patients; and (3) pilot testing for construct validation and internal consistency reliability testing among 130 cancer patients.
Results: Three assessment questionnaires utilizing weighted single-response or multiple-response choice formats or 4-point Likert scale was developed for 3 critical domains: (1) Needs Assessment Questionnaire (NAQ) which explored emotional health, healthcare needs, symptoms, medications, feeding, nutrition, social support, access to healthcare, ambulatory capacity and functional disability; (2) Acceptance Assessment Questionnaire (AAQ) which explored socio-demographic variables, attitude towards tool, perceived logistic capacity and competency to use it, and willingness to acquire or access materials, equipment, knowledge; and (3) Readiness Assessment Questionnaire (RAQ) which explored computer and Internet access, use, skills training and perceived competence. Expert review and initial administration of the tool determined the relevant items and items that needed modification. The analyses of results of pilot testing of the modified tools revealed that all questionnaires have good construct validity (absence of complex item upon principal component analyses) and acceptable internal consistency reliability (NAQ Cronbach alpha= 0.84; RAQ Cronbach alpha=0.77; AAQ Cronbach alpha=0.71)
Conclusion: The WPROCS – NARA is a valid and reliable 46-item tool in understanding the needs, acceptance and readiness among Filipino adult cancer patients for a web-based patient-reported outcomes capture system.
Funding Source: None

L-339 - Turning Evidence Into Opinion: An EU Scientific Committee Review And Risk Assessment Of Ultraviolet Radiation From Sunbeds

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Purpose: The European Commission requested the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) to review recent evidence on ultraviolet (UV) radiation from sunbeds and provide an updated opinion of the risk.

Methods: Information was primarily obtained from peer reviewed papers and reports covering epidemiologic, experimental and cell culture studies.

Results: UV emissions from sunbeds vary widely, with a tendency more recently towards higher UVA irradiance and are estimated to correspond to an UV index of 12, i.e. equivalent to midday tropical sun. The prevalence of sunbed use varies greatly by country being higher in white-skinned populations from Northern Europe, and in younger women.

Both UVA and UVB have an immunosuppressive effect on the skin and also a systemic immunosuppressive effect. Exposure to UVA and/or UVB enhances aging of the skin. There is consistent evidence of increased risk from cutaneous melanoma associated with sunbed use, with a dose-response proportional to the number of sessions and frequency of use. From a smaller number of studies there is also consistent evidence that sunbed use increases the risk of squamous cell carcinoma, especially when exposure takes place at a younger age, and to a lesser extent for basal cell carcinoma.

Evidence for carcinogenicity of UV exposure is supported by experimental animal and mechanistic studies. UVA has been shown to be as much involved as UVB in DNA damage and mutation induction.

In Europe, 3,438 (5.4%) of annual newly diagnosed cases of melanoma may be related to sunbed use (68% women).

Conclusions: The SCENIHR concluded that UV is a complete carcinogen, both an initiator, and a promoter and that, because of this evidence and the nature of skin cancer induction (no indications for threshold levels of UV-irradiance and UV–dose), a safe limit for UV irradiance from sunbeds could not be established.

L-340 - Process Evaluation Of The Native Womenís Health Project (NWHP)

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Purpose: To describe the process evaluation of an innovative, culturally-sensitive, theory-based and complex intervention, the Native Women's Health Project (NWHP). The NWHP, a community-driven program, incorporated clinic and community based intervention strategies and aimed to increase mammography rates. The intervention lasted for 4 months; however, design, implementation, and evaluation occurred over 3 years and utilized a community-based participatory research approach. Methods: The priority population consisted of breast cancer-free American Indian (AI) women aged 52-74 years, with no recent screening mammogram, and who lived in rural Oklahoma. Process evaluation planning consisted of the construction of a comprehensive evaluation plan to address key process evaluation components (i.e. context, reach, dose received, dose delivered, and fidelity), the design of evaluation tools, and identification of relevant evaluation questions. Process evaluation data collection included focus groups with research participants, individual interviews with key informants, logs, and survey administration. Data analysis consisted of descriptive statistical analysis and content analysis. The Plan, Do, Study, Act (PDSA) change cycle was used for continuous quality improvement. Results: Process evaluation revealed a shallow implementation of the clinical component; the community component was implemented as planned. The PDSA change cycle was helpful in refining primarily the community component. Focus group research showed participants overall were satisfied with program implementation. Weaknesses of the NWHP included contextual factors, its short duration and insufficient exposure to the broader AI community. The NWHP was feasible to implement in "real-world" settings. Conclusion: Implementation research is challenging, as one has to balance methodological rigor with practical constraints. Nevertheless, it is important in strengthening the quality of a program during implementation and thus it increases its chances of being effective. Information derived from this study can assist others in the development of similar studies promoting breast health among indigenous populations worldwide. Funding Source: Susan G. Komen®.

L-341 - Using A Mass Media Campaign To Raise Awareness Of The Link Between Alcohol And Cancer: Cross-Sectional Pre And Post-Intervention Evaluation

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Given the increasing evidence linking alcohol consumption with cancer risk we sought to evaluate the effectiveness of a population-based, state-wide public health intervention designed to improve women's awareness and knowledge of the link between alcohol and cancer. The 'Alcohol and Cancer' mass media campaign ran from May 2010 to May 2011 and consisted of three waves of paid television advertising with supporting print advertisements.

We used a cross-sectional samples of Western Australian women aged 25-54 years before the campaign (n=136) and immediately after wave I (n=206) and wave III (n=155) of the campaign.

We assessed campaign awareness; knowledge of drinking guidelines and the link between alcohol and cancer; intentions towards drinking.

Prompted recognition of the campaign increased from 67% following wave I to 81% following wave III (adjusted OR [adj OR]=2.31, 95% CI 1.33 to 4.00, p=0.003). Improvements in women's knowledge that drinking alcohol on a regular basis increases cancer risk were found following wave I (adj OR=2.60, 95% CI 1.57 to 4.30, p<0.001) and wave III (adj OR=4.88, 95% CI 2.55 to 9.36, p<0.001) compared with baseline. Knowledge of the recommended number of standard drinks for low risk in the long term increased between baseline and wave I (adj OR=1.68, 95% CI 1.02 to 2.76, p=0.041), but not baseline and wave III (adj OR=1.42, 95% CI 0.84 to 2.39, p=0.191). Among women who drink alcohol, the proportion expressing intentions to reduce alcohol consumption increased significantly between baseline and wave III (adj OR=2.38, 95% CI 1.11 to 5.12, p=0.026).

Results indicate a population-based mass media campaign can reach the target audience and raise awareness of links between alcohol and cancer, and knowledge of drinking guidelines. However, a single campaign may be insufficient to measurably curb drinking behaviour in a culture where pro-alcohol social norms and product marketing are pervasive.

L-342 - Web-Based Patient-Reported Outcomes Monitoring For Adult Filipino Cancer Patients: A Cross-Sectional Analysis Of Needs, Acceptance And Readiness

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Purpose: Information and communications technology (ICT) applications have been employed to overcome difficulties in symptom monitoring and management among cancer patients. The objective of this study was to determine the needs, acceptance and readiness of adult Filipino cancer patients towards use of ICT for monitoring of patient-reported outcomes (PROs) **Methods:** This is a cross-sectional descriptive study that included adult cancer patients from outpatient radiotherapy and chemotherapy units, multidisciplinary tumor clinics, medical and surgical oncology wards, and pain and palliative unit of University of Santo Tomas Hospital-Benavides Cancer Institute. Demographic data were obtained using semi-structured interviews using the Web-Based Patient-Reported Outcomes Capture System - Needs, Acceptance and Readiness Assessment (WPROCS – NARA) questionnaires. While clinical data were collected through records review.**Results:** There were 130 respondents (23.08% males and 76.92% females) with mean age of 45.95+10.57 (28-80) years old. In terms of needs, majority of the participants reported to have moderate to severe overall health condition (44.62%) and mental or emotional health (50.77%) with 1-3 active symptoms (46.92); needed at least 30 minutes to access closest hospital (65.38%); and do not have anyone who provides them professional health care and advice outside hospital or clinics (94.62%). In terms of attitudes, majority of the respondents reported that they feel (94.62%) and think (96.15%) that use of such is a good idea; willing to acquire materials (87.69%), learn system (90.77%), and reported intention to use of such system (98.46%). Lastly, in terms of readiness, majority of the participants reported to currently have internet access (96.92%) and often utilize it for different reasons like communication (90%), access to information (70%), and civic and political participation (50%), and learning (83.85%).
Conclusion: The possible use of ICT for monitoring of PROs was found to be needed, accepted, and feasible by Filipino adult cancer patients.
Funding Source: None

L-343 - Partners In Action: Integrating Shade Design In Public Places For Cancer Prevention

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Purpose: Social media is a key tool in promoting cancer prevention. The provision of shade is one of the key methods of preventing skin cancer, caused by environmental ultraviolet radiation. Public policy to support the creation of shade is one component of skin cancer prevention. The Toronto Cancer Prevention Coalition Ultraviolet Radiation Working Group (TCPC – UVRWG) successfully put shade on the city's cancer prevention agenda. Consequently Toronto is the first city in Canada to implement a shade policy. To advance this policy, a film was produced to present the members of this group, describe its workings, discuss the policy and demonstrate the necessity of multi-disciplinarity for skin cancer prevention.
Methods: The Shade Policy Committee of the UVRWG secured funding to hire a documentary film maker. Together this group prepared a film script that would encapsulate the rationale for shade, the necessity of including a range of expertise in shade creation, present the views of shade promoters and present examples of shade in Toronto.
Results: The film was shot and produced in 2013, and released publicly on You-tube in 2014. Entitled "Partners in Action: A Shade Policy for the City of Toronto", it won the 2014 Canadian Dermatology Association Public Education Award.
Conclusions: Activity in Toronto for shade creation represents a successful synergy linking UVR awareness and skin cancer prevention with public health, city planning, urban forestry, civic design and health promotion policy. The use of social media extends the reach of health promoters to a larger audience and is an effective tool for skin cancer prevention.
Funding source: The City of Toronto / Toronto Public Health

L-344 - Architectural Responses For UVR Protection ñ Creating Prototypes For Interactive Architecture For Shade Design

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Purpose: Toronto has Canada's first policy on shade to support prevention of skin cancer, caused by environmental UVR. Shade is a key component of skin cancer prevention. An architectural studio produced prototypes of interactive structures for shade for evaluation by parks planners and testing in a park setting.
Methods: The architecture studio applied Australian methods and techniques for designing and evaluating shade. Consultations with park users and managers identified site constraints and needs. Recreation facilities and activities on the site were mapped. Locations for placing shade devices to maximize their effectiveness were located. A typology of interactive approaches was developed and applied to shade structure design. Designs were produced, digital and scale models built, and schemes were evaluated as to their effectiveness in producing shade in desired locations.
Results: Twelve designs demonstrating six methods of interactivity were presented for a five specific recreational sites within the park. Computer renderings simulated shade creation during diurnal cycles of peak UVR in these locations. Feedback was elicited from park users and managers and was applied to policies developed for capital projects in Toronto parks.
Conclusions: Successful collaboration between health promoters, parks planners and architects can create UVR protection through shade. Architectural interactivity is an innovative tool for shade creation.
Funding: Ryerson University Department of Architectural Science.

L-345 - Implementation Of Torontoís Shade Policy And Guidelines Through The Cityís Parks, Forestry And Recreation Division

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Purpose: Shade protects people from overexposure to ultraviolet radiation (UVR) and decreases the risk of skin cancer. Following the approval of a Toronto-wide Shade Policy (the first of its kind in Canada) and development of Guidelines, the City's Parks, Forestry and Recreation Division (PF&R) took the lead in implementation through the development of design standards that prioritize shade in high UVR exposed recreation sites in City-owned parks and facilities.

Methods; PF&R researched and developed a taxonomy of shade structures and design standards, and utilized an evaluation matrix to assess viability of approaches. Data was reviewed internally and tested through a focused stakeholder workshop. The resulting design standards include detailed design specifications, UVR protection factors and cost estimates for the proposed shade solutions.

Results: A catalogue of tested and approved products, and concomitant design solutions for natural and constructed shade, allows ease of implementation of shade design by PF&R supervisors, capital project coordinators and landscape architects for park projects. A wide variety of shade solutions are now available, which are being implemented in PF&R capital projects.

Conclusions: Annually Toronto spends $CAD350 million on parks capital improvements. Time pressures and tight budgets of park development projects limit the opportunity for PF&R staff to easily and effectively incorporate sun safety measures into facility planning. This project supports implementation by making background research accessible, demonstrating successful design alternatives, and providing a pre-selected list of shade provision options that adhere to City requirements. By standardizing provisions for shade designs, the City is able to provide shade in more public places and at cost savings, through efficiencies in design and project delivery.

Funding source: Ryerson University, City of Toronto, Department of Parks, Forestry and Recreation, Toronto Public Health

L-346 - Evaluation Of The International Standardized 24-Hour Dietary Methodology (GloboDiet) For Potential Applications In African Research And Surveillance Settings

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Purpose: The International Agency for Research on Cancer (IARC/WHO) is the owner of an international standardized 24-hour dietary recall methodology (GloboDiet) aiming to cover the lack of standardized dietary tools for nutritional monitoring and surveillance in the global context of rapid increasing of obesity and related comorbidities including cancers. The objective of this project was to evaluate the GloboDiet methodology and its potentials for use in the specific African context.

Methods: A panel of 29 African and international experts in food consumption field participated in six e-workshop sessions upon invitation of the Dietary Exposure Assessment Group (DEX) of IARC/WHO, to comment on the GloboDiet methodology and its features. Each expert completed afterwards an online questionnaire.

Results: The experts expressed their overall satisfaction on the suitability of the GloboDiet as potential tool for collection of dietary consumption data in Africa for surveillance and research purposes. The different sections of the interview methodology were acknowledged as adapted or/adaptable to the African context. Notwithstanding, the experts made specific requirements for additional figures regarding local African foods and recipes description. The experts also unanimously expressed the need to address individual quantification in the context of shared-dish eating habits, of major relevance throughout Africa.

Conclusions: The consultation of the experts provided constructive comments on the ability of the GloboDiet methodology to cover the African specific needs for food consumption data collection. There is, however, a need to adapt some of the sections to local specificity and particularly study how to address individual consumption from a shared plate.

Funding source: The work was undertaken during the tenure of a postdoctoral fellowship from the IARC, partially supported by the European Commission FP7 Marie Curie Actions–People–Cofounding of Regional, National and International Programmes (COFUND)

L-347 - Thyroid Cancer Screening: Fukushimaís Experience

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Purpose: Thyroid cancer screening does not reduce mortality, and its legitimacy has been questioned in countries with extensive implementation of increased diagnostic surveillance programmes. The thyroid ultrasound examination programme started after the radiation emergency in Fukushima in 2011 detected 152 suspected/confirmed malignant cases in 300,476 children (ages 0-18) screened by the end of 2015. This result is often interpreted as an effect of radiation exposure, rather than of the mass screening. We aimed to address impact of the thyroid screening in Fukushima on thyroid cancer incidence, prevalence, as well as potential for over-diagnosis/overtreatment.
Methods: We reviewed relevant scientific papers, government reports, newspaper and popular magazine articles published in Japanese or English between March 2011 and December 2015.
Results: Legitimacy of thyroid screening in Fukushima has been questioned in scientific papers in English since early stages, while rarely discussed in Japanese. Little has been published on thyroid cancer incidence and mortality in general Japanese population before the accident, potential effects of cancer screening, including thyroid cancer over-diagnosis/overtreatment. Comparisons between thyroid cancer screening after Fukushima and Chernobyl seldom addressed differences in survey methodologies, diagnostic criteria and radiation exposure conditions.
Conclusions: Lack of discussion on impact of the thyroid screening may have created and reinforced unnecessary anxiety among the affected population in Fukushima. Some of the discourses in Japanese mass media were not built on scientific evidence, but likely to be more influential information source for the general population. Enhanced information provision in the Japanese language may help affected people start discuss necessity of thyroid screening and make informed decisions.
Funding source: This work was undertaken during the tenure of a Postdoctoral Fellowship from the International Agency for Research on Cancer, partially supported by the European Commission FP7 Marie Curie Actions - People - Co-funding of regional, national and international programmes (COFUND).

L-348 - Implementing HPV DNA Testing Into A Public Cervical Cancer Screening Program In El Salvador

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Purpose: CAPE (Cervical Cancer Prevention in El Salvador) introduces a low-cost HPV-DNA test into a public sector program. During phase 2 of the project, 8 thousand women were expected to be part of the project. To increase adherence to screening, different interventions of recruitment strategies were adopted. For the management of HPV positive women, two treatment algorithms were compared to select the best management for HPV+ women. The results of this phase would help decision making on the scale up of the project.
Methods: Health promoters were trained on HPV and cervical cancer in order for them to educate and recruit women aged 30-49 at the community. 8205 women were contacted at home to participate in the screening. Additional methods were used, such as home visits and opportunistic screening at the health units in order to screened 8,000 women targeted for this phase. Women with HPV+ results followed two treatment strategies, colposcopy management (CM) or screen and treat (ST) if they were cryotherapy eligible.
Results: 8,050 women were screened in this phase. 81.1% (6,656/8,025) of women recruited at the community attended to their appointment, 1,062 women had an opportunistic screening and 332 women were screened at home. Of the women screened, 489/3,963 (12.3%) and 465/4,087 (11.4%) of women in the CM and ST tested HPV-positive respectively. In the CM all were referred for colposcopy—and 216/489 (44.2%) attended within 6 months. In the ST, 397/465 (85%) received immediate treatment.
Conclusions: Training and education, as well as combination of different recruitment techniques shows a higher adherence to screening. The ST strategy outcome vs the ST, allowed stakeholders to adopt screen and treat modality for the scale up of the project.
Funding source: Einhorn Family Trust Fund, Union for International Cancer Control

L-349 - Prospective Study Of Factors Which Determine The Extent And Pace Of Implementing And Disseminating The European Code Against Cancer

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Background: The European Code Against Cancer (ECAC), a series of recommendations of primary and secondary prevention, is a key instrument for translating the available information and knowledge into 12 ways to reduce cancer incidence and mortality aimed at the general public. The 4th edition of the ECAC aims to enhance its effectiveness by facilitating implementation of healthy lifestyle habits and risk-reducing behaviours. This study aims at deciphering the factors that determine the effective implementation and dissemination of the ECAC, and identifying gaps or barriers that impede a successful translation of the scientific knowledge into cancer prevention attitudes and practice. The potential combined impact of a set of recommendations for cancer prevention such as offered by ECAC has been never systematically evaluated.

Aims and objectives: To identify and study the individual and structural factors that would influence the successful implementation and adoption of the ECAC as a cancer prevention tool: (1) at individual level, the adoption and impact of effective adherence to the ECAC, by measuring changes in citizens' knowledge and attitudes towards cancer prevention and risk-reducing behaviours; (2a) at structural level, the ECAC dissemination in the media (e.g. mass and social media); and (2b) the adoption and maintenance of the ECAC implementation by stakeholders (e.g. use of knowledge in practice decision-making, incorporation into policy decisions and cancer control programs, allocation of resources).

Methods: Cross-sectional survey at several times in different EU countries, to investigate decision-making processes, and to test receptivity and usefulness of dissemination strategies directed towards the general public.

Conclusions: The update of the ECAC presents an excellent opportunity to study the appropriate and effective methods to implement and disseminate cancer prevention strategies and tools. Advantage can be taken of the fact that EU countries have requested the 4th edition and are therefore eager to make use of it.

L-349-1 - A Global Cancer Project Map Integrating Global Cancer Statistics to Guide International Efforts

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Purpose
In response to the growing burden of cancer, Global Oncology, Inc., and the National Cancer Institute Center for Global Health launched a free, online, interactive map, the Global Cancer Project Map (GCPM) [http://gcpm.globalonc.org], to allow policy makers, researchers, and civil society around the world to search this central repository of international cancer control and research projects. The GCPM serves to catalyze collaboration in cancer research and clinical care, as well as inform research and care gaps.

Methods
In addition to search options by project attributes, the GCPM provides map overlays of epidemiological measures using IARC's GLOBOCAN cancer-specific estimates of incidence, prevalence, and mortality, cancer disability-adjusted life-years, and UN Human Development Index country values. Currently, the map displays projects with international collaborators collated from the NCI, NCI-Designated Cancer Centers, UICC and ASCO.

Results
The GCPM search options offer countless angles of looking at projects worldwide. Of the 1479 currently-mapped projects, 44.8% have investigators or collaborators in less-developed countries (LDCs) (as defined by the UN). Of the 1218 with a project type classification, 104 relate to capacity building and/or training, with 69 of these projects (66.3%) occurring in LDCs. Utilizing the cancer type search options, the GCPM currently displays 54 cervical cancer projects with LDC collaborators, where the cervical cancer mortality age-standardized risk is more than 2.5 times higher for LDCs than more-developed countries.

Conclusions
The GCPM is a real-time needs assessment tool to allow the cancer community to visualize international efforts in cancer control and link need to action. To better address the growing burden of cancer, the partnership is actively seeking collaboration and additional project submissions. Utilized with cancer statistic overlays, the GCPM can help develop regional priorities in cancer research and control.

Funding
NCI Contract No. HHSN261200800001E and resourced by in-kind volunteer hours of Global Oncology members.

M-350 - Factors Influencing The Recommendation Of The Human Papillomavirus Vaccine By South African Doctors Working In A Tertiary Hospital

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Purpose: In South Africa, the HPV vaccination programme was incorporated recently into the school health system. Since doctors are the most trusted people regarding health issues in general, their knowledge and attitudes regarding HPV infections and vaccination are very important for the HPV vaccine programme nationally, as this influences parental decisions regarding vaccine acceptability in their adolescents. The objective of this study was to investigate factors contributing to recommending HPV vaccines to patients.
Methods: A quantitative cross-sectional study was conducted among 320 doctors, using a self-administered anonymous questionnaire.
Results: The average age of the participants was 39 years. All the doctors were aware of HPV and knew that HPV was transmitted sexually. Their overall level of knowledge regarding HPV infections and the HPV vaccine was poor, but most intended to prescribe the vaccine to their patients. Doctors who knew HPV 6 and 11 are responsible for > 90% of anogenital warts, their patients will comply with the counseling regarding HPV vaccination, and received sufficient information about HPV vaccination were 5.68, 4.91 and 4.46 times respectively more likely to recommend HPV vaccination to their patients compared to their counterparts ($p<0.05$).
Conclusions: There was a knowledge gap about HPV infection and HPV vaccine among the doctors. For the HPV vaccination programme to be successful in the country, there is an urgent need to educate doctors about it.
Funding source: There was no funding received for this study.

M-351 - The Fraction Of Oropharyngeal Cancer Potentially Preventable By Controlling HPV Infection

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Background:
Human papillomavirus (HPV) is a recognized cause of oropharyngeal squamous cell carcinoma (OPSCC). Strategy to prevent HPV infection including vaccination might decrease the incidence of OPSCC, but the impact is likely to vary between populations according to the fraction of HPV-associated cases. This study analyzed this potentially preventable fraction in a southern Chinese (Hong Kong) population.

Methods: 207 patients which constituted 63.5% of all newly diagnosed OPSCC in Hong Kong during a 5-year period from 2005 to 2009, were examined for the presence of HPV DNA, and with E6/7 mRNA test to verify their oncogenic role.

Results: Molecular features of HPV involvement were found in 20.8% (43/207) of OPSCC. All HPV-positive cases were HPV-16, except one (HPV-18). HPV-associated OPSCC were significantly younger than HPV-negative cases (mean age: 59.8 vs 63.9 years, P=0.05). Multivariate analyses showed that HPV-associated OPSCC was more likely to occur in non-smokers (39.5 vs. 15.1%, OR: 2.89, P=0.05), non-drinkers (52.5 vs. 25.6%, OR: 2.72, P=0.04), originate from the palatine tonsils (83.7 vs. 53.7%, OR: 3.88, P=0.01), present with an early primary tumor (T1/2) (79.1 vs. 47.6%, OR: 3.81, P=0.004), and exhibit basaloid differentiation (33.3 vs. 7.3%, OR:19.74, P=0.006). HPV positivity was an independent predictor for better prognosis for both 5-years overall and 5-year disease-specific survivals (63.0% vs 29.7%, HR: 0.33, P<0.001, and 87.8% vs 42.6%, HR: 0.16, P<0.001, respectively).

Conclusion: The estimated age-standardized incidence of OPSCC in Hong Kong during the period 2005-2009 was 0.6/100,000/year, of which 20.8% were attributed to infection with high-risk HPV. The main risk factors for OPSCC in Hong Kong are still smoking and alcohol, whereas HPV attributed to a minor fraction.

M-352 - Involvement Of HPV Infection In Cervical And Head & Neck Cancers And Its Association With Genetic Predisposition In Saudi Arabia

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Purpose: Human papillomavirus (HPV) is implicated in several carcinomas including cervix uterine, anogenital and subgroup of oropharyngeal cancers. We studied the extent of HPV involvement in these cancers and the association with genetic single nucleotide polymorphisms (SNPs), presumed to predispose to cancer. The aim is to provide health authorities with guidelines for prevention.
Methods: 213 cervix and 200 oropharyngeal cancers were included. HPV detection and genotyping were carried out using HPV Linear Array, which enables the detection of 37 most common high- and low-risk HPV genotypes. Genetic polymorphisms were compared with 300 normal volunteers with no history of cancer (controls). SNPs in 9 candidate genes (*CDKN1A* (p21) C31A, *TP53* C72G, *ATM* G1853A, *HDM2* promoter T309G, *HDM2* A110G, *DNA Ligase IV* A591G, *XRCC1* G399A, *XRCC3* C241T and *TGFβ1* T10C) were genotyped by direct sequencing.
Results: HPV was detected in 160 cervix and 4 oropharyngeal cancer patients (75% and 2%; respectively). Seven different single HPV genotypes (16, 18, 31, 45, 56, 59, 73) and 5 double infections (16/18, 16/39, 16/70, 35/52, 45/59) were detected. The most common genotype was HPV-16 (71%), followed by 31 (7%), and 18, 45, 73 (4% each). Cancer predisposition (n=100) showed significant association for *XRCC1* (P=0.02, OR=1.69; 95%CI=1.06–2.66). More interestingly, nested analysis revealed a preponderance of HPV-positivity in patients harboring the *TP53* codon 72 risk allele *G* with a borderline significant association (*P* = 0.06), and deviation from Hardy-Weinberg equilibrium (*P* = 0.07).
Conclusions: The rate of HPV infection was lower than estimated worldwide. HPV 16 and 18 were the most common genotypes. Current HPV vaccines could protect two-third of cervical cancer in Saudi Arabia. Genetic predisposition suggest that HPV-associated cancer occurrence is not random in the population and that certain genetic SNPs favors its development.
Funding: Supported by NSTIP-KACST Grant#12-MED2945-20 (RAC#2130025).

M-353 - Emerging Oncogenic Viruses In HNCs From Romanian Patients

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Background: Head and neck cancer (HNC), with an estimated global burden of approximately 700 000 incident cases, is the sixth most common malignancy reported worldwide and has a high case fatality rate of 380 000 deaths per year. Alcohol consumption, smoking, poor oral hygiene, and genetic features are key risk factors for HNC development. Oncogenic viruses are recognized to be related with HNC: MCPyV, EBV and HPV. There are no data from Romania.
Purpose: to evaluate the prevalence of oncogenic viruses in different HNCs from Romanian patients.
Methods: we tested 26 fresh tumors (6/26 women) from 3 surgical departments from Iași, Romania with HNCs (cancers of hypopharynx, oropharynx, oral cavity, larynx and skin from head/neck region). The samples were tested at IARC by LUMINEX multiplex genotyping for the presence of specific DNA from 61 viral agents by using type-specific multiplex genotyping (TS-MPG) assays, which combine multiplex polymerase chain reaction (PCR) and bead-based Luminex technology (Luminex Corp., Austin, TX, USA). Multiplex type-specific PCR used specific primers for the detection of 19 probable/high-risk alpha-HPV types, 2 low-risk alpha-HPV types, 25 genus-beta HPV types, 10 polyomaviruses and 5 herpesviruses. The assay also includes assessment of the β-globin gene, to evaluate the presence and quality of extracted DNA.
Results: 23/26 patients were positive for one or more viruses. In total, we detected 8(30.7%) MCV, 1(3.8%) HPyV6, 16(61.53%) EBV1, 1(3.8%) EBV2, 6 (23.07%) CMV, 8 (30.7%) HHV6, 12 (46.15%) HHV7 and 2 (7.69%) HHV8.
Conclusions: our results suggest an association between the presence of viral DNA and HNCs. Additional research are required for clarifying the natural history of these viruses in HNC, as virus detection would have a decisive impact on diagnostic/decisional algorithms.
Acknowledgement: *The work reported in this paper was undertaken while hosted as Visiting Scientist by the International Agency for Research on Cancer.*

M-354 - Human Papillomavirus (HPV) Genomics Project: Exploring The Carcinogenicity Of HPV Worldwide

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Objectives: High-risk HPV types, as well as variant lineages of HPV16, differ considerably in carcinogenicity despite close evolutionary relatedness. However, methods to assess the genetic basis of such variation have been lacking. We seek to leverage the type of next-generation sequencing technologies and analyses that have been developed for human genomics, to study the viral genetic component of cervical cancer risk.
Methods: Using an Ampliseq and Ion Torrent-based method developed at NCI U.S.A., we are sequencing DNA derived from FFPE, frozen biopsies or cervical cell samples from 2364 HPV16-positive women: 1521 cervical cancer cases, 213 CIN2/3, and 630 controls. Cervical samples have been collected worldwide from 37 diverse populations during 30 years by the International Agency for Research on Cancer (IARC) studies on HPV and cancer. Using case-control comparisons, we are evaluating associations between viral genetic variation and cancer risk, including (1) comparison of viral lineages and sublineages, (2) individual SNPs, and (3) gene-level associations. We are also studying human genetic variation and ancestry in relationship to HPV16 genetic variation and cancer risk.
Results: At the time of abstract submission, whole viral genome sequences have been obtained and analyzed for 1,550 HPV16-positive samples (1,044 cervical cancer cases, 118 CIN2/3, and 388 controls). Variation in the HPV16 E1 and URR regions are strongly and significantly associated with cervical cancer risk. Completed findings for 2,364 HPV16-positive women in the IARC biobank will present the final results at the meeting.
Conclusions: Based on preliminary data, the chance of this approach defining viral genetic determinants of cervical cancer risk appears high, and we are planning to apply it to other high-risk HPV types. This technology now permits much larger studies and more complete genotype-phenotype examinations of HPV genomes than previously possible.

M-355 - Risk Factors For Cervical Cancer In Ghana

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Purpose
To study the risk factors associated with cervical cancer in Ghana.

Methods
Incident cases of histologically confirmed invasive cervical cancer were identified in two large hospitals where most of cervical cancer cases are diagnosed and treated. Inclusion criteria for controls included no past or current history of cervical cancer, aged 18-95 years, residence in Ghana for at least three years, not vaccinated for HPV and disease not related to cervical cancer. Questionnaires were administered to the women after which a request for a cervical smear was made for reporting of cytological abnormalities and laboratory detection of HPV DNA and genotypes. Age, age at first marriage, region of residence, ethnicity and the presence of high-risk HPV were identified as confounding variables.

Results
Overall, 206 cases and 230 controls were recruited. HPV DNA testing was performed for 84 cases and 174 controls. The prevalence of HPV was 80.9% and 52.3% among women with and without cervical cancer respectively. Parity was a risk factor in this study (OR for 5 or more children = 7.88; 95% CI: 2.25-27.56). The risk increased with number of children (p for trend <0.001). Women reporting the use of a homemade sanitary towel during menstruation showed a seven-fold increased risk of cervical cancer compared with a pad (OR: 7.34; 95% CI: 2.45-21.98). Lack of genital hygiene and the use of OC were associated with the risk of cervical cancer.

Conclusions
High parity and poor personal hygiene were the main contributory risk factors, after high-risk HPV positivity. These results will be used to inform policy decisions around the implementation of HPV testing for screening and changes to lifestyle in Ghanaian women.

Funding source
The Director's Cancer Research Trust, Hugh Adam Cancer Epidemiology Unit, and the Department of Preventive and Social Medicine, University of Otago, New Zealand, provided funding.

M-356 - Ultraviolet Radiation Awareness Activities And Ultraviolet Radiation Protection Policies In Ontario Public Health Units

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Purpose: A funded study determined the scope and depth of skin cancer prevention initiatives in Ontario Public Health Units (PHUs), which are at the forefront of delivery of ultraviolet radiation (UV) awareness and skin cancer prevention activities in Ontario. These PHUs have formed networks to collaborate, enhance communications, share information and promote skin cancer prevention. The study aggregated data on the range, scope and type of initiatives in skin cancer prevention by PHUs to determine the level of their activities and to provide future direction to collaborating networks.

Methods: In 2009, a survey was conducted of Ontario 36 PHUs to determine the levels of activity with regard to UV awareness activities and protection policies. This survey was repeated in 2013 by a sub-group of PHUs to determine if significant changes in activities or policies had occurred.

Results: 31 of 36 PHUs participated, thus including PHUs responsible for the health of 85% of Ontario's population. A range of involvement and activities by health care professionals to address skin cancer prevention was found. Activities are developed to target diverse groups and respond to locally determined needs and conditions. Respondents reported the presence of policies and guidelines in support of UV awareness and skin cancer prevention. They identified barriers to delivery of programs and activities, as well as impediments to policy and guideline development, notably lack of resources and public perceptions of the issue. Few programs were evaluated for their effectiveness. In 2013 no substantive changes in activity levels or perceived barriers were found.

Conclusions: PHU professionals utilize multiple strategies whose implementation is constrained by resources and perceived and actual barriers. The lack of program evaluation prevents full assessment of activity outcomes and thus constrains ongoing health promotion planning.

Funding: Canadian Cancer Society (Ontario Division), Ryerson University

M-357 - Immune Response To Non-Targeted HPV Subtypes, After Varying Doses Of Quadrivalent HPV Vaccine Administration

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Purpose
Evaluation of immune-responses of quadrivalent HPV vaccine against non-targeted HPV-types.
Methods
The cohort study carried out at 9 Indian sites enrolled unmarried girls aged 9-18 years. We compared four cohorts of girls receiving 3 doses on days 1, 60 and 180 or later (3-dose); 2 doses on days 1 and 180 or later (2-dose); 2 doses on days 1 and 60 by default (2 doses/D); and 1 dose by default (1 dose/D). The primary outcomes considered were immunogenicity demonstrated by level and avidity of L1-binding antibodies, levels of neutralizing-antibodies for non-vaccine-targeted HPV-types related to HPV-16 (papillomavirus species a9: HPV-31/33/35/45/52/58) and HPV-18 (species a7: HPV-45).
Results
The 2-dose protocol induced high peak geometric mean immune-responses non-inferior to the 3-dose protocol at month-7 after first dose for the non-vaccine-targeted HPV-31/33/35/52/58/45. These responses in both dose groups dropped to or below seropositivity levels by the 48th month after first dose, except for HPV-31. Geometric mean immune-responses in 2 doses/D groups at month-18 after first dose were non-inferior, whereas the responses of the 1-dose/D group were inferior to 3-dose group for all 7 non-vaccine targeted HPV-types analyzed. Avidity indices above 50% were observed at month-18 after first dose in different dose groups for these 7 HPV-types except in 1-dose/D for HPV-33, and 2-dose, 2-doses/D and 1-dose/D for HPV-35. Proportion of samples with detectable concentrations of neutralizing antibodies for 3-dose, 2-dose, 2-dose/D and 1-dose/D vaccination cohorts at month-18 after first dose were 51%, 39%, 29% and 5% for HPV-31, 12%, 12%, 3% and 3% for HPV-33, 8%, 5%, 3% and 7% for HPV-45, and 2%, 0%, 0% and 2% for HPV58, respectively.
Conclusions
These observations need to be correlated with genital HPV DNA status and disease end-points as the immune correlates of protection are still unknown
Funding source
Bill and Melinda Gates Foundation

M-358 - Epidemiological Modelling Of Cervical Cancer Control In High- & Low-Resource Settings

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Purpose. Cervical cancer is the third most-common cancer in women worldwide, approximately 530,000 new cases have been estimated to occurred in year 2012. The incidence of cervical cancer is expected to increase to approximately 756,000 new cases by year 2035. Current changes of sexual behaviors in populations undergoing socio-economic transition are also expected to increase the risk of cervical cancer. In absence cancer control programs, most of the increase of cervical cancer incidence will occur in less developed countries.
We have developed a set of HPV transmission and cervical cancer progression models to support the introduction or modification of cervical cancer control programs both in high- and low resources settings. These models have been used in combination with biostatical analyses to provide an epidemiological interpretation of findings from field studies conducted in high- and low resources settings.
Methods. We calibrated and validated the models against large sets of data from high-resource settings. The validated models were subsequently adapted to a set of high- and low-resource countries. For each country we have simulated the introduction of vaccination combined or not with screening. We have assessed the impact of different levels of coverage, catch-up, and gender-neutral vaccination, across different populations.
Results. The effort necessary to obtain an effective control of HPV is directly dependent of the magnitude of the herd immunity effect, which is not constant across populations. Catch-up of older cohorts accelerates the impact of vaccination among older women and maximizes the chances of HPV elimination. Gender-neutral vaccination maximizes the herd immunity effect in populations with suboptimal vaccination coverage and improves the resilience of vaccination programs.
Conclusions. Epidemiological modeling is a flexible and informative approach to support the development and assessment of cervical cancer prevention methods in high- and low resources settings.
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M-359 - Cancer Risk Among 21st Century Blood Transfusion Recipients

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Purpose
Some carcinogenic infectious agents, such as hepatitis viruses, are known to be transmissible by blood transfusion. In most countries transfused blood is intensively screened for hepatitis B and C, HIV, and HTLV1 viruses. In the UK, high-sensitivity nucleic acid amplification tests for hepatitis C were introduced in 1999 and it was thought that this would reduce, and possibly eliminate, transfusion-related liver cancer. Here we report cancer incidence among 21st century transfusion recipients in a prospective study of one million UK women.
Methods
Overall 11,274 women without prior cancer or precancerous conditions, such as hepatitis, had a first hospital record of one or more blood transfusions in 2000 or later; 1648 of them were diagnosed with cancer during follow-up to 1 January 2014. Cox regression yielded relative risks (RRs) for 11 site-specific cancers, with age as the underlying variable and adjusting for year of birth, region, socioeconomic status, height, smoking, body mass index, and alcohol consumption. Because some women may have had preclinical cancer at the time of blood transfusion, the first 5 years follow-up after transfusion was excluded from the analyses.
Results
Five or more years (mean 8 years) after blood transfusion, there were significant excess risks for liver cancer (adjusted RR= 2.63, 95%CI 1.45-4.78) and for non-Hodgkin lymphoma (adjusted RR=1.74, 95%CI 1.21-2.51). The reasons the transfusions were done in all the women who developed these cancers appear unrelated to the cancer: for example, a third of the transfusions were associated with hip or knee replacement surgery.
Conclusions
In this cohort of UK women, 21st century blood transfusions are still associated with excess risks of liver cancer and non-Hodgkin lymphoma. The role of infectious agents, other than those for which there is routine screening, needs to be considered.
Funding Source
UK Medical Research Council and Cancer Research UK

N-360 - Community-Based Specimen Collection And HPV Testing For Cervical Cancer Screening; Lessons From A Cross-Sectional Study In Ghana

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Background: The implementation of existing cervical cancer screening strategies has reported different rates of success in different countries. These have been mainly due to the experience of different factors including population specific factors that limit women's participation. We report observations and the development of a community-based specimen collection approach as a result of interactions with women in the study communities following an initial low response to a cervical cancer screening activity.
Method: In this cross-sectional study, women were initially recruited by a household survey and invited to report at a hospital either within a week or after a week for self-specimen and health personnel specimen collections. However, due to low reporting rate and an interaction with women, another approach was developed that required recruited women report at a central location within their respective communities for both specimen collections.
Results: Of the 174 participants who opted to report after a week (long duration group) for specimen collection at the hospital, 49 (37.9%) reported. Of the 100 participants who opted to report within 1 week (short duration group) for specimen collection at the hospital, 53 (53.0%) reported. Of the 103 participants were invited to report at a specified location within the community (instead of the hospital) for specimen collection, 99 (96.1%) reported. An overall response rate of 60.7% was attained. Although almost 90.0% of the owmen performed both self and health personnel sample collection, post-performance preference for health personnel sample collection was higher (55.9%) than for self-sample collection (22.4%).
Conclusion: A community-based approach with self-specimen collection and HPV testing holds great potential for increasing women participation in cervical cancer screening in Ghana and other developing countries. The patterns of the distribution of the risk factors are suggestive of a potentially high HPV prevalence for this community.

N-361 - Colposcopy As An Adjunct To Cytology In The Diagnosis Of Cervical Pre-Cancer And Cancer In An Executive Health Care Set-Up: A Retrospective Study In Mumbai, India

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Purpose: Cervical cancer is one of the major public health problem in India. There is no organized screening in place. Cytology performed sporadically in various centres throughout the country, which has its own limitations. Colposcopy, of late has shown promise in the detection of cervical pre cancers and cancers as an adjunct to cytology.

Methods: This is a hospital based retrospective study conducted in a corporate hospital in Mumbai, India. Women attending the Obstetrics and Gynaecology department during August 2010 to July 2012 were included in the study based on history and clinical findings. The Pap smear which was part of health care package was collected and processed by conventional method and reported by Bethesda system. The results of Pap smear were given to women when they returned within a month of Pap smear examination. Whatever the cytology report was, the women in the age group of 25-70 years with history of chronic leucorrhoea, post coital bleeding, post-menopausal bleeding, irregular or inter menstrual bleeding and whose cervix appeared unhealthy on examination as well as those whose pap report was abnormal, colposcopy was performed. Histopathology was considered as reference standard to compare the results of cytology and colposcopy.

Results: A total of 143 women attended the hospital. About 57% of women had come for routine examination. Comparison between Pap smear and colposcopy showed fair agreement. Pap smear showed only 9.09% sensitivity and 88.57% specificity when compared with histopathology. Positive predictive value was 20% and negative predictive value was 75.61%. Colposcopy showed 100% sensitivity and 74.28% specificity when compared with histopathology. Positive predictive value was 55% and negative predictive value was 100%.

Conclusions: Colposcopy is an ideal method to diagnose cervical pre cancer and cancer when used as an adjunct to cytology.

Funding source: Nil

N-362 - Symptomatic Presentations In Primary Care Before Cancer Diagnosis: Opportunities And Challenges For Colon And Rectal Cancers Diagnosed As Emergencies

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Purpose: To examine patterns of symptomatic presentation in primary care prior to colorectal cancer diagnosis comparing patients diagnosed following emergency presentation (EP) and non-EP.
Methods: Cohort study using cancer registry data individually linked to primary care records for colorectal cancers diagnosed in England in 2005-2006 (latest linked cohort with up to 10-year clinical records before cancer diagnosis).
Results: Among the 1029 colon and 577 rectal cancers, EP occurred in 35% and 15%, respectively. EP and non-EP had similar patterns of primary care consultations up to 2 years before cancer.
The year before diagnosis, over 95% of EP and non-EP patients had consulted their doctor for any reason, but significantly less frequently for a relevant symptom among EP (48% versus 71% among EP and non-EP colon cancers ($p<0.001$); 49% versus 61% among EP and non-EP rectal cancers ($p=0.043$)). EP also had less frequently 'red flag' symptoms (e.g. among rectal cancers, rectal bleeding was recorded in 9% versus 24% among EP and non-EP ($p=0.002$)). 18% of EP colon cancer and 23% of rectal cancer patients had 'red flag' symptoms recorded the year before diagnosis.
Multivariable analysis confirmed the above findings showing a lower likelihood of EP for patients with 'red flag' symptoms (change in bowel habits, rectal bleeding, anaemia) during the year before cancer diagnosis. Women, older and more deprived patients were more likely to present as emergencies.
Conclusions: Patients with EP and non-EP have a similar 'background' primary care consultation history until a few months before diagnosis. Emergency presenters with colon and rectal cancer have different symptom signatures and patient characteristics. A non-ignorable proportion of emergency presenters have previously consulted with 'red flag' symptoms. Patient and healthcare factors may be implicated with missed opportunities for earlier diagnosis in this subgroup.
Funding Source: Cancer Research UK - EDAG [C48748/A18667].

N-363 - Testing The Efficacy Of Peer-PN For Latinos On Colonoscopy Screening Uptake

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Purpose: Colorectal cancer (CRC) mortality is preventable through endoscopic screening. Unfortunately Latinos have lower rates of CRC screening compared to whites and other United States (US) racial groups and, as a result, are also more likely than whites to be diagnosed with advanced-stage CRC. Providing patients with help navigating the health care system (i.e., patient navigation [PN]) is related to cancer screening completion. However, very few hospitals provide PN for colonoscopy; partly because of the costs associated with professional-led PN. Peer-led PN may be a less costly, effective alternative. The purpose of this pilot was to investigate the efficacy of a culturally adapted peer-led PN intervention to increase CRC screening among Latinos.
Methods: Latino participants at a primary care clinic aged 50 and older (N= 75) were referred for a screening colonoscopy by their physician. Participants were randomized to receive navigation assistance from (1) a professional PN (PRO; n=36) or (2) a trained peer-patient PN (PEER; n=39). PEER PNs were bilingual Latinos who had undergone a colonoscopy, and were able to discuss how they overcame barriers.
Results: Both groups were equivalent in terms of socio-demographic measures (i.e. gender, education, insurance). A total of 54 participants (72.0%) completed a screening colonoscopy. In the PEER group (intervention) 53.7% (N=29) completed compared to 46.3% (N=25) in the PRO group (control) (p=0.80).
Conclusions: Both navigation groups were equivalent in terms of screening completion; the two groups did not differ statistically. This culturally adapted intervention has the potential to increase CRC screening rates of Latinos and would be useful to the development of future large-scale interventions adapted for other cultural groups. Given the low cost, peer-led PN is a promising approach for the early detection and prevention of colorectal cancer in low-resource settings.
Funding Source: This work was supported by the American Cancer Society (124141-PF-13-018-01-CPPB).

N-364 - Evaluating The Performance Of Mobile Units In A Breast Cancer Screening Program In São Paulo State, Brazil

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Purpose: To evaluate the impact of a population-based breast cancer screening programme implemented with mobile units in urban and rural regions of São Paulo state, Brazil, using performance indicators.

Methods: We studied women ages 40-49 screened annually and 50-69 screened biennially by two-view mammography on one of four mobile units in 2011-2015. We estimated coverage rates using census data. The hospital cancer registry was used to compare clinical characteristics at diagnosis of 656 screen-detected cases with 832 clinically-detected cases arising from the same population eligible for the screening program (aged 40-69 in regions serviced by the units).

Results: In total, 193,101 mammograms were performed on mobile units: 122,640 (63.5%) in initial screening and 70,461 (36.5%) in subsequent screening rounds. The average coverage rates were 35% among women ages 40-49 (annual) and 55% among women 50-69 (biennial). For initial and subsequent screenings, recall rates were 11.2% and 6.3% and cancer detection rates were 4.1/1000 and 2.1/1000, respectively. Biopsies were performed on 2,455 women. The positive predictive values were 18.3%, 29.6%, and 42.9% among women ages 40-49, 50-59, and 60-69, respectively. Breast cancer cases detected through the screening program had more favourable prognosis than clinically-detected cases, including smaller tumour size (53% vs. 36% of invasive tumours were <20mm), and a greater probability of detection below clinical stage II (Odds Ratio = 2.13, 95%CI: 1.69, 2.71).

Conclusions: Our findings show that a breast cancer screening program implemented with mobile units is a viable model for screening in urban and rural areas of Brazil. The mobile units increased access to cancer prevention services and the referral service was effective in guiding patients with suspected breast cancer through appropriate diagnostic steps.

Funding source: McGill Integrated Cancer Research Training Program, McGill Faculty of Medicine, McGill Institute for Health and Social Policy: McBurney, Mitacs Globalink Research Award

N-365 - Association Between Immigration Status & Cervical Cancer Screening: Systematic Review & Meta-Analysis

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Background: In developed countries, much invasive cervical cancer, and the highest mortality rates occur in women who never had a Pap test. Immigrants appear less likely to have been screened for cervical cancer than non-immigrants due to various factors such as education, income, knowledge etc.
Objective: We aimed to determine the magnitude of association between immigration status and cervical cancer screening (ever been screened) among women in developed countries.
Approach: The search used guidelines of the Center for Reviews and Dissemination, using a combination of keywords related to cervical cancer and screening. Data was extracted using the 2009 PRISMA checklist. The Newcastle-Ottawa Quality Assessment Scale was used for confounding and quality assessment.
Results: From 7426 citations, ten articles were included in the systematic review and eight in meta-analysis. The studies were published between 2001 to 2013 from Australia, UK, USA, Canada & Spain. Immigrants are less than half as likely to have ever been screened as non-immigrants in Canada (pooled OR = 0.44; 95% CI:0.386- 0.511), Spain (OR = 0.41; 95% CI: 0.365-0.467), and Australia (OR = 0.44; 0.376-0.508). In the UK, the ratio is worse (OR = 0.23; 0.210-0.244) In the USA, the trend was similar but not significant (polled OR = 0.62; 0.190-2.083). Demographics showed immigrants are less likely to be educated, have lower income and are uninsured. Women born in Asia had lower odds of ever being screened compared to other immigrant groups.
Conclusion: A statistically significant association was found between immigration status and cervical cancer screening but there are limitations due to data reporting. Efforts to increase cervical cancer screening should focus on newly arrived immigrants, immigrants with low levels of education, with low household annual income, and particularly from Asian background. Improving access to care is important to increase cervical screening practices among immigrant populations.

N-366 - Identifying Barriers To Cervical Cancer Screening Among South Asian Muslim Immigrant Women

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Objectives: We sought to identify the barriers to cervical cancer screening among South Asian Muslim immigrant women in Calgary. Understanding their ideas and needs will enable development of educational programs and services so they can benefit from screening and reduce the effect of this disease.

Approach: Qualitative, semi-structured in-depth interviews, by purposive sampling, were conducted with South Asian Muslim immigrant women of Calgary who were unscreened or infrequently screened for cervical cancer. Thematic analysis was conducted for data analysis using Microsoft Word.

Results: 18 women were interviewed and the majority (66%) never had a Pap test. Findings were categorized into five major themes: Attitude, knowledge & beliefs, healthcare seeking practices, experience with healthcare system & services, barriers and strategies to Pap testing. Major findings include: misunderstanding about Pap test reminders, strong preference for a female physician who also speaks their language, seeking symptomatic treatment not prevention, negative experiences with healthcare providers including painful Pap test experience. Major barriers involved: lack of knowledge about cervical cancer and the term cervix, fatalist beliefs, dependence on husband, transportation, language and unavailability of female physicians. Separate centers for Pap testing, awareness and encouragement by social workers and family physicians to get tested were strategies participants suggested.

Conclusion: Different healthcare strategies are needed at the system and provider level to improve healthcare experience of these women and to promote cervical cancer screening. Providing female physicians, knowledge and resources such as transportation and a separate center, and screening reminders that explain the procedure and the disease in detail could potentially increase screening practices.

N-367 - Geographical Variation In Stage At Diagnosis Of Colorectal, Lung And Ovarian Cancers In England, 2008-2013

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Purpose: Stage at diagnosis is a key predictor of cancer survival and a key component for cancer control policy. Clinical Commissioning Groups (CCGs), which plan health services in England, are required to report the proportion of tumours diagnosed at early stages as an indicator of their cancer management quality. However, information on stage in population-based registries often remains incomplete. We seek to investigate the recent variation in stage at diagnosis of colorectal, lung and ovarian cancers between CCGs in England.
Methods: Clinical and socio-demographic information on cancer cases was retrieved from various population-based sources. CCG characteristics were obtained from official publications and sources. Multiple imputation was performed to derive the likely stage when missing. Random intercept models were fitted to quantify variations in stage between the 211 CCGs and identify patient and CCG factors which could explain between-CCG variation.
Results: The study included 99,942 patients diagnosed with colorectal cancer (2010-2012), 203,215 with lung cancer (2008-2013), 14,641 with ovarian cancer (2011-2013). Among those with known stage, proportions of stage I-II were 41.6% for colorectal, 21.1% for lung, 33.9% for ovarian cancer. Variation in the stage distribution exists between CCGs and the results describe the potential roles in this variation of individual factors (deprivation, tumour characteristics and comorbidities), and system features at CCG level (availability of specialists and tests, and percentage of budget spent on cancer).
Conclusions: A thorough understanding of the extent and the nature of geographic variations in stage at diagnosis is relevant from a cancer policy perspective. These findings will help identify individual and system factors responsible for differences in CCG outcomes and hence inform public health interventions aimed at shifting diagnosis to earlier stages, ultimately improving cancer survival.

N-368 - Volumetric Breast Density And The Risk Of Screen-Detected And Interval Breast Cancer

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Purpose: In light of breast density legislation and discussions about supplemental screening it is important to know not only one's risk of breast cancer, but particularly the risk of a tumor that is not detected through mammographic screening. We investigated the relationship between volumetric breast density and the risk of screen-detected and interval cancer within a digital mammography (DM) screening program.

Methods: Mammographic density was automatically assessed with Volpara version 1.5.0 (Matakina, New Zealand) on the first available digital mammogram of 43,211 women (50-75 years) participating in the Dutch biennial breast cancer screening program (2003-2009). Screen-detected and interval breast cancer information was obtained from the screening registration system and through linkage with the Netherlands Cancer Registry. We estimated risks of screen-detected and interval cancers in relation to breast density using multinomial logistic regression analysis (adjusted for age). No other confounders were available in this routine screening database.

Results: 413 screen-detected and 150 interval tumors were identified. Screen-detected breast cancer risk was significantly higher in the higher breast density categories compared to the lowest (OR: 1.65, 95% CI: 1.21-2.24, OR: 1.78, 95% CI: 1.29-2.47, OR: 1.69, 95% CI: 1.08-2.63, for density categories 2 to 4 respectively compared to 1). Interval cancer risk increased with increasing breast density (OR: 2.45, 95% CI: 1.20-4.99, OR: 5.24, 95% CI: 2.59-10.59 and OR: 6.86, 95% CI: 3.12-15.11, for density categories 2 to 4 respectively compared to 1). The relationship with interval cancers was statistically significantly stronger than with screen-detected cancers ($p<0.01$) for density categories 3 and 4.

Conclusions: Although higher breast density is related to a higher risk of a screen-detected breast cancer, it is particularly strongly related to the risk of a breast cancer that is not detected through mammographic screening (interval cancer).

Funding source: European Union's Seventh Framework Programme and Dutch Cancer Society.

N-369 - Vaginal Human Papilloma Virus Genotype Distribution: A Profile Of Zimbabwean Women Reporting For Routine Cervical Cancer Screening

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Purpose: The aim of this study was to determine the type specific prevalence of HPV in self collected vaginal swabs (VS) from Zimbabwean women reporting for routine Cervical cancer (CC) screening. There is paucity of data on type specific prevalence of HPV in Zimbabwe. Developed countries have successfully introduced HPV DNA testing for CC screening to compliment cytology; therefore our setting is looking at adopting similar algorithms.
Methods: A cross sectional study carried out at a tertiary hospital in the capital city of Zimbabwe. Women at least 18 years old reporting for routine CC screening, using visual inspection with acetic acid and cervicography (VIAC), were consecutively enrolled and trained for sample collection. Each participant provided a spot self-collected vaginal swab. Dacron swabs with a plastic applicator were used, which were broken into a cryotube with 500 microliters of guanidine thiocyanate for storage. DNA was extracted using the standard chloroform/phenol method. Illumina sequencing using the MiSeq kit and PGMY primers was done on the 450bp L1 region for HPV genotyping.
Results: Sample size was 144. Age range was 18-83 (median 38). All samples were positive for beta globin, a house-keeping gene for quality control. Overall HPV prevalence was 72%(104/144). Of the HPV positive samples the most common high risk genotypes were; HPV 18(24%), 52(23%) and 16(21%). The low risk genotypes were HPV 6(15%), 61(13%) and 53(8%).
Conclusions: HPV prevalence is relatively high. Since this was a cross sectional study it is difficult to separate new and persistent infections. Knowing the common genotypes in our setting will contribute towards design of HPV DNA screening tools and the decision on the most suitable HPV vaccine to use.
Funding source: Letten foundation funded the research in collaboration with UZ-UCSF and Akershus University hospital in Norway.

N-370 - Delay In Breast Cancer Diagnosis And Treatment In Africañ A Review To Improve Design And Reporting Of Studies

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Purpose
Delay in breast cancer diagnosis and treatment is a major problem in Africa, as it results in advanced stage and poor prognosis for patients. Several studies have measured time of delay in presentation, diagnosis and treatment and analyzed corntributing factors. This study reviewed the literature on delay in breast cancer in Africa to compare methods and to summarize findings.
Methods
A systematic literature research was conducted in PubMed to identify studies analyzing time delay in presentation, diagnosis or treatment of female breast cancer patients in Africa. The Aarhus statement, a recent recommendation to promote greater precision and transparency in studies on early cancer-diagnosis, were used as a basis to evaluate methods. The Model of Pathway were used to compare time intervals and influencing factors.
Results
From 261 search results, 23 studies were included for final analysis. Methods of studies varied widely. 14 studies analyzed delay from symptom recognition until first medical consultation, 12 until diagnosis and 3 until treatment. The percentage of women delays less than 3 months were 11 to 69% until first consultation, 9 to 30% until diagnosis and 10-19% until treatment.
Conclusions
The analyzed literature showed a significant delay in presentation, diagnosis and treatment of breast cancer patients in Africa. However, the time of delay varied widely between studies and comparisons are difficult due to variations in methods and reporting of results. This study gives simple recommendations to improve on standardization of studies in future.
Funding source
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N-371 - Family History And The Risk Of Colorectal Cancer: The Importance Of Patientsí History Of Colonoscopy

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Background: Studies that examined the risk of colorectal cancer (CRC) for persons with a family history (FH) mainly focused on the absolute number of first-degree relatives (FDR) and did not take personal history of colonoscopy of the study participants (HCS) into account.

Methods: We conducted a population-based case-control study in the Rhine-Neckar region of Germany from 2003 to 2014, including 4,334 patients with a first diagnosis of CRC (cases) and 4,232 subjects without CRC (controls). We used multiple logistic regression analyses to assess the association between FH and risk of CRC with odds ratios (OR) and the resulting 95% confidence intervals (95% CI).

Results: Of 7,469 eligible study participants, a total of 1,408 persons reported a FH of any relative, which was associated with a 41% increase in risk of CRC (OR 1.41, 95% CI 1.25-1.59) after adjustment for sex and age. The OR substantially increased to 1.68 (95% CI, 1.48-1.92) when the model was adjusted for HCS. Irrespective of their FH status, persons with positive HCS had a lower risk for CRC compared to persons without HCS and without family history (OR 0.25, 95% CI, 0.23-0.28 for persons without FH of CRC and OR 0.42, 95% CI, 0.35-0.51 for persons with FH of CRC).

Conclusions: In an era of widespread use of colonoscopy, especially among high risk groups, adjusting for HCS is crucial for deriving valid risk estimates of the role of FH in CRC risk. Colonoscopy effectively reduced most of the excess risk of people with a FH of CRC.

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N-372 - Increase In Thyroid Cancer Prevalence In Fukushima After The Nuclear Disaster In 2011 ñ A Potential Overdiagnosis?

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A thyroid ultrasound examination program has been conducted in Fukushima Prefecture, Japan after the nuclear disaster in 2011. Though high prevalence of thyroid cancer was observed, relevant quantitative evaluation was not conducted. We aimed to calculate the observed/expected (O/E) ratio of thyroid cancer prevalence for the residents aged ≤20 years. Observed prevalence was the number of thyroid cancer cases detected by the program through the end of April, 2015. Expected prevalence was calculated as cumulative incidence by a life-table method using the national estimates of thyroid cancer incidence rate in 2001-2010 (prior to the disaster) and the population of Fukushima Prefecture. The observed and estimated prevalence of thyroid cancer among residents aged ≤20 years was 160.1 and 5.2, respectively, giving an O/E ratio of 30.8 (95% confidence interval (CI): 26.2, 35.9). When the recent increasing trend in thyroid cancer was considered, the overall O/E ratio was 22.2 (95% CI: 18.9, 25.9). The cumulative number of thyroid cancer deaths in Fukushima Prefecture, estimated with the same method (annual average in 2009-2013), was 0.6 under age 40. Combined with the existing knowledge about radiation effect on thyroid cancer, our descriptive analysis suggests the possibility of overdiagnosis. Further evaluation including individual-level analysis is required to clarify the contribution of underlying factors.

N-373 - The Feasibility Study Of The Randomized Cancer Screening Trial In China

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Purpose: Lung cancer has been the leading cause of cancer death in China. The US National Lung Screening Trial (NLST) showed a 15-20% mortality reduction in a high-risk population with annual Low-Dose Computed Tomography (LDCT). China hasn't yet developed national guidelines for lung and colorectal cancer screening and needs scientific evidence from the Chinese population for making policy. The aim of this study is to obtain information necessary to design a long-term randomized lung and colorectal cancer screening trial in China.
Methods: Individuals at elevated risk in three centers were randomized into three arms: ① annual LDCT and baseline colonoscopy; ② every other year LDCT plus annual fecal immunochemical test (FIT); ③ annual FIT plus Septin-9 test. The randomization was stratified on gender and 5 age groups (50-74). This study was approved by Ethics Committee of Cancer Hospital, Chinese Academy of Medical Science in June, 2014 and registered in Chinese Clinical Trial Registry.
Results: From August, 2014 to March, 2015, 2696 eligible participants were recruited at baseline. The rate of adherence to screening was 90.0%. 1598 participants received LDCT. The abnormality rate was 77.4% with LDCT and suspicious rate for lung cancer were 6.5% and 6.1% for arm 1 and arm 2, respectively. 2150 participants received colorectal cancer screening. The positivity rate was 34.1% with colonoscopy screening, 9.7% with FIT, and 5.8% with Septin9 test.
Conclusions: This is the first randomized trial of lung and colorectal cancer screening in China. The feasibility study will help develop a practical design for the Large-scale Randomized Cancer Screening Trial in China.
Funding resource: International Cooperative Project by Ministry of Science and Technology, China

N-374 - The Distribution And Risk Estimate Of Esophagogastric Junction Adenocarcinoma And Precursors Lesions In Linzhou: A Prospective Cohort Study

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Background：The incidence of esophagogastric junction adenocarcinoma (EGJA) has shown a significantly upward trend in China, especially in traditional high-risk areas of esophageal cancer. However, the literature on incidence and mortality of EGJA is limited.
Purpose：To understand the epidemic state of EGJA and precursor lesions in high-risk areas of China.
Methods：Endoscopy with Lugol's iodine staining was performed on 10328 local residents aged 40 to 69 years old in Linzhou of Henan province from 2005–2009 and followed up until 31 March 2014. We estimated the relative risk of developing EGJA for each of the initial histological diagnoses.
Results：A total of 9941 subjects were enrolled in this study, about 144 incident cases and 32 death case of GCA were identified between 2005-2014. The incidence rate of non-atrophic gastritis(NAG), atrophic gastritis(AG), mild dysplasia(mD), severe dysplasia(SD), EGJA were 0.29% (9/3 108), 0.93% (9/965), 1.17% (10/858), 11.38% (19/167), 81.05% (77/95). And relative risks (95% confidence intervals) for incidence of EGJA, by initial histological diagnosis, were: NOR 1.0 (reference), NAG 0.69(0.31-1.50), AG 2.21(1.03-4.76), mD 2.77(1.34-5.72), SD 27.01(17.89-40.78), and EGJA 192.42(159.82-231.67). Moreover, the mortality of NAG, AG, mD, SD, EGJA were: 0.16% (5/3 108), 0.31% (3/965), 0.35% (3/858), 2.40% (4/167), 14.74% (14/95) and the relative risks for mortality of this tumor were: NOR 1.0 (reference), NAG 2.55(0.64-10.12), AG 4.92 (1.16-20.81), mD 5.53(1.34-22.89), SD 37.91(15.30-93.92), and EGJA 233.24 (149.26-364.45).
Conclusions：Up to 20.97% residents were asymptomatic were suffered from EGJA or precursor lesions in Linzhou. And increasing grades of dysplasia were strongly associated with increasing risk.
Funding source：National Natural Science Foundation of China

N-375 - Long-Term Follow-Up Study Of The Optimal Starting Age Of Endoscopic Screening Program And Its Effect On Mortality Of Esophageal Cancer In High Risk Population In China

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Purpose
There are no global screening recommendations for esophageal squamous cell carcinoma (ESCC). We previously reported the effectiveness of endoscopic screening in reducing mortality and incidence caused by ESCC in an endoscopic screening cohort. This study is aim to evaluate effects of endoscopic screening in different age groups and further confirm the optimum starting age for ESCC screening.
Methods
Based on the previous endoscopic screening cohort study, 6825 residents aged 40-69 years in the intervention communities were recruited as the subjects. Subjects were assigned to either the screening group of underwent baseline screening by endoscopy with Lugol's iodine staining and biopsies of the unstained lesions or the control group received usual medical care. The primary analysis compared ESCC mortality rates in the screening group and the control group of different starting age groups.
Results
The 14-year risks of ESCC fatality were 1 in 55, 1 in 17 and 1 in 9 for a person in the starting age group of 40-, 50- and 60- year. The screening groups had significantly lower cumulative mortalities of ESCC versus control groups in starting age 40 years group (1.42% vs 2.38%, p=0.0331) and 50 years group (4.18% vs 7.13%, p=0.0053).The relative risks for subjects underwent screening were 0.60 (95% CI 0.37-0.97) and 0.59 (95% CI 0.40-0.86) for the starting age groups of 40- year and 50- year. The numbers needed to invited for screening to save 1 life were 104 (95% CI 51-1520) and 34 (95% CI 20-114) for subjects aged 40 to 49 years and 50 to 59 years respectively.
Conclusions
Considering overall conditions of high risk regions of ESCC, we recommend high risk population should have screening once at their 50 years. 40 years will be preferable defined as the starting age to screening in the developed areas with sufficient health resources.
Funding source
This study was supported by grants (2006BAI02A15, and 81241091) from the Ministry of Science and Technology of PRC.

N-376 - Optimal Strategies For Mass Screening Of Breast Cancer In India Through Markov Model And Survival Analysis Induced From Multistage Models

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Purpose: The aim is to evaluate and assess different strategies of mass screening for breast cancer (BC) using mathematical model, since BC has survival rates around 31-54% in India as compared to over 90% in developed countries like USA. Also to formulate optimal age window for “once in a lifetime” (OL) and “twice in a lifetime” (TL) individual policies for resource limited setting in India.
Methods: Natural history of BC with inter-stage transition was simulated using a mathematical model to evaluate various biennial and triennial screening policies that also had different age for initiating and terminating screening. Clinical Breast Examination (CBE) followed by clinical ultrasound, is the suitable screening method, recommended for Indian population where BC incidence peaks at a younger age was evaluated along with standard mammography using specificity and sensitivity values reported for pilot screening programs in India. Markov Chain transition model was used to model the natural history of BC progression through different clinical stages.
Results: Initiating age of screening from 37 years for biennial policy increased average life expectancy by 30 days, and by 24 days, compared to average life expectancy at the age of 37 years, in triennial policies. For resource limited strategies such as “once in a lifetime” the optimal age window was 42 to 46 years and that for “twice in a lifetime” it was from 41 to 44 years and from 46 to 51 years, previously not investigated or recommended. False positive rates were 58% and 53% respectively for OL and TL. False positive rates declined after 45 years of age with use of mammography compared to CBE.
Conclusions: The proposed optimal strategies can be considered for BC awareness and design and planning of mass screening programs in India.
Funding Source: Indian Institute of Science, Bangalore, India

N-377 - Prospective Cohort Study Of The Effect Of Endoscopic Screening In TNM Stage Of Esophageal Cancer Patients

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Purpose:To investigate whether an endoscopic screening and intervention program could make patients to be diagnosed in earlier TNM stage.
Methods:This study was on the basis of a preliminary study from January 1,2000 to December 31,2009, which selected fourteen villages as the intervention communities and ten villages not geographically adjacent to intervention villages for comparison. Participants in the intervention group were screened once by endoscopy with Lugol's iodine staining, and those with dysplasia or occult cancer were treated. A retrospective analysis was performed on the clinical data of 168 patients with esophageal cancer, which come from the intervention group and control group. The c2 test was used to analysis the difference of TNM stage between two groups, the Kaplan-Meier curve compared survival rate of patients in two groups, the risk factors of death in patients of two groups were analyzed through Cox regression analysis.
Results:We collected 168 case reports in Cixian cancer hospital and Cixian county people's hospital range from 2000 to 2013, among them 166 case reports had detailed information to estimate their TNM stage, which contained 78 cases from the intervention group and 88 cases from the control group. There was significant difference of the TNM stage between intervention group and control group.Survival analysis using Kaplan-Meier methods showed that the 1-year survival rates and 5-year survival rates in intervention group and control group were 65.0%,60.3% and 10.0%,6.3% respectively, with significant differences (P=0.042) between the survival curves of two groups. The multivariate analysis showed that intervention measure was the independent prognostic factor.
Conclusions:We showed that endoscopic screening and intervention significantly made esophageal cancer patients to be diagnosed in earlier TNM stage. And this can be the medium-term indicator for evaluating the effectiveness of screening.
Funding source:National Natural Science Foundation of China

N-378 - Development Of A Non-Melanoma Skin Cancer GP Referral Guideline; An Evidence-based Approach

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Purpose
Non-melanoma skin cancer is the most common cancer in the Republic of Ireland. Ireland's incidence and mortality are steadily increasing; 9000 cases are diagnosed each year. Incidence will escalate; by 2040 it will increase by up to 356% in males and 235% in females (NCRI, 2014).

Achieving better patient outcomes depends on early recognition, prompt and appropriate referral, and multi-disciplinary specialist management. The National Cancer Control Programme (NCCP) identified a need for a referral guideline to assist General Practitioners (GPs) in the recognition of high risk non-melanoma skin cancer (NMSC) and advise on management and referral pathways.

Methods
An Expert Group was set up with representation from general practice, dermatology and surgery/plastic surgery. Key clinical questions were agreed for the literature review. Publications were appraised using either the AGREE II instrument or a methodology checklist for systematic reviews and meta-analyses. The guideline was developed by the Expert group prior to public consultation. Currently the guideline is in the final stages of development.

Results
GPs should endeavour to identify high risk tumours at the earliest opportunity and refer patients with clinical or pathological features of high risk NMSC for specialist management and discussion at a Multi-disciplinary Meeting (MDM). Low risk lesions may be excised in Primary Care. The guideline clearly defines features of high risk basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) including images of the clinical features of these cancers. Pathways for management and referral of BCCs and SCCs are outlined. There is brief advice on primary prevention and early detection for patients.

Conclusions
This guideline has been devised by an Expert Group following critical appraisal of current evidence and public consultation. It will be circulated to all GPs and used to promote evidence-based pathways of care for patients presenting to their GP with NMSCs.

Methods

N-379 - Future Burden Of Cervical Cancer Preventable By Screening In Central And Eastern European Countries

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Purpose: Cervical cancer (CC) incidence is particularly high in Baltic and Central/Eastern European (BCEE) countries mainly because of the historical absence of mass screening programmes. We estimate the future burden of CC that could theoretically be prevented by 2040 if effective screening programmes were introduced.
Methods: Age-period-cohort models were applied within a Bayesian framework to selected BCEE countries. Projected rates in a scenario where the current status quo of no effective screening will persist were obtained by extrapolating, using spline functions, the two major risk factors affecting CC rates. Cohort-specific effects, reflecting mainly the increasing risk of human papillomavirus (HPV), are rising in many European countries. Conversely, period-specific effects have strongly declined in countries with long-standing screening programmes, e.g., the Nordic countries, but are absent in countries without existing CC prevention strategies, e.g., BCEE. A gradual impact of screening is hypothesized, assuming declines in period-specific effects equal to those observed in Denmark following implementation of screening in the late 1960s. Introduction of screening programmes at different future dates was assessed.
Results: Projected CC rates will continue increasing substantially in many BCEE countries, reaching age-standardized rates of ≥50 cases per 100.000 in all studied countries in 2036-2040. Particularly high rates are expected in Lithuania (88 per 100,000), Latvia (68 per 100,000), Belarus (67 per 100,000) and Estonia (64 per 100,000). Effective screening programmes might, however, change dramatically these figures. The number of CC cases possibly preventable up to 2040 through improvements in screening programmes varies from almost 1,500 in Estonia to over 150,000 in the Russian Federation. The beneficial effects of screening will increase progressively over time reaching reductions of 50-60% of the projected rates in 2040.
Conclusions: The improvement of screening programmes might prevent a HPV-driven CC epidemic in several BCEE countries in the next 25 years.
Funding source: None.

N-380 - Semi-Quantitative HPV Viral Load Estimation In Colposcopy Practice: A Pooled Analysis Among Chinese Population

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Purpose To evaluate the role of high human papillomavirus (HPV) viral load in detection of the cervical cancer and precancer lesions (CIN2+) which were missed by cloposcopy in HPV positive women.
Methods We analyzed the pooled database of 17 population-based cross-sectional studies which were conducted across China from 1999 to 2008. In total, 30,371 women aged 17-59 participated in these studies and received liquid-based cytology test (LBC), HPV testing and visual inspection with acetic acid (VIA). Women with any positive result were referred to colposcopy, among them, 15,287 women with completed HPV testing and cloposcopy examination were included in the analysis. HPV positive women were categorized into three groups (low, intermediate and high viral load) based on relative light unit/ cut off ratios. The risk of CIN2+ and the correlation between viral load and the grading of cloposcopy were analyzed with the golden standard of pathological diagnosis .
Results 10652, 1661, 1369 and 1590 women were categorized into the groups of RLU< 1, 1-10, 10-100 and 100+, respectively. 34.7% (307/886) of CIN2+ and 30.0% (138/460)of CIN3+ cases were missed by colposcopy, respectively. The majority (84.7% of CIN2+, 87.7% of CIN3+) were categorized into the intermediate and high viral load groups. Risk of CIN2+ for women with intermediate and high viral load was 74.8 and 174.0 times higher than that of HPV negative women, respectively, even their colposcopy results were apparently normal.
Conclusions About one third cervical cancer and precancer lesions might be missed by colposcopy among Chinese screening population. The HPV viral load could assist to improve the detection of lesions in colposcopy practice based on the high risk of CIN2+ estimated for these women with intermediate and high HPV viral load, even they have normal colposcopy impression.

Funding source National Natural Science of Foundation of China (No 81322040)

N-381 - Socioeconomic Position And Breast Cancer Stage In Switzerland

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Purpose
This study aims to investigate the association between socioeconomic position (SEP) and breast cancer stage at diagnosis in Switzerland.

Methods
The study used population-based breast cancer incidence data from the cantonal cancer registries of Geneva, Valais and Zurich 2001-2008 (N=11,150) linked to the Swiss National Cohort. Stage at diagnosis was classified by Surveillance, Epidemiology, and End Results Program (SEER) summary stage (in situ, localized, regional, distant). We used highest education level attained to estimate SEP (compulsory or less, upper-secondary, upper-tertiary education). Logistic regression models examined the association between cancer stage at diagnosis and SEP. The adjusted model reports odds ratios (OR) with 95% confidence intervals (95%CI) and included *age* at diagnosis (<50, 50-70, >70 years), canton with organized *screening program* (yes/no), *civil status* (single, married,…), *nationality* (Swiss, non-Swiss), and an interaction term for *age* and *screening program*.

Results
Odds of later stage at breast cancer diagnosis were increased for women with upper-secondary (OR 1.11, 95%CI, 1.01-1.22) and compulsory or less education (OR 1.24, 95%CI 1.11-1.39) compared to women with upper-tertiary education. Women living in a canton without an organized screening program were also more likely to be diagnosed at later stages (OR 1.54, 95%CI 1.31-1.82). Further, women outside the targeted screening age (<50 years: OR 1.39, 95%CI 1.18-1.64; >70 years OR: 1.83, 95%CI 1.37-2.46) and single/widowed/divorced women showed elevated risks for later stages (OR 1.15 (95%CI 1.04-1.27) - 1.19 (95%CI 1.06-1.34)).

Conclusions
Characteristics associated with later stage breast cancer diagnosis in Switzerland were lower SEP, being unmarried, being below 50 or above 70 years of age and living in a canton without an organized breast cancer screening program. Appropriate intervention strategies are needed in order to reduce sociodemographic inequalities and improve early detection of breast cancer.

Funding source
This work was funded by Cancer Research Switzerland (KFS-02553-02-2010).

N-382 - Risk Assessment To Guide Cervical Screening Strategies In A Large Chinese Population

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Purpose: Three different cervical screening methods (cytology, human papillomavirus (HPV) DNA testing, and visual inspection with acetic acid (VIA)) are being considered in China for the national cervical screening program. To guide cervical cancer screening in China, we compared risks of CIN3 and cervical cancer (CIN3+) for different results, which can inform test choice and management guidelines.
Methods: We evaluated the immediate risk of CIN3+ for different screening results generated from individual and combined tests. We compared tests using a novel statistic designed for this purpose called Mean Risk Stratification (MRS), in a pooled analysis of 17 cross-sectional population-based studies of 30,371 Chinese women screened with all 3 methods and diagnosed by colposcopically-directed biopsies.
Results: The 3 tests combined powerfully distinguished CIN3+ risk; triple-negative screening conferred a risk of 0.01%, while HPV-positive HSIL+ that was VIA-positive yielded a risk of 57.8%.Among the 3 screening tests, HPV status most strongly stratified CIN3+ risk. Among HPV-positive women, cytology was the more useful second test. In HPV-negative women, the immediate risks of CIN3+ ranged from 0.01% (negative cytology), 0.00% (ASC-US), 1.1% (LSIL), to 6.6 (HSIL+). In HPV-positive women, the CIN3+ risks were 0.9% (negative cytology), 3.6% (ASC-US), 6.3% (LSIL), and 38.5% (HSIL+). VIA results did not meaningful stratify CIN3+ risk among HPV-negative women with negative or ASC-US cytology; however, positive VIA substantially elevated CIN3+ risk for all other, more positive combinations of HPV and cytology compared with a negative VIA.
Conclusion: All 3 screening tests had independent value in defining risk of CIN3+, different combinations can be optimized as pragmatic strategies in different resource settings.
Funding: Our work was supported by the National Natural Science of Foundation of China (No 81322040).

N-383 - The Program For Cancer Detection, Diagnosis, And Treatment Technologies For Global Health: Translating Affordable Point-Of-Care Technologies To Less-Resourced Settings

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Cancer kills more people worldwide than HIV/AIDS, tuberculosis and malaria combined, with low-and-middle income countries (LMICs) largely bearing this burden. While success in detection, diagnosis and treatment has been reported in LMICs through the use of low-cost point-of-care (POC) technologies, these technologies have been largely overlooked by industry and venture capital, as low-cost solutions offer less incentive for investment. The program presented here funds multidisciplinary teams to adapt and validate technologies for cancer detection, diagnosis and treatment in low-resource settings, providing these technologies a pathway to market.

Each project consists of an adaptation phase (2 years: $500k total costs/year) and validation phase (3 years: $1M total costs/year). Projects are selected through NIH peer review process by a carefully-selected special emphasis panel. Projects are competitively vetted for validation phase funding based on completion of adaptation phase milestones.

The program currently supports seven technologies for cancer detection, diagnosis and treatment. For oral cancer, the program supports a LED-based photodynamic therapy device with similar in vivo and ex vivo efficacy as existing laser phototherapy. For cervical cancer detection, an automated high-resolution microendoscope is supported, displaying a 90%+ histological concordance in detecting CIN3. Two cervical cancer cryotherapy projects are funded: a cryopen which achieves ~4.0 mm depth of necrosis (>90% of disease), and a cryopop device that consumes >10% theCO_2 consumed by commercial devices, while exhibiting comparable efficacy in ballistic gel studies. The program also supports POC tests for HPV and Hepatitis C viral antigen level/viral load detection, and a breast cancer triaging device/algorithm with 95% sensitivity and a 40% false positive reduction rate of.

The program is adding eight projects this year, and by year seven of the program, at least nine projects will have progressed through optimization, clinical validation, and business planning for commercialization, uniquely accelerating these technologies for successful clinical translation.

N-384 - Long-Term Risk Of Cervical Cancer Or Precursor For Type-Specific Human Papillomavirus In Chinese Women

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Purpose： The role of high-risk human papillomavirus (HR-HPV) including HPV16 and 18 in predicting the cervical cancer and triaging the HPV positive women in the screening has been well demonstrated by many cohort studies and clinical trials. However these risk patterns of individual HPV types especially HPV 52 and 58 are not clear in China, therefore we evaluated the long-term risk for type-specific HPV in developing cervical cancer or precursors based on a population-based cervical cancer screening cohort in mainland China.
Methods：We analyzed the cohort database of Shanxi Provincial of Cervical Cancer Screening Study from 2005-2014, 1734 women aged 45–55 were screened by the Hybrid Capture 2 (HC2) and liquid based cytology (LBC) tests. The prevalence rate (PR) of individual type-specific HR-HPV tested by SPF10-LiPA V2 assay in HC2 positivity in 2005 was calculated and the cumulative incidence rates (CIR) of cervical intraepithelial neoplasia 2 or worse (CIN2+) for individual type-specific HR-HPV from 2005-2014 was estimated.
Results：Compared to HR-HPV negativity women(CIR= 2.1%), higher prevalence and risk of developing CIN2+ with 9 years following a positive test were observed in HPV16 (PR=32.8%; CIR=32.3%), HPV31 (PR=8.5%;CIR=27.8%), HPV58 (PR=12.8%; CIR=19.2%), HPV39 (PR=5.1%;CIR=18.2%), HPV52 (PR=15.7%;CIR=14.3%), HPV33 (PR=9.8%;CIR=13.6%), and HPV18 (PR=8.9%;CIR=9.5%).
Conclusions：Our results indicate that HR-HPV genotyping may provide accurate risk stratification of HPV positive women. Specific prevalent and HR-HPV type in China including HPV16, 31, 58, 39, 52, 33 and 18, should be taken into consideration when the HPV-based cervical cancer screening and vaccination are applied.
Funding source：Our work was supported by the National Natural Science of Foundation of China (No 81322040).

N-385 - Understanding Pathways To Breast Cancer Diagnosis: A Qualitative Exploration Of Symptom Appraisal And Health Seeking Behaviour

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Purpose: Timely diagnosis of breast cancer is important to improve survival. The aim of this study was to explore and understand women's pathways to breast cancer diagnosis and factors influencing this journey.

Methods: In-depth interviews were conducted with 20 newly diagnosed breast cancer clients attending a tertiary level breast cancer clinic in Cape Town, South Africa. Issues explored included: interpretation of breast changes, signs and symptoms; perceived risk; social and family support; triggers to seeking care; access to health care; use of various levels of care; and commonly held community beliefs. A thematic analysis was performed underpinned by the theoretical concepts of the Model of Pathways to Treatment framework.

Results: The average time between discovery of bodily changes to breast cancer diagnosis was 8.5 months. Deficits in breast self-awareness and knowledge of breast cancer symptoms delayed women's interpretation of bodily changes as being abnormal. All women first noticed breast lumps, however many did not perceive it as abnormal until additional symptoms were present. General good health, attribution of symptoms to ageing and past benign breast disease resulted in women being complacent about bodily changes. Disclosure to family members served as a trigger to seek health care. The initial type of primary level care services women accessed was influenced by perceptions of care each provided, finances, structural factors, and personal safety related to the physical location of services.

Conclusion: Symptom appraisal and interpretation contributed significantly to delayed presentation. To improve timely diagnosis of breast cancer, interventions that increase women's confidence in detecting breast changes, improve knowledge of breast cancer symptoms, address myths and encourage prompt help-seeking behavior are required.

Funding source: Cancer Association of South Africa (CANSA) and the University of Cape Town, Faculty of Health Sciences

N-386 - Cancer Screening Program In Urban China

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Purpose
Cancer is the leading death cause in China, especially in urban China. Since 2012, Chinese government has initiated a new national key public health program called Cancer Screening Programs in Urban China (CanSPUC). Its main purpose is to carry out the screening on several top cancers in urban China including lung, breast, colorectal, oesophageal/stomach and liver cancers.

Methods
The subjects aged 40-69 years in urban cities were invited to participate in the program. After the questionnaire interview, the subjects will be evaluated as high-risk or not high-risk to 1 or more cancers. If the participants are high risk to 1 or more cancers, they will be screened with low-dose computed tomography (LDCT) for lung cancer, ultrasound and mammography for breast cancer, colonoscopy followed by biopsy collection and pathological diagnosis for colorectal cancer, endoscopy followed by biopsy collection and pathological diagnosis for esophageal/ stomach cancers, and AFP test plus abdominal ultrasound for liver cancer. Once the above tests find some suspicious lesions, the participants will be directed to get the further diagnosis and treatment in the professional hospitals.

Results
Till July 31, 2015, nearly 1.5 million subjects aged 40-69 years participated in the questionnaire interview. Of them, 360,000 subjects were evaluated as high risk to 1 or more cancers and received the screening including 120,000 for lung cancer, 70,000 for breast cancer, 70,000 for liver cancer, 60,000 for esophageal/stomach cancers and 40,000 for colorectal cancer.

Conclusion
This is the first and large-scale cancer screening program in urban China, which will reveal a lot of evidence on the cancer prevention and control in urban China.

Funding resource
It is funded by Chinese Ministry of Finance with the central governmental budget and administered by National Health and Family Plan Committee.

N-387 - Cost-Effectiveness Of Different Cervical Screening Strategies In I. R. Iran: A Middle-Income Country With A Low Incidence Rate Of Cervical Cancer

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Objective: Invasive cervical cancer (ICC) is the fourth most common cancer among women worldwide. Cervical screening programs have reduced the incidence and mortality rates of ICC. We studied the cost-effectiveness of different cervical screening strategies in the Islamic Republic of Iran, a Muslim country with a low incidence rate of ICC.
Methods: We constructed an 11-state Markov model, in which the parameters included regression and progression probabilities, test characteristics, costs, and utilities; these were extracted from primary data and the literature. Our strategies included Pap smear screening and human papillomavirus (HPV) DNA testing plus Pap smear triaging with different starting ages and screening intervals. Model outcomes included lifetime costs, life years gained, quality-adjusted life years (QALY), and incremental cost-effectiveness ratios (ICERs). One-way sensitivity analysis was performed to examine the stability of the results.
Results: We found that the prevented mortalities for the 11 strategies compared with no screening varied from 26% to 64%. The most cost-effective strategy was HPV screening, starting at age 35 years and repeated every 10 years. The ICER of this strategy was $8,875 per QALY compared with no screening. We found that screening at 5-year intervals was also cost-effective based on GDP per capita in Iran.
Conclusion: We recommend organized cervical screening with HPV DNA testing for women in Iran, beginning at age 35 and repeated every 10 or 5 years. The results of this study could be generalized to other countries with low incidence rates of cervical cancer.
Keywords: Cervical cancer, human papillomavirus, cost-effectiveness, screening, Iran

N-388 - Comparison Of Three Management Strategies For Patients With Atypical Squamous Cells Of Undetermined Significance

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Background:
In Albania an average of 2.9% per year, receive an equivocal cervical cytological diagnosis (atypical squamous cells of undetermined significance [ASCUS]). Effective colposcopy triage strategies are needed to identify the minority of women who have clinically significant disease while avoiding excessive follow-up evaluation for others.
Methods: This study summarizes the cross-sectional enrolment results of 141 women with a referral diagnosis of ASCUS during 2009-2012. Randomised yield 49 (34.8%) in the immediate colposcopy, 53 (27.7%)in the HPV triage arm, and 39 (37.6%) in the conservative management. This randomized trial comparing the sensitivity and specificity of the following three management strategies to detect cervical intraepithelial neoplasia (CIN): 1) immediate colposcopy (considered to be the reference standard), 2) triage to colposcopy based on human papillomavirus (HPV) results and cytology results, or 3) triage based on cytology results alone. Results: Among participants with ASCUS, the underlying prevalence of histologically confirmed CIN was 46.8%. Sensitivity to detect CIN or above by testing for cancer-associated HPV DNA was 78%, with 69.8% of women referred to colposcopy. The sensitivity will increase (using a threshold of positive cytology base in age more than 30 years) 100% (95% CI = 20% to 85%), with 24.5% referred to colposcopy. Sensitivity of a single repeat cytology specimen was 30.3% with 14.2% referred. Conclusions: HPV testing for cancer-associated HPV DNA is a viable option and cost efective in the management of women with ASCUS bases and the age of the patients. It has greater sensitivity to detect CIN or above and specificity comparable to a single additional cytologic test indicating ASCUS or above.

N-389 - Risk Prediction Models For Breast Cancer Subtypes Defined By Hormonal Receptor Status In The European Prospective Investigation Into Cancer And Nutrition

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Purpose: Several breast cancer (BC) risk models have been developed since the initial work by Gail in the late eighties. The discriminatory power (C-statistic) of these models is around 60% using questionnaire-based risk factors and 70% after combination with genetic variants. In this study, we investigated whether the predictive power could be improved by accounting for BC heterogeneity in the European Prospective Investigation into Cancer and Nutrition (EPIC).
Methods: Prospective data from 301,550 women were analyzed. Preliminary subtype-specific models included age, menopausal status, age at menopause, age at menarche, full term pregnancy (FTP), number of FTP, age at first FTP, breast feeding, hormone replacement therapy, height, body mass index (BMI), and the interaction between menopausal status and BMI. First primary cancers of other sites and non-BC mortality were considered as competing events. The predictive power was evaluated with a five-fold cross-validation.
Results: During an average follow-up period of 15 years, 13,164 BC cases were identified (ER+: 7,295; ER-: 1,613; unknown: 4,256). FTP, number of FTP, age at first FTP, and height showed differential associations between ER+ and ER- tumors. The five-fold cross-validation showed an average C-statistic of 69% (95% confidence interval: 66%, 72%) for ER+ and 56% (50%, 62%) for ER- tumors, and calibration values (expected/observed BC) were 1.14 (1.10, 1.19) and 0.98 (0.90, 1.07), respectively. Adding alcohol consumption and a composite dietary score to our models slightly improved the discriminatory power for ER- tumors (C-statistic: 59%; 53%, 65%).
Conclusion: Our subtype-specific models yielded higher predictive power for ER+ tumors than the previous overall models, although the predictive power for ER- tumors remained limited. Data on BC-related biomarkers, i.e. specific hormones and sets of fatty acids, as well as genetic variants available in EPIC nested case-control studies, will be integrated to the models.
Funding sources: IARC fellowship program.

N-390 - Molecular Pathological Features Of Colorectal Cancer Detected At Screening And After Occurrence Of Symptoms: Are There Relevant Differences?

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Background. Colorectal cancer (CRC) screening aims at both prevention and early detection of CRC. CRCs detected earlier through screening may have divergent molecular pathologies than symptom-detected cancers. Knowledge about the molecular pathology can help improve screening examinations and technologies. Thus, we aimed to compare molecular characteristics of screening- and symptom-detected CRCs according to molecular pathological characteristics.

Methods. Mode of detection was assessed in 1,260 CRC patients of a large population-based case-control study from Germany (DACHS) with available information on molecular pathological features analysed in the tumor tissue of the patients (microsatellite instability (MSI), CpG island methylator phenotype (CIMP-high), *KRAS* and *BRAF* mutations, estrogen receptor (ER) beta expression). Multivariable logistic regression analyses were employed to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CI).

Results. The study participants were on average 69 years old. MSI-high, CIMP-high, *KRAS* and *BRAF* mutations showed associations with age, sex, stage and location of CRC as expected. In multivariable analyses adjusting for the latter factors and other patient characteristics, CIMP-high CRC was detected more often at screening (17%) than after occurrence of symptoms (10%) (OR 1.70, 95% CI 1.07-2.71). On the contrary, CRCs lacking ER beta expression were detected less often at screening (36% versus 48%; OR 0.56, 95% CI 0.40-0.80). Risk reduction of CRC after colonoscopy was found to be stronger for KRAS mutated than for KRAS wildtype CRC in the proximal colon.

Conclusion. In this first study exploring differences of major molecular characteristics in screening- and symptom-detected CRCs, screening was less effective in detecting CRCs with lack of ER beta expression, a finding which would have prognostic relevance. Other large studies are required to confirm these first results.

N-391 - An Investigation Of Routes To Cancer Diagnosis In Ten International Jurisdictions ñ Survey Development And Implementation Of ICBPM4

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Purpose: International differences in cancer survival, reported previously by the International Cancer Benchmarking Partnership (ICBP), may be linked to differences in time intervals from first symptom(s) until diagnosis and start of treatment, and routes to diagnosis of cancer patients. Module 4 of the ICBP will provide the first robust international comparison of these parameters. We present the study design and recruitment processes, and report reliability testing and response rates of the developed questionnaires.
Methods: A prospective study involving questionnaires from newly diagnosed patients and their primary care physicians (PCPs) and cancer treatment specialists (CTSs) was undertaken. Patients were identified through cancer registries data in each jurisdiction. The recruitment target was 200 breast, lung, colorectal and ovarian patients, diagnosed through a symptomatic route in each of ten participating jurisdictions in 6 countries. Data on screen-detected patients was also collected. Screened patients were also recruited as it was not possible to identify these patients through cancer registry data in all jurisdictions. Data and audit information from treatment records or databases supplemented the questionnaire data. Hierarchal ‘data rules’ were applied to combine and reconcile conflicting information.
Results: Analysis of colorectal and breast cancer data showed that intervals for screened and symptomatic patients can be compared between jurisdictions. Reliability testing broadly showed good agreement for items within the patient questionnaire, and response rates to the questionnaires were comparable with similarly published questionnaires in some jurisdictions.
Conclusion: An international questionnaire-based survey of patients, PCPs and CTSs was undertaken in ten jurisdictions. This is the first attempt to describe and compare between countries the patient journey from symptom onset to a cancer diagnosis and treatment. ICBPM4 could provide unique insights into cancer survival differences, and identify areas where improvements may be made in health systems.
Funding source: Provided by various sources from each participating jurisdiction.

N-392 - From First Symptom To Treatment For Breast Cancer ñ An International Comparative Study (ICBPM4)

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Purpose: International differences in breast cancer survival and stage at diagnosis, reported previously by the International Cancer Benchmarking Partnership (ICBP), may be linked to differences in time intervals and routes to diagnosis. ICBP Module 4 reports the first international comparison of routes to diagnosis for breast cancer patients and the time intervals from symptom onset until the start of treatment. Data from ten jurisdictions across six countries (Canada, the UK, Norway, Sweden, Denmark and Australia) is included.
Methods: Patients were identified via cancer registries. Data on symptomatic and screened patients was collected – with a target of 200 symptomatic patients. Questionnaire data from patients' primary care providers (PCPs) and specialists, as well as audit information from treatment records or databases, supplemented data from the patient questionnaire.
Routes to diagnosis and the key time intervals were estimated and compared using quantile regression.
Results: A total of 3,470 breast cancer patients diagnosed between May 2013 and November 2015 are included in the analyses. Preliminary analyses show that the main route to diagnosis was symptomatic presentation, most often to primary care, with half experiencing a lump.
The median patient interval ranged from 4 to 31 days. The primary care interval was short with a median of 0 days with a few important exceptions. For symptomatic women the median diagnostic interval ranged from 8 to 36 days and the median total interval from first symptom to treatment from 42 to 93 days between jurisdictions. The total interval was similar between jurisdictions when screen detected cases were included.
Conclusion: ICBM4 was able to demonstrate important differences in routes to diagnosis and time intervals between ten jurisdictions. Preliminary results will be presented at the conference.
Funding source: Provided by various sources from each participating jurisdiction.

N-393 - A Randomized Controlled Trial Comparing Self-Collected HPV Testing To VIA for Cervical Cancer Screening In Uganda: Uptake And Preliminary Results

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Purpose: Although visual inspection with acetic acid (VIA) is standard for cervical cancer screening in many low resource settings, self collected samples for high risk human papillomavirus (HR-HPV) DNA has emerged as a promising alternative. In this randomized controlled trial we compared community based self-collection of HR-HPV testing to VIA to determine the optimal screening method for cervical cancer screening in Kisenyi, Uganda.

Methods: 500 women recruited by outreach workers in the community between April-June 2014 in Uganda were randomized to self-collection or VIA. Women randomized to HPV self-collection were given a swab, completed screening and returned it immediately to the worker. Women who tested HPV positive were referred to VIA. Women randomized to VIA were referred for VIA at the local health unit where VIA positive women were provided cryotherapy at time of screening. Women in both arms were referred to colposcopy when indicated. Uptake rates were compared with Fisher's exact test.

Results: Uptake in HR-HPV arm was 99.2% (248/250), compared to 48.4% (121/250) in VIA arm ($p<0.01$). In HR-HPV arm 29.4% (73/248) tested positive for HR-HPV, 45.2% (33/73) of whom attended VIA for follow up. Of those, 7 screened positive and 5 received treatment. In the VIA arm, 13.2% (N=16/121) screened positive; 7 received cryotherapy, 3 refused treatment, 5 were referred to colposcopy, and 1 woman was suspected of cervical cancer and received treatment after confirmatory testing.

Conclusions: Self collection-based high risk HPV testing had a significantly higher uptake rate compared to VIA alone in a low resource setting. This suggests that self-collection based screening is both feasible and acceptable among women in this setting.

Funding Source: University of British Columbia, BC Centre for Disease Control Foundation, Women's Health Research Institute

N-394 - MIRNA As Markers Of CIN Risk And Persistence For Optimization Of HPV-Based Cervical Cancer Screening

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Cervical cancer (CC) is caused by oncogenic human papillomaviruses (HR-HPVs) infection and exhibits well-defined clinical stages associated with different steps of tumorigenesis. Screening for CC based on HPV is more effective than cytology, but it may increase costs and over treatment of spontaneously regressive high-grade lesions (hgCIN). Thus triage of HPV positive women is needed. Several microRNAs (miRNAs) are dysregulated in CC and hgCIN. However, the studies so far are based on miRNA candidate genes or array approach, mainly in tumor/healthy tissues.
The aim of this study is to investigate miRNA profiles by next-generation sequencing in exfoliated cervical cells of HPV-positive women in relation to the presence of hgCIN lesions or as predictors of persistence/progression of CIN lesions.
The study is nested in a large Italian multi-centre randomised controlled trial recruiting women in population-based screening programs that actively invite women aged 25-64 years. The study population includes HPV-positive women with CIN2 and CIN3 or without hgCIN lesion. For the discovery phase libraries of 100 samples of exfoliated cervical cells have been set up for miRNA sequencing. For the validation an additional set of 200 samples has already been selected.
Preliminary results shows that, after correction for multiple testing, 44 miRNAs resulted dysregulated in women with vs. those without prevalent hgCIN. This set includes some miRNAs previously reported in the literature, such as miR-100, and other additional miRNAs. The association of miRNAs with occurrence of hgCIN and clearance of infection during follow up is being investigated.
The high stability of miRNAs, in contrast to the fast degradation of mRNA and proteins, allows their accurate determination also in samples of exfoliated cervical collected during screening. Validation of the results, associations with other investigated markers and with HPV genotypes will be performed.

Study supported by Italian Association on Cancer Research (AIRC, IG2013 N.14119).

N-395 - Comparison Of hr-HPV Test, HPV16/18 Genotyping And p16/ki67 Immunocytochemistry Performance For Detecting High-Grade Lesions (CIN2 +) In Women Referred To Colposcopy In MedellÌn, Colombia

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Purpose:
High-risk HPV (hr-HPV) testing is more sensitive than cytology in detecting high-grade cervical intraepithelial neoplasia (CIN2+); however, it is less specific. HPV16/18 genotyping and p16/Ki-67 immunocytochemistry have shown promise in identifying women at higher risk of CIN2+ than hr-HPV test, so these have been proposed as strategies to triage HPV-positive women. We compared the performance between hr-HPV test, HPV16/18 genotyping and p16/ki67 for detecting CIN2+ in women referred to colposcopy in Medellin-Colombia.

Methods:
441 women referred to colposcopy because ≥ASCUS cytology and/or HPV+ were enrolled into the study. Prior to colposcopy, one cervical sample was obtained using a Cervex broom and placed in PreservCyt medium. An aliquot was used for p16/Ki-67 immunocytochemistry, and remaining sample was used for HPV testing and genotyping. The main outcome measures were sensitivity, specificity, positive (PPV) and negative predictive values (NPV).

Results:
All samples were adequate for HPV testing and p16/Ki-67 immunocytochemistry. For CIN2+(n=59) detection, hr-HPV test had 84% sensitivity (95%CI: 75-95), 48% specificity (95%CI: 43-51), 20% PPV (95%CI: 15-25) and 95% NPV (95%CI: 92-98). HPV genotyping had 58% sensitivity (95%CI: 44-71), 82% specificity (95%CI: 79-86), 33% PPV (95%CI: 24-43) and 93% NPV (95%CI: 90-95). p16/ki67 had 66% sensitivity (95%CI: 53-79), 77% specificity (95%CI: 72-81), 31% PPV (95%CI: 23-39) and 94% NPV (95%CI: 91-97). Among hr-HPV-positive women, the sensitivity increased to 68% (95%CI: 54-81) and 72% (95%CI: 58-85), and the PPV to 34% (95%CI: 24-43) and 37% (95%CI: 27-47) for HPV16/18 and p16/Ki-67, respectively.

Conclusions:
Although sensitivity is lower than hr-HPV test, p16/Ki67 and HPV16/18 had higher PPV and identified a lower number of positives among normal and CIN1 lesions. These results suggest that HPV16/18 and p16/Ki-67 had similar performance to triage hr-HPV positive women. Further work is needed to confirm these findings with a larger sample size.

Funding source:
CODI-Universidad de Antioquia; COLCIENCIAS.

N-396 - HPV Information Centre: A New ICO And IARC Joint Collaboration To Prevent And Control HPV-Related Diseases

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Purpose:
The HPV Information Centre, www.hpvcentre.net, is an initiative that was initially launched by the Catalan Institute of Oncology (ICO, Barcelona) in 2007 in collaboration with the World Health Organization.
In 2014, ICO and IARC signed a collaborative agreement to support ongoing maintenance and enhancement of the existing Centre that will be identified as the ICO/IARC Information Centre on HPV and Cancer.
Methods/Results:
The Centre will continue to routinely monitor, capture, process, analyse, and disseminate key data for the prevention of HPV-related cancers, worldwide and for countries and regions. Interactive web-based data queries and country-specific reports are routinely produced and made available to users.
The new centre will develop new contents and will redesign the website according to identified end-user needs. A Scientific Advisory Board has been created to periodically select and decide on the most relevant indicators to be updated and disseminated.
Conclusions:
The Centre's approach is novel because it combines detailed information on three elements: the risk factor (HPV), the diseases associated with the risk factor, and the strategies developed to prevent and control both the risk factor and its related diseases. The website usage, with an average of 1311 visits per month in 2014, exemplifies how this kind of knowledge resource is useful and in increasing demand. A challenge of the Centre is however to adapt to the fast-growing knowledge and changes that occur in the field of HPV epidemiology and prevention, including the description and impact of cervical cancer screening and HPV vaccination strategies.
Funding source:
PATH (USA); ISCIII, AGAUR(Spain)

N-397 - Interobserver Reproducibility Of Cervical Histologic Interpretations Among Pathologists Of Colombian Health System And An Expert Panel Of Pathologists: A Preliminary Report Of A Pragmatic Randomized Trial (ASCUS-COL Trial)

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-Purpose
Accurate cervical histopathology diagnosis is critical to cervical cancer prevention programs. Little is known about the reproducibility of cervical histological diagnosis in Latin America. Therefore, the reproducibility of diagnostic interpretation under routine clinical conditions of biopsies, loop electrosurgical excision procedures (LEEPs) and endocervical curettages (EECs) between pathologists and an expert panel was determined.

-Methods
396 colposcopic biopsy, 28 LEEP, and 93 ECC specimens from women enrolled in ASCUS-COL trial during 2011-2015 were recovered from pathology labs that served 3 major Health Medical Organizations of Medellin, Colombia. The specimens were independently reviewed by an expert panel of 2 well-trained observers pathologists. Reproducibility was measured using agreement percentage as well as unweighted and weighted Kappa values interpreted as Fleiss (1991).

-Results
Biopsy specimens had 56.3% (95%CI: 51.4-61.1) agreement and moderate weighted k (0.62; 95%CI: 0.55-0.69). LEEPs specimens had 46.4 (95%CI: 29.5-64.2) agreement and moderate weighted k (0.50 95%CI 0.33-0.67). ECCs had 90.5% (95%CI: 82.3-95.1) agreement and excellent weighted k (0.75; 95%CI, 0.51-0.98). Using the CIN2+ cut-off, biopsy specimens had 64.3% (95%CI: 58.5-68) agreement and moderate weighted k (0.62; 95%CI: 0.55-0.69). LEEPs specimens had 67.9 (95%CI: 49.3-81.1) agreement and poor weighted k (0.20 95%CI 0.0-0.41). ECCs had 91.7% (95%CI: 83.8-95.9) agreement and moderate weighted k (0.64; 95%CI, 0.36-0.93)
-Conclusions
Moderate reproducibility of biopsies and LEEPs specimens are within the ranges of previous studies. Major source of interpretative variability was the tendency of the expert panel to review pathologists CIN1 and negative biopsy interpretations as CIN2/CIN3 since Colombian Pathologists undercalled 30% of CIN2/3 biopsy specimens. Good reproducibility of ECC specimens may be due to over representation of negative diagnosis (93%) in the sample. These results need to be confirmed in a bigger sample size.

-Funding source.
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N-398 - Risk Factors For Interval Advanced Colorectal Neoplasia After Screening Colonoscopy: 10-Year Follow-Up Of A Prospective, Multi-Center Cohort In The United States

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Purpose: Colorectal cancer is the fourth leading cause of cancer-related deaths globally. Knowledge of risk factors could inform risk reduction and screening strategies. We report baseline risk factors for advanced colorectal neoplasia (AN) up to 10 years after baseline screening colonoscopy in asymptomatic participants.
Methods: Among a cohort of 1010 participants aged 50-75, we identified factors associated with interval AN during a 10-year follow-up period. From 1994-1997, 3121 participants underwent baseline screening colonoscopy at 13 Veterans Affairs Medical Centers; 1010 participants had a repeat colonoscopy 5.5-10 years after screening. AN included adenomas ≥1cm, villous histology, high-grade dysplasia, or carcinoma. Risk factors were self-reported at baseline. We performed multivariable logistic regression analysis of risk for 10-year incident AN, adjusting for age, body mass index, alcohol use, colorectal cancer in first-degree relatives, baseline screening and five-year colonoscopy findings, cardiovascular disease, and diabetes.
Results: Participant characteristics were described previously (Lieberman, NEJM 2000). At 10 years, 267 participants (26.4%) had small adenomas <1cm and 66 participants (6.5%) had AN. In univariate analyses, African American race, >50 pack-year smoking history, colon cancer history in ≥ 2 first degree relatives, AN on baseline screening colonoscopy, and small adenoma or AN on 5-year colonoscopy were associated with 10-year interval AN. In multivariable analyses, risk for 10-year interval AN was only associated with 5-year findings of a small adenoma (OR, 4.45; 95%CI, 1.94-10.23) or AN (OR, 4.04; 95%CI, 1.53-14.07), while baseline screening colonoscopy findings were not significant.
Conclusions: This study provides the longest follow-up of patients after screening colonoscopy. We conclude: 1) 5-year colonoscopy findings are more strongly associated with AN risk than baseline screening colonoscopy findings over time and 2) small adenoma and AN at last colonoscopy confer similar risk of interval AN up to 10 years after screening colonoscopy.
Funding sources: U.S. Department of Veterans Affairs

N-399 - A Personalized, Web-Based Decision Aid For Lung Cancer Screening

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PURPOSE
Informed decision making has been highlighted as an important aspect of lung cancer screening programs. This study seeks to assess the efficacy of a web-based patient decision aid for lung cancer screening, www.shouldiscreen.com.

METHODS
A before-and-after study (August through December 2014) was conducted where participants navigated a web-based decision aid that provided information about low-dose computed tomography lung cancer screening. Using an established prediction model, the decision aid computed baseline lung cancer risk and an individual's chances of benefiting from, and risk of being harmed by, screening. Outcome measures included knowledge of lung cancer risk factors and lung cancer screening, decisional conflict, concordance, and acceptability of the decision aid. Data were collected from 60 participants who were current or former smokers, had no history of lung cancer, and had not received a chest computed tomographic scan in the previous year. Analysis took place in 2015.

RESULTS
Knowledge increased after seeing the decision aid compared with before ($p<0.001$), whereas the score on the Decisional Conflict Scale decreased ($p<0.001$). Concordance between a participant's preference to screen and the U.S. Preventive Services Task Force recommendation improved after seeing the decision aid ($p<0.001$). Risk perceptions among the screen-ineligible group changed (n=49), contrary to those who were eligible (n=11). Ninety-seven percent of the participants reported that the decision aid was likely useful for lung cancer screening decision making.

CONCLUSIONS
The web-based decision aid should be a helpful resource for individuals considering lung cancer screening, as well as for practitioners and health systems with lung cancer screening programs.

FUNDING SOURCE
Elizabeth A Crary Fund of the University of Michigan Comprehensive Cancer Center

N-400 - Acceptability Of HPV Self-Sampling For Cervical Cancer Screening In An Indigenous Community In Guatemala

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Purpose: Rates of cervical cancer in Latin America are higher than those in developed countries, likely due to low prevalence of screening. Specifically, the screening rates are particularly low in indigenous communities in Guatemala. Current screening strategies, Pap smears and Visual Inspection With Acetic Acid (VIA), might not be the most effective methods for controlling cancer in these settings. So we investigated the potential of self-collection of vaginal specimens for human papillomavirus (HPV) testing for cervical cancer prevention.
Methods: A community representative random sample of 202 women aged 18-60 who resided in Santiago Atitlan, an indigenous community in Guatemala, were surveyed during July 2015 to assess knowledge of and risk factors for HPV. Women then collected a vaginal sample for HPV testing to assess infection prevalence and acceptability of self-sampling as an alternative screening method.
Results: Of 202 women who completed the survey, 178 (88%) provided a sample. After collection, 100% reported they were willing to perform this test periodically as a method of screening. 31 (17%) samples tested positive for at least one of 13 high-risk HPV types. 8 samples (4.5%) were positive for HPV 16/18.
Conclusions: Self-collection HPV testing was very well accepted in this community, suggesting it is a plausible alternative modality for cervical cancer screening. Further studies are needed to assess rates of follow-up screening after receiving a positive result on an HPV test and determine if these results extend to other indigenous and non-indigenous communities in Guatemala and Latin America.

N-401 - Opportunity In Diagnosis Of Breast Cancer In Colombian Women

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Objective: To describe the time between different stages for diagnosis of breast cancer in women attending in health care services. Methods: Descriptive, longitudinal and retrospective study. The information was reported to High Cost Diseases Fund in 2015. Women with diagnosis of malignant breast tumor considering the International Classification of Diseases -ICD-10 (C500, C501, C502, C503, C504, C505, C506, C508, C509), aged between 18 and 80 years and women were in treatment (radiation therapy, systemic therapy, surgery or a combination of these) in time data recollection were included. 3 opportunities were measured by determining the time between 1) the first symptoms and admission to the health care institution for making the diagnosis, 2) time from the histopathology and the result of the histopathological study and 3) result of the histopathological report and consultation with the attending physician of the disease. Opportunities with some demographic and clinical variables (age at diagnosis, stage) through statistical analysis were related. Results: 13.691 women diagnosed with breast cancer were included. The average time for first opportunity was 95.9 days (3.2 months), for the second time opportunity was 27.5 days and for the third 76 days (2.6 months). In women aged 18 to 34 years at diagnosis, the time between the first symptoms and admission to health care institution for diagnosis was lower than women over 65 years. Conclusions: In Colombia, women with breast cancer have a diagnostic process with multiple stages due to operation of the health care system, the implementation of actions for the reduction in the time between each of these, are stages is essential to ensure the timely access, quality of care and a better prognosis. Funding: No funding.

O-403 - Indicators Of Long-Term Survival And Cure Of Cancer

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PURPOSE
To provide estimates of indicators of long-term survival and cure for 50 cancer types, presently lacking.

METHODS
Data from 1.6 million Italian cancer patients, diagnosed until 2010 (AIRTUM), were included. Validated statistical models were used to estimate four population-based original indicators of cancer cure, by sex, age, and period:
1.Cure fraction: Proportion of patients expected to reach the same death rates of the general population;
2.Time to cure: Years after cancer diagnosis necessary to eliminate the excess mortality of patients vs the general population. This occurs when 5-year conditional relative survival (CRS, probability of surviving an additional 5 years) becomes>95%;
3. Already cured patients: Proportion of patients who have survived longer than Time to cure;
4. Cure prevalence: Proportion of all prevalent cases who will not die of that cancer.

RESULTS
The cure fractions ranged from>90% for patients aged<60 years with thyroid and testis cancers to <10% for those with liver and pancreatic cancers. For several cancers they increased >10% from the 1980s to 2000s. Five-year CRS>95% was reached in <10 years by patients with cancers of the stomach, colon–rectum, pancreas, corpus and cervix uteri, and Hodgkin lymphoma. Mortality rates similar to the ones reported by the general population were reached after approximately 20 years for breast and prostate cancer patients. Five-year CRS remained <95% for >25 years after cancer diagnosis in patients with liver and larynx cancers, non-Hodgkin lymphoma, myeloma, and leukaemia. Time to cure was reached by 27% (20% in men and 33% in women) of all people living after a cancer diagnosis, defined as already cured. Therefore, the cure prevalence was 67% in men and 77% in women.

CONCLUSIONS
The availability of these indicators has a high potential impact on health planning, clinical practice, and patients' perspective.

FUNDING SOURCE
Italian Association for Cancer Research (AIRC)

O-404 - Population-Based Factors Associated With Death After Liver Resection For Hepatocellular Carcinoma In Queensland, Australia

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Purpose: Accurately identifying patients with poorest prognosis from hepatocellular carcinoma (HCC) may prevent futile, quality-of-life impairing surgery. Little is known of the social determinants of poor survival after liver resection for HCC. Using a population-based-linked cohort of HCC patients we examined factors associated with early death after resection.
Methods: Cancer registry (1584 HCC cases), hospital admission and viral hepatitis notification data were used.
Results: Bivariate analysis showed that the proportion of patients dying within 12 months of diagnosis reduced over time (66% (1996-2000), 61% (2001-2005), 53% (2006-2011), P<0.001). Poorer HCC survival was seen with more social disadvantage (P<0.001) and living more remotely (P<0.001). Patients with hepatitis B and C infection had better survival than non-infected patients (P<0.001). While there was no significant evidence that Indigenous people had poorer HCC survival than non-Indigenous Australians (p=0.225), they had poorer overall survival (all deaths) (p=0.012). The 236 patients who underwent liver resection had better survival than those who did not (median HCC survival 1537 vs 173 days; P<0.001). 50/236 (21%) patients who had resection died within 12 months of diagnosis (42 HCC deaths/8 non-cancer deaths). On multivariate analysis, poorer HCC survival after resection was associated with social disadvantage (HR=2.5 95%CI 1.15-5.53 most disadvantage vs most affluent), earlier diagnosis period (2001-2005 vs 2006-2011, HR=1.6 95%CI 1.02-2.61), and male sex (HR=2.0 95%CI 1.12-3.44). Remoteness, hepatitis B diagnosis, Indigenous status and age were not associated with HCC-specific or overall survival.
Conclusions: Social determinants are important in early HCC death. Early HCC death (<12 months) after HCC diagnosis and survival after resection have improved over time. Reduced early HCC death-rates may reflect improved screening. With better recognition and assessment of underlying liver disease in patients with HCC, better patient selection, operative techniques and post-operative care may underlie improved post-resection survival.
Funding: NHMRC Fellowships (1083090/1052622/105534/1058522).

O-405 - Population-Based Long-Term Cause-Specific Mortality Among 34,489 5-Year Survivors Of Childhood Cancer In Great Britain

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Purpose
The recent extension of the British Childhood Cancer Survivor Study (BCCSS) to include 5-year survivors of childhood cancer diagnosed from 1992 to 2006 provides an opportunity to investigate risk of death in relation to treatment era and mortality beyond 50 years of age.

Methods
The BCCSS, a nation-wide population-based cohort of 34,489 5-year survivors of childhood cancer diagnosed from 1940 to 2006 in Great Britain, is the largest cohort to assess late mortality.

Results
Overall, 4475 deaths were observed, which was 9-times that expected and corresponded to 64 excess deaths per 10,000 person-years. The number of excess deaths from all-causes declined among those treated more recently; those treated 1990-2006 experienced 30% of the excess number of deaths experienced by those treated before 1970. The corresponding percentages for the decline in excess deaths from recurrence/progression and non-neoplastic causes were 30% and 60%, respectively. Among survivors aged 50-59 years, 41% and 22% of excess deaths were attributable to subsequent primary neoplasms (SPNs) and circulatory conditions, respectively, whilst the corresponding percentages among those aged 60+ years were 31% and 37%, respectively.

Conclusions
The net effects of changes in cancer treatments, and surveillance and management for late effects, over the period 1940 to 2006 is to reduce the excess number of deaths from both recurrence/progression and non-neoplastic causes among those treated more recently. For the first time we provide evidence that among survivors aged 60+ years the excess number of circulatory deaths exceeds the excess number of SPN deaths; this is unsurprising because in the general population aged 60+ years circulatory conditions account for substantially more deaths than neoplasms. The critically important message here for the evidence-based surveillance aimed at preventing excess mortality and morbidity in survivors aged 60+ years is that circulatory disease overtakes SPNs as the leading cause of excess mortality.

O-406 - Estimation Of Cure Rate In Iranian Breast Cancer Patients

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Purpose: Although the Cox's proportional hazard model is the popular survival analysis to investigate the significant risk factors of cancer patient's survival, this model would not appropriate in the case of log-term disease free survival. Recently, cure rate models, introduced to distinguish between clinical determinants of cure and variables associated with the time to event of interest. The aim of this study was to use these cure rate model to determine the clinical associated factors on cure rate of patients with breast cancer (BC).
Methods: This is a prospective cohort study on 305 patients with breast cancer, admitted at Shahid Faiazbakhsh Hospital, Tehran, during 2006 to 2008 and followed until April 2012. The case of patients' death was confirmed by telephone contact. For data analysis, non-mixed cure rate model with Poisson distribution and Negative Binomial distribution were employed. All analysis carried out using a developed Macro in WinBugs. The DIC criteria employed to find the best model.
Results: The overall 1-year, 3-year and 5-year relative survival rate was found as 97%, 89% and 74%. Metastasis and stage of BC were the significant factors, but age was significant only in Negative Binomial model. The DIC criteria showed that the Negative Binomial model had a better fit.
Conclusion: This study indicated that, metastasis and stage of BC were identified as the clinical criteria of cure rate. There are limited studies on BC survival, which employed these cure rate models to identify the clinical factors associated with cure. These models are better than Cox, in the case of long-term survival, even thought there are no cured patients.

O-407 - Evaluation Of Parametric Models By The Prediction Error In Colorectal Cancer Survival Analysis

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Purpose: Survival models are statistical technique to estimate or predict the overall time up to specific events. Prediction is important in medical science and the accuracy of prediction is determined by a measurement, generally based on loss functions, called prediction error. The aim of this study is using parametric models to determine the factors influencing predicted survival time for patients with colorectal cancer (CRC) and select the best model by predicting error's technique.
Methods: 600 colorectal cancer patients whom admitted to the Cancer Registry Center of Gastroenterology and Liver Disease Research Center, Taleghani Hospital, Tehran, who were followed at least for 5 years and have completed information selected for this study. Body Mass Index (BMI), Sex, family history of CRC, tumor site, stage of disease and histology of tumor included in the analysis. The survival time was compared by the Log-rank test and multivariate analysis was carried out using parametric models including Log normal, Weibull and Log logistic regression. For selecting the best model, the prediction error by apparent loss was used.
Result: Log rank test showed better survival for females, BMI more than 25, patients with early stage at diagnosis and patients with colon tumor site. Prediction error by apparent loss was estimated indicated that Weibull model was the best one for multivariate analysis. BMI and Stage were independent prognostic factors according to Weibull model.
Conclusion: In this study, Weibull regression showed a better fit according to prediction error. Prediction error would be a criterion to select the best model with ability to make prediction of prognostic factors in survival analysis.

O-408 - Relative Survival Of Prostate Cancer Patients In The Canton Of Zurich, Switzerland ñ A Population Based Study

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Purpose: Prostate cancer is the most frequent incident cancer in men in Switzerland. The purpose of this study was to estimate relative survival (RS) of prostate cancer patients who lived in the Canton of Zurich focusing on treatment choices, grade and age of the patients.

Methods: Population based data from the Cancer Registry Zurich and Zug were used. Relative survival of 1512 prostate cancer patients diagnosed in 2000 and 2001 were estimated according to the Ederer II approach using life tables for Switzerland.

Results: Compared to other treatments (radiotherapy, hormonal therapy, active surveillance, no treatment), surgical procedures were more prevalent in patients aged <70 years (65%) than in patients aged ≥70 years (39%, p<0.001). 61% of patients with low grade, 55% with intermediate grade and 49% with high grade underwent surgical procedures compared to other treatments. Overall, 1-, 5- and 10-year RS were 96%, 94% and 93%, respectively. 1- and 10-year RS of patients aged <80 years was close to 100%, for patients aged ≥80 years RS decreased (1 year: 79%, 10 years: 54%). Patients with low grade had an RS of 100% after 1 year, and above 100% after 5 and 10 years. A decreasing RS was observed in patients with high grade (1 year: 94%, 10 years: 63%). For patients who underwent surgical procedures, RS was approximately 100%, RS of patients undergoing other treatments decreased over time (1 year: 91%, 10 years: 79%).

Conclusions: Our results confirm findings from previous studies, stating that prostate cancer patients have a good RS if cancer is diagnosed at an early stage. We observed a trend in age- and grade-related treatment choices as recommended in official guidelines. RS above 100% could indicate a selection bias regarding the PSA screening, which tends to be more often used by men with a health-conscious behavior.

O-409 - Inequalities In Colorectal Cancer Risk And Prognosis In Victoria, Australia

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Purpose: Assess inequalities in colorectal cancer (CRC) incidence and outcomes by sex, socio-economic status (SES) and geographic remoteness using population-based registry data.

Methods: Incident cases diagnosed between 2004 and 2013 were identified through the Victorian Cancer Registry and linked to the state death registry up to 31st December 2014. SES and remoteness were determined from the population census. Associations with incidence were assessed by multivariable Poisson regression. Associations with survival were assessed by multivariable Cox regression.

Results: Overall 35,638 incident cases of CRC were ascertained, 15,540 of whom died during median follow-up of 3.2 years (interquartile range: 1.4-6.0). Average CRC incidence per 100,000 was higher in men (45 versus 31), in persons with lower SES (41 for lowest quintile [Q1] versus 34 for Q5) and in those living outside major cities (41 versus 36). The association with SES was stronger for men. The association with remoteness was not apparent for people with higher SES. Male cases, and cases with higher SES, were more likely to be diagnosed with early stage disease.
Men with CRC had worse prognosis (HR for all-cause death, 1.22 [95%CI, 1.16-1.27]) as did cases with lower SES (HR for Q1 versus Q5, 1.44 [1.33-1.55]); the latter appeared to attenuate with increasing time since diagnosis (p=0.035). A survival disadvantage for non-metropolitan cases observed in univariable analysis was largely accounted for by SES. These associations were independent of disease stage and grade, age at diagnosis and calendar year.

Conclusions: Sex, geographical remoteness and SES interact as determinants of CRC risk in Victoria. Sex and socio-economic inequalities are also apparent in outcomes for people who develop CRC, which appear to be unrelated to disease stage and grade at diagnosis. Further work is required to understand and address these disparities.

Funding sources: Cancer Council Victoria, Victorian State Government

O-410 - The Scottish Audit Of Head And Neck Cancer (SAHNC): Determinants Of 12-Year Survival Of Head And Neck Cancer Patients In Scotland

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Purpose
Factors affecting the survival outcomes of head and neck cancer patients beyond five years are unclear. The SAHNC cohort provides the opportunity to complete a comprehensive analysis to determine which patient, tumour, and treatment factors are independently associated with the 12-year survival outcome of head and neck cancer patients.

Methods
The SAHNC national cohort data was collected between September 1999 and August 2001, and in September 2014 the cohort was linked to 12-year mortality records (n = 1895). We assessed the independent influence of several variables collected at diagnosis on patient (age, sex, socioeconomic status, smoking behaviour, alcohol consumption, and WHO performance status), tumour (anatomical site and stage), and treatment (modality and location/region of Scotland) factors associated with 12-year survival outcomes.

Results
12-year overall survival was 25.5% (95% CI 23.5% - 27.5%). The factors independently associated with the long-term overall survival outcomes of head and neck cancer patients were age at diagnosis ($p<0.001$), stage ($p<0.001$), treatment ($p<0.001$), WHO performance status ($p<0.001$), alcohol consumption ($p<0.001$), smoking behaviour ($p<0.001$), and anatomical site ($p<0.001$).

Conclusion
In conclusion, 25% of patients were alive 12-years after their diagnosis. The key determinants associated with long-term survival included age, stage, treatment modality, WHO performance status, alcohol consumption, smoking behaviour, and anatomical site. These patient, tumour, and treatment factors should be considered by clinicians when informing patients of the long-term prognosis associated with head and neck cancer.

Funding source
NHS National Services Scotland (NSS) PhD Studentship
British Association of Head and Neck Oncologist (BAHNO) data linkage grant

O-411 - Restrictions In Activities And Societal Participation Of Long-Term Colorectal Cancer Survivors In The Encore Study

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Purpose
Persisting health and functioning problems in colorectal cancer (CRC) survivors due to the cancer and its treatment can influence societal participation, and thereby their role functioning. Insight into the number and nature of restrictions is needed as input for targeted intervention strategies. As part of the Energy for life after ColoRectal cancer (EnCoRe) study, we aimed to evaluate current satisfaction with societal participation and associations with HRQoL, and to explore the nature and perceived impact of activity limitations and participation restrictions of CRC survivors.

Methods
A mixed method approach was applied in the cross-sectional EnCoRe study in 151 stage I-III stage CRC-survivors 2-10y post-diagnosis. Self-reported satisfaction with societal participation and role functioning were assessed by questionnaire. Associations of self-reported satisfaction with societal participation (current satisfaction with paid job, non-paid job, household activities, and hobbies), with role functioning subscales (RAND36-Health Survey, physical and emotional role functioning) were analysed by multivariable logistic regression models. The impact of activity limitations and participation restrictions was explored by semi-structured face-to-face interviews in a sub-sample of 10 CRC survivors from the EnCoRe study, who had reported participation restrictions.

Results
Dissatisfaction with societal participation was reported by 19% of CRC survivors. Better self-reported physical functioning was significantly associated with lower likelihood of reported dissatisfaction with participation (OR: 0.4, 95%CI: 0.2-0.5). Reported activity limitations were in the areas of undertaking tasks, mobility, self-care, and domestic life. Participation was restricted in the areas of interpersonal relationships, work and employment, and social and civic life. Restrictions were mainly related to neuropathy, pain, lack of muscle strength, fatigue, digestion and defecation.

Conclusions
CRC survivors partly reported dissatisfaction with societal participation. The observed association of participation with physical functioning and the reported activity limitations and participation restrictions offer possible targets for intervention.

Funding sources
Dutch Cancer Society and Kankeronderzoekfonds Limburg

O-412 - Better Lung Cancer Stage Distribution In More Deprived Areas Of Wales Offset By Much Worse Stage 1 And 2 One Year Survival

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BACKGROUND
Lung cancer is a priority in Wales because of poor outcomes. We examined stage at diagnosis and one-year relative survival by stage. We considered the effect of several demographic factors.

METHODS
We identified residents of Wales diagnosed with lung cancer in 2010-2012 from our cancer registry. We described the distribution of cases by stage, sex, age, area deprivation and health board. We calculated one year survival by stage and the same factors.

RESULTS
Over two-thirds of 2,373 lung cancer patients were at stages 3 or 4 compared to a fifth at stages 1 or 2. Others had unknown stage. Men were slightly more likely to have a later stage. Stages 1 and 2 accounted for a slightly higher proportion as age increased. Stage distribution was slightly more favourable as area deprivation increased (early stage 16% in least deprived, 19% most deprived). Stage distribution varied by health board (early stage 14% in worst, 21% in best). Nearly a third of patients survived at least one year. Survival by stage varied considerably (stage 1 78%, stage 4 14%). Almost a third of women and a quarter of men survived at least one year. Survival decreased with age. Deprivation had little effect on all-stage one-year survival, but one-year stage 1 survival was 91% in least deprived areas, 74% in the most.Stage 2 had large variation in survival by deprivation, but later stages varied little.

CONCLUSIONS
Although most people are diagnosed at late stages, a large minority have potentially treatable early stage lung cancer in Wales.Despite slightly more favourable stage distribution in more deprived areas, survival is considerably higher in less deprived areas for stages 1 and 2.Many factors such as health seeking behaviour, referral practice, access to diagnostics and treatment, as well as comorbidity may contribute. This needs further exploration and action.

O-413 - 20-Year Cancer Prevalence In The UK By Cancer Type: Exploring Variations Between Short-Term And Long-Term Survivors In The Cancer Population

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Purpose
An estimated 2.5 million people are living with cancer in the UK, predicted to increase to four million by 2030. The Macmillan-NCIN Cancer Prevalence project aims to provide the most granular understanding of the cancer population in the UK.
Patient needs and experiences vary over time from those recently diagnosed likely to be in active treatment, to long-term survivors who may still require health or social care and support.

Methods
We used the National Cancer Data Repository (UK cancer registrations linked to mortality records) to identify people diagnosed with cancer between 1991 and 2010, and still alive on 31st December 2010.
We analysed the data to show variations in time since diagnosis distributions across: cancer type, age at diagnosis, gender, deprivation and geography. Counts are based on the first diagnosis of a specific cancer within the 20 year period; a person is counted more than once if diagnosed with more than one cancer type within the period, but just once if diagnosed again with the same cancer type.

Results
There were 1.8 million people living with cancer in the UK diagnosed between 1991 and 2010.
Breast cancer was the most prevalent cancer, and 32% of women with breast cancer were long-term survivors (still alive 10-20 years after diagnosis). Cervix cancer had the highest proportion (46%) of long-term survivors. Almost half of those diagnosed with pancreatic cancer had been diagnosed within the previous year, and had the lowest proportion of long-term survivors (10%).

Conclusions
Our analysis provides a more granular understanding of the UK cancer population. Segmenting the cancer population in this way can help better planning and tailoring of health and social care, but further information on the health and experiences of long term survivors is still needed.

O-414 - A New Way Of Counting Cancer Prevalence To Understand The Prevalence Of Multiple Primaries In The UK

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Purpose
An estimated 2.5 million people are living with cancer in the UK, predicted to increase to four million by 2030. The Macmillan-NCIN Cancer Prevalence project aims to provide the most granular understanding of the cancer population in the UK.
Previous cancer prevalence analyses have largely been based on a person count and a 'first diagnosis-only' method, but second/subsequent cancer diagnoses present new treatment and support needs. We aim to capture the prevalence of people diagnosed with more than one type of primary within a specified 20-year period.

Methods
We used the National Cancer Data Repository (UK cancer registrations linked to mortality records) to identify people diagnosed with cancer between 1991 and 2010 and still alive on 31st December 2010.
We calculated prevalence based on the first diagnosis of a specific cancer type and then identified whether they then had a second/subsequent diagnosis of a different type of cancer within the 20-year period.

Results
The most prevalent cancers (breast, colorectal and prostate) accounted for the largest absolute number of people who had a second/subsequent diagnosis of another cancer type. Lung cancer was the ninth most prevalent, but had the highest proportion of second/subsequent diagnoses. One in 13 people diagnosed with lung cancer had received a previous cancer diagnosis of a different type, compared to 1 in 46 females with breast cancer.
We will explore variations within and between UK nations and cancer types.

Conclusions
Initial analysis suggests that cancers with poorer prognosis potentially have higher proportions of people who have had a previous diagnosis and warrants further exploration. This analysis allowed us to quantify and capture the different groups which are more likely to experience more than one cancer diagnosis, helping us better understand need to inform health and social care provision.

O-415 - Mortality Among Children And Young People Who Survive Cancer In Northern Ireland

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Introduction
While survival rates for childhood cancers are excellent it is known that these patients have an increased risk of death from disease recurrence and other causes. We investigate patterns and trends and survival of cancers in children and young adults in N. Ireland.

Methods
20 years (1993, 2013) of cancer incident data including non malignant brain tumours from the N. Ireland Cancer Registry for persons age 0-24 years was analysed using joinpoint for trend and Kaplan Meier method for survival analysis examining with excess mortality calculated at one and five years after first cancer diagnosis using standardised mortality ratios.

Results
2633 children and young people were diagnosed with cancer, 1386 (52%) male and 1247 female with 1140 (43.3%) aged 0-14. 59 patients 2.2% had a record of a second cancer. While trends were increased over time they did not reach statistical significance except in the 15-24 group for all persons combined. The most common cancers for age 0-14 were brain, eye and CNS and leukaemia with skin the most common in 15-24 age group. Survival was high 90.7% at 1 year, better among females and similar for older and younger groups. Excluding the primary cancer there was an excess mortality of from all causes with non cancer deaths twice that of the background level, however a significant contribution to deaths was congenital malformations.

Conclusion
While survival from childhood cancers is excellent this work in common with larger studies highlights the need for ongoing monitoring of cancer survivors. Preventable skin cancer was identified as a problem.

O-416 - Nutrition, Physical Activity And Cancer: Influence Of Social Determinants Across The Lifecourse In Women From The 1958 British Birth Cohort Study

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Purpose: The etiological role of diet and physical activity in the development of cancer is now well established. Socioeconomic factors could influence nutritional behavior and then, the occurrence of cancer. The objective of the present study was to examine the influence of social determinants across the lifecourse in the relationship between nutrition patterns and cancer occurrence in women.
Methods: Data collected from the National Child Development Study (NCDS), a prospective British birth cohort. Thirty-seven items regarding diet, alcohol and physical activity were registered as frequencies at ages of 33 and 42 years. Nutrition patterns were obtained by principal component analysis. Cancer odds ratios (OR) were estimated by logistic regression for the highest versus the lowest tertile of nutrition pattern score. Social determinants from birth to adulthood were introduced in logistic models using a lifecourse approach.
Results: 6169 women were included and 237 women reported cancer diagnosis at 46, 50 or 55 years old. Four nutrition patterns were identified: “Healthy active”, “Drinker”, “Sweet tooth” and “Western”. An association between the “Drinker” pattern and cancer was found (lifestyle-adjusted OR of tertile 3 vs 1: 1.65; 95%CI: 1.17-2.33; P trend=0.017). This association persisted but was slightly attenuated, statistically, after adjustment for social determinants (OR=1.54; 95%CI: 1.08-2.18; P trend=0.054). Having parents from manual social class at birth (P=0.014) or a low educational level at 23 years old (P=0.003) was related to a decreased cancer risk.
Conclusions: An increased risk of mid-life cancer was found in British women adhering to an alcohol-related pattern and social determinants over the lifecourse explained a moderate part of this association. Socioeconomic conditions are related to cancer incidence and should be taken into consideration in cancer research and prevention policies.
Funding: Project grant (#12-D-019) from the French Food and Health Fund [Fonds Français pour l’Alimentation et la Santé]

O-417 - To Compare Survival Models And Their Application In Breast Cancer Patients

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Currently, cancer is one of the most important of problems in worldwide. Due to increasing of incidence in types of cancer, it is important to deal with them. Breast cancer is the most common cancer of women in worldwide. The cancer is the major cause of cancer deaths in women, so that more than one million new cases of cancer are diagnosed in women and 3/37% of cases lead to death in 2000. Asian women's risk of breast cancer of women in North America or Western Europe is 0.1 to 0.2. Breast cancer is not common under the age of 25; however, its incidence is rapidly increased to 50 years. To model the censored survival data is usually done with Cox regression in clinical research. One of the most widely used Cox proportional hazard model analysis of survival data. The Cox proportional hazards model is one of the most common methods to analyze of survival data. In short follow-up studies the assumption of a constant ratio is very reasonable. It means that an important assumption in this model is proportional of risk over time. However, it may not be very appropriate assumption in long-term follow-up studies and the time somehow influences the risk ratios. When the proportional hazards assumption is violated then Cox model is not reliable and other models should be considered such as extended Cox model with time-dependent variables, the frailty and cure models. We use a data set 1148 women having BC referred to Shiraz Namazi Hospital, south of Iran. The main object of this study was to evaluate and compare different models on the breast cancer survival in southern Iran and to find the key factors in the disease. The researchers used R-3.1.2 software to carry out statistical analyses.

O-418 - Serological Response To Human Papillomavirus (HPV) Type 16 E6 And E7 And Survival In Oropharyngeal And Non-Oropharyngeal Cancer Patients, São Paulo, Brazil, 1998-2008

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Purpose: To evaluate overall survival in patients with head and neck squamous cell carcinoma (HNSCC) according to serological response to human papillomavirus (HPV) type 16.
Methods: Patients with HNSCC from five hospitals in São Paulo diagnosed between 1998 and 2008 and followed-up until June of 2009 were included in this study. Multiplex Luminex was used in order to determine serological response to HPV16 E6 and E7. Frequencies and percent were calculated for all variables and chi-square or Fisher's exact test were performed for evaluate association between demographic and clinical variables and HPV16 E6 and E7. Kaplan-Meier method for overall survival was performed and log-rank test was used for compare survival curves from serological response to HPV16. Descriptive level (p-value) <0.05 was considered as statistically significant.
Results: Serological response to HPV16 E6 was 3% in non-oropharyngeal cancer and 10.6% for oropharyngeal cancer. On the other hand, 21.2% was positive to HPV16 E7 in oropharynx compare to 13.7% in non-oropharynx cancer. Differences between survival curves for interaction between anatomical site and serological response to E6 were statistically significant (p=0.0197). No statistically differences were observed for serological response to HPV16 E7 (p=0.1125). However, patients with serological response negative to E6 showed worst survival.
Conclusion: Serological response to HPV16 E6 could be a biomarker for better prognostic in patients with oropharyngeal cancer. The epidemiological profile of Brazilian patients is related with risk factors classic (tobacco and alcohol consumption) and not showed a high prevalence of serological response to HPV16 as other studies had been showed in Europe and USA.
Funding source: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (grant nos.: 10/50733-6; 09/52031-1 and 04/12054-9).

O-419 - Trends In Survival From Ovarian Cancer In Six European Latin Countries: Results From The SUDCAN Population-Based Study

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Purpose: The SUDCAN study is an initiative of the GRELL in collaboration with EUROCARE. Suboptimal survival results on ovarian cancer (European 5-year net survival 37.6%) make necessary major efforts to detect differences in survival trends and improve prognosis. We studied the trends in 1 and 5-years net survival from ovarian cancer over the 1992-2004 period in six participating European Latin countries.

Methods: The data were extracted from EUROCARE-5 database (end of follow-up: 01/01/2009). The results are reported from 1992 to 2004 in France, Italy, Spain, and Switzerland and from 2000 to 2004 in Belgium and Portugal. Analyses included 33,178 cases from 28 registries. Exclusions (mainly DCO) ranged from 0% to 3.4% depending on the country. Trend analyses were performed using an original flexible excess rate modelling strategy applied for each country. A model was selected among 19 that differed in the modelling of the effect of the year of diagnosis in terms of linearity, proportionality and change with age, based on the Akaike Information Criterion.

Results: In 2004, the 5-year age-standardized net survival (ASNS) was about 38% in Spain, Switzerland and Italy and about 42% in France, Portugal, and Belgium. Between 1992 and 2004, 1 and 5-year ASNS improved substantially in all countries; the absolute increases ranged from 7% to 12% and from 5% to 8%, respectively. In Belgium and Portugal, the 5-year ASNS increased too between 2000 and 2004. Differences in 1-year ASNS between countries were maintained along the study-period whereas differences in 5-year ASNS widened, especially in the most recent years, due to lower increases in Switzerland and Spain.

Conclusions: Improvements in survival from ovarian cancer were seen across Latin European countries but some differences between countries remain. These results underline the necessity of studying the variability in ovarian cancer care.

Funding source: French Ligue contre le Cancer.

O-420 - Monitoring Oral, Oropharyngeal And Larynx Cancer Survival In A Tertiary Cancer Center ñ ACCamargo Cancer Center (ACCC) São Paulo, Brazil

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Introduction: Analyse survival rates from specialized cancer centers is an important activity to measures treatment outcomes, in cancer patients. Oral, Oropharyngeal and larynx cancer are a malignancies in which a multidisciplinary therapeutic approach is mandatory. Although there was improvement for cancer care survival rates remain almost unchanged for these malignancies.
Purpose: To describe survival rates in two periods from 2000 to 2010 at ACCCC/Brazil, and to verify mortality trends in the city of Sao Paulo 1998 to 2012.
Methods: Data was stratified in two periods 2000-2004 and 2005-2010 .Variables analysed were gender, age, clinical stage, treatment specific and overall survival. Mortality data was abstracted from datasus.
Results: Oral Tongue was the most common site (42%) followed by Floor of mouth (18%). Stage I and II proportion increased from 26%, 2000 to 2004 to 37% in the period 2005 to 2010 ($p<0.001$). Five years cancer specific survival rates was 61% in 2000 to 2004 and 59% 2005-2010 (p 0.659).
Oropharynx Tonsil was the most common site (34%) followed by base of tongue (30%). Early stage (I e II) decrease 1% from 11%, 2000 to 2004; to 10% from 2005 to 2010. Five years cancer specific survival was 52% 2000 to 2004 and 66% (p 0,004) 2005-2010.
Larynx Glotis was the most common site (53%) followed by supraglotis (20%). Early stage proportion (I and II) increased from 39% (2000 - 2004) to 41% in 2005 to 2010. Cancer specific survival at 5 years was 73% 2000 to 2004 and 75% 2005-2010 (p 0,523).
Mortality trends remained almost unchanged in the population of Sao Paulo.
Conclusion: Survival of oral and larynx, remain unchanged, while for oropharyngealincreased; mortality rates remains stable in Sao Paulo.

O-421 - Socioeconomic Status And Head And Neck Cancer Survival In A National Cohort, Scotland (1999 ñ 2013)

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Background: Socioeconomic status (SES) is associated with risk and prognosis of head and neck cancer (HNC). The association of SES with the survival of head and neck cancer patients are rarely considered beyond five years. We aim to investigate the influence of socioeconomic status on overall survival at 5- and 12-years in Scotland – where there is universal healthcare provision.

Methods: The Scottish Audit of Head and Neck Cancer (SAHNC) is a national clinical cohort which recruited incident cases and baseline data between 1999 and 2001 (n=1895 participants; 77% case ascertainment of Scottish Cancer Registry). We assessed the association of SES (via Carsairs2001 area-based socioeconomic deprivation index) on 5- and 12-year survival outcomes, while also considering the influence of baseline covariates including patient (age at diagnosis, sex, smoking behaviour, alcohol consumption, WHO performance status), tumour (anatomical site and stage), and treatment (modality and geographic location of cancer centre) factors. Survival was measured using the Kaplan-Meier method, and the independent association of SES was determined from a multivariate Cox regression model.

Results: Overall survival at 5- and 12-year was 45.0% and 25.5% respectively. The 5-year survival inequality for the highest SES (47.6%; 95%CI 41.3%, 53.6%) and lowest SES (38.8%; 95%CI 32.4%, 45.2%) was greater (p=0.006) than at 12-years where the highest SES (26.0%; 95%CI 20.7%, 31.6%) and lowest SES (22.4%; 95%CI 17.1%, 28.1%) were converging (p=0.048). There was no independent association of SES after adjusting for other patient, tumour and treatment factors.

Conclusions: SES was associated with 5-year overall survival for HNC, but it had substantially reduced by 12-years, and the effect was lost after adjusting for age at diagnosis, sex, smoking/alcohol, WHO performance status, tumour site/stage, and treatment modality/location.

Funding: NHS National Services Scotland (NSS) PhD Studentship; and British Association of Head and Neck Oncologist (BAHNO) data linkage grant.

O-422 - Understanding Geographic Variation In Mortality Within 30 Days Of A Cancer Diagnosis In England, 2008-2013

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Purpose: Hazard of death tends to be high in the first 30 days after cancer diagnosis, which has a strong long-term influence on metrics such as net survival from cancer. Geographic variation in 30-day mortality following cancer diagnosis observed in England may be partly explained by organisational differences between the 211 Clinical Commissioning Groups (CCGs) which are responsible for local cancer management. This project aims to inform policies which could reduce inequalities by measuring and explaining geographic variation in 30-day mortality in England in 2008-2013, whilst taking account of the role of patient and CCG characteristics.

Methods: Socio-demographic and clinical information (deprivation, stage at diagnosis, and co-morbidities) on patients with lung, ovarian and colorectal cancer was retrieved from population-based sources. Multiple imputation was performed to complete stage information. CCG characteristics including number and specialisation of clinicians, facilities available, and spend on cancer services were retrieved from official sources. Random intercept logistic regression models were fitted to quantify between-CCG variation in 30-day mortality. The changes in the random intercept variance, as covariates were added to the model, were used to measure the proportion of geographic variance each patient or CCG factor could explain.

Results: The study included 99,942 patients diagnosed with colorectal cancer (2010-2012), 203,215 with lung cancer (2008-2013), and 14,641 with ovarian cancer (2011-2013). Adjusted 30-day mortality for the CCGs and avoidable deaths due to different factors are presented, alongside geographic maps showing variation and graphics displaying how much variation different factors account for.

Conclusions: Health system factors are partly responsible for geographic variation in 30-day mortality, and policy changes to remedy these could improve outcomes and reduce inequalities.

Funding source: Cancer Research UK

O-423 - Efficacy Of An Adapted Physical Activity And Diet Counseling Intervention In Women Treated For Breast Cancer: Results Of The Long-Term ìAPAD1î Randomized Controlled Trial

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Purpose: The adoption of healthy diet and regular physical activity has been advanced as non-pharmacological interventions to relieve cancer therapy-related side effects and improve cancer prognosis. A clinical trial carried out at the Cancer Institute of Montpellier (France) has investigated the effect of an Adapted Physical Activity and Diet counseling (APAD) intervention on fatigue, physical, anthropometric and quality-of-life (QoL) outcomes in women undergoing adjuvant therapy for breast cancer.
Methods: 143 women diagnosed with breast cancer were randomized to APAD or Control (usual care) group. The APAD group received an intervention including 3 weekly exercise sessions and 9 dietetic consultations in the course of the 26 weeks of chemotherapy and radiotherapy. Patient-reported outcomes (PROs) and objective outcomes (measured by assessors), such as anthropometric, muscular and cognitive variables, have been measured at baseline, 18 and 26 weeks (end of intervention), and at 52- and 78-week of follow-up. Mixed effects models were used to assess the efficacy of the intervention.
Results: Beneficial effects of the APAD intervention were observed on all PROs i.e., fatigue, QoL, anxiety, depression and leisure physical activity at 18 and 26 weeks, with persistent significance at 52- and 78-week follow-up for some outcomes. Significant improvements were also observed on body mass index, fat mass, muscular strength and cognitive flexibility at 26 weeks. Subgroup analyzes revealed that beneficial effects on anthropometric variables, mental fatigue, anxiety/depression, and QoL were predominantly observed in overweight/obese or socially disadvantaged women. It was not necessary to be physically active at baseline to obtain favorable effects from the intervention.
Conclusion: The APAD1 study relieved breast cancer patients from adjuvant therapy-related side effects at short and long term. Overweight/obese, socially disadvantaged or inactive women at baseline particularly benefited from the intervention.
Funding: Ligue contre le Cancer (PI: G.Romieu); M.Carayol is supported by the Fondation de France (grant#2014-00050542)

O-424 - Pre-Diagnostic Meat And Fibre Intake In Relation To Colorectal Cancer Survival In The European Prospective Investigation Into Cancer And Nutrition

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Purpose: Improvements in colorectal cancer (CRC) detection and treatment have led to greater numbers of CRC survivors, for whom there is limited evidence on which to provide dietary guidelines to improve survival outcomes. Higher intake of red and processed meat and lower intake of fibre are associated with greater risk of developing CRC, but there is limited evidence regarding the nature of the association between these dietary exposures and survival after CRC diagnosis.

Methods: Among 3,789 CRC cases in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, pre-diagnostic consumption of red meat, processed meat, poultry, and dietary fibre was examined in relation to CRC-specific mortality (n=1,008) and all-cause mortality (n=1,262) using multivariable Cox regression models, adjusted for CRC risk factors.

Results: Pre-diagnostic red meat, processed meat, or fibre intake (defined as quartiles and continuous grams per day) were not associated with CRC-specific or all-cause mortality among CRC survivors. Pre-diagnostic poultry intake was inversely associated with all-cause mortality among women [hazard ratio (HR) per 20 g/d 0.92, 95% confidence interval (CI) 0.84-1.00], but not among men (HR 1.00, 95% CI 0.91 – 1.09) (P for heterogeneity = 0.10).

Conclusion: Pre-diagnostic intake of red meat, processed meat, or fibre is not associated with CRC survival in the EPIC cohort. There is suggestive evidence of an inverse association between poultry and mortality among female CRC survivors, however, further research using post-diagnostic dietary data is required to confirm this relationship.

O-425 - Incidence Of And Net Survival From Rare Cancers Diagnosed In England, 2000-2013

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Purpose: Rare cancers are relatively under-researched, with little information available on survival despite cancers with an annual incidence of <6 per 100,000 representing almost a quarter of all cancer diagnoses in adults. We report the net survival of selected rare cancers in England.
Methods: Data were analysed from 138,313 patients diagnosed from 2000-2013 with a primary, invasive malignancy of one of 13 cancers: tongue, oral cavity, salivary glands, oropharynx, hypopharynx, small bowel, anal, gallbladder, sinus, bone, vagina, penis or eye. Net survival analysis was performed, corrected for patients' expected mortality. Specific rules were put in place to restrict the net survival analysis to periods of follow-up with sufficient available data to make robust estimates.
Results: Average annual incidence of the cancers ranged from 0.8 per 100,000 for sinus to 3.1 per 100,000 for tongue. Incidence across the period rose slightly for anal, markedly for oral, small bowel, and gall bladder cancers, and particularly steeply for oropharynx and tongue cancers. Gallbladder, hyphoparynx and small bowel cancers had the poorest net survival overall at 43%, 61% and 66% at one year after diagnosis respectively, with eye cancer the highest at 95%. At five years, eye cancer survival was 70%, while gallbladder was 17%, hypopharynx 28% and small bowel 44%. Anal, oral and salivary cancers showed significantly worse survival at both one and five years for men, while women's survival was worse for gallbladder cancer at one year, but not significantly different from men at five years. Full results are presented.
Conclusions: The estimation of survival from rare cancers presents specific methodological challenges. We report robust quantification of recent survival from rare cancers for use by clinicians, patients and policy makers.
Funding source: Cancer Research UK

O-426 - Examining Variation In The Burden Of Lung Cancer Across GP Clusters In Wales

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PURPOSE
Examining variation in the burden of lung cancer across groups of GP practices developing collaborative working (GP clusters) in Wales.

METHODS
We extracted data from the Welsh Cancer Intelligence and Surveillance Unit's Cancer Registry for patients diagnosed with lung cancer between 2009 and 2013 living in Wales and registered with a Welsh GP at diagnosis. Population figures were obtained from NHS Wales Informatics Service for each GP practice. The Welsh Index of Multiple Deprivation 2014 was used to assign a deprivation half to lung cancer patients, and also to the population of each GP practice. We calculated crude incidence rates and one-year relative survival rates for GP clusters by sex, deprivation half and stage.

RESULTS
The highest crude incidence rate in men was two and a half times higher than the lowest (119.2 and 46.9 per 100,000 population respectively). In women, the highest incidence rate was almost three times higher than the lowest rate (100.9 and 35.3 per 100,000 population respectively).

For relative survival, there was a 29.5 percentage point difference in men and a 25.5 percentage point difference in women between the highest and lowest relative survival.

Crude incidence rates were generally higher in the most deprived half of each GP cluster. There was no clear relationship between deprivation and survival.

For the majority of GP clusters, most lung cancer patients were diagnosed at a late stage (stages 3 and 4) where relative survival was statistically significantly lower than relative survival from early stage lung cancer (22.5% and 71.2% respectively for Wales).

CONCLUSIONS
There was wide variation in incidence and survival between GP clusters when considering sex, deprivation and stage. There is still work to be done to improve survival across Wales, including increasing the number of lung cancer cases diagnosed at an early and potentially treatable stage.

O-427 - Innovative Culinary Intervention To Reduce Treatment-Induced Side Effects In Cancer Patients

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Purpose
Cancer cachexia and treatment-induced side effects can contribute to deterioration in nutritional status in patients declining the quality of life and survival rates by 25%. Culinary practices may provide new strategies to minimize the symptoms.
The objective of the NEODIA study was to understand the occurrence of treatment-related side effects as well as culinary and dietary habits in cancer patients and to develop a culinary practice and web-based educational program for the patients, families and health care staff.

Methods
Data were collected cross-sectionally in 197 cancer patients (31,6% colorectal cancer, 27,6% breast cancer, 7,9% non-Hodgkinien lymphoma, 7,5% esophageal/gastric cancer, 6,6% liver cancer, 5% lung cancer, and others) who were receiving treatment at the department of oncology of the Beauvais city hospital, France. The validated 145-item questionnaire inquired the frequency and occurrence of treatment-induced side effects, frequency and consumption of food and beverages as well as culinary habits.

Results
60% of the participants have reported at least one treatment-induced side effect and expressed their need for culinary practices. The data-driven development of the culinary practice and web-based educational program was monthly evaluated by 3 scientists and 10 female patients for perceived ease of use and acceptability of the culinary solutions. This study describes the program «vite fait Bienfaits®», available at http://vite-fait-bienfaits.fr as well as smartphone application. Results include more than 100 validated culinary solutions to minimize nausea, vomiting, diarrhea, constipation, dry mouth, fatigue and alterations in food preferences.

Conclusion
Overall, this study supports the feasibility and performance of culinary education as new preventing strategies to prevent and minimize treatment-induced side effects in cancer patients.

Funding source
The NEODIA study is supported by the regional health agency of Picardy, France (ARS Picardie), the French National Program of Nutrition (PNA) and the French league against cancer (departmental committee of Oise)

O-428 - Colorectal Cancer Survival Is Affected By The Public Hospital Type Where Patients Underwent Surgery In Brazil

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Purpose: The aim of this study was to analyze the effect of hospital specialization on five-year overall survival (5y-OS) of patients with surgically treated colorectal cancer. Methods: Study sample included all patients aged 20 years or older with colorectal cancer (tumor sites ICD-O-3 C18-C20 and morphologies 8000/3-8576/3) diagnosed and submitted to surgery during the period 2000-2010. Cases were retrieved from the Central hospital-based Cancer Registry from the state of Sao Paulo, Brazil, summing 18,537 cases who received care in institutions affiliated with the universal health care system (public or non-profit). Patients were classified according to hospital complexity where they received the oncologic surgical care: Centers for High Complexity Care in Oncology (CHCCO), Oncology Care Specialized Units (OCSU) and General Hospitals (GH) (more specialized to less specialized). Clinical group staging (TNM) was available for 17,831 patients. Five-year overall survival was estimated using Kaplan-Meier method and curves were compared using log-rank test. For all statistical tests, alpha=5% was used. Results: Higher 5-y OS was noted for patients treated at CHCCO, compared to those treated at OCSU and GH (53.9% versus 46.9% and 46.3%; $p<0.001$, respectively). When stratified by clinical stage, differences remained significant, with the same gradient: Stage I = 53.9% versus 46.9% and 46.3%; ($p<0.001$); Stage II = 68.9% versus 60.5% and 54.5%; ($p<0.001$); Stage III = 52.2% versus 45.7% and 32.9%; ($p<0.001$); Stage IV = 13.9% versus 12.1% and 0.0%; ($p=0.004$). Conclusions: Colorectal specialization was associated with improved survival, irrespectively of disease stage. Our results suggest a relationship between volume and outcome in colorectal cancer surgery, based on hospital and surgeons specialization. These data can contribute to the reorganization of referral system for colorectal cancer diagnosis and treatment in Brazil.

O-429 - The Impact Of Chronic Disease Combinations On Mortality Rate Advancement Periods In Older Adults

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Purpose: The number of older people living with chronic conditions is increasing and previous studies have indicated that patients with multiple chronic conditions have higher mortality rates. Yet, little is known about how specific combinations of chronic conditions impact mortality.
Methods: A total of 22,741 participants (62% women) aged 65 years of age and older from four cohorts were followed-up for vital status for an average of 10.0 years. Information on chronic disease status and confounding variables (smoking, education) was harmonized across cohorts. Using self-reported history of five chronic conditions with high mortality rates at baseline (cancer, hypertension, stroke, myocardial infarction, and diabetes), mutually exclusive groups of disease combinations were created. Cox proportional hazards models were used to estimate the rate advancement period (RAP) and corresponding 95% confidence intervals (95%CI) for all-cause mortality associated with specific disease combinations.
Results: At baseline, 58% of participants reported having two or more chronic conditions. Compared with individuals without any of the five conditions, the rate of death was advanced by 2.09, 5.56, 10.02, and 11.13 years for participants with 1, 2, 3, or ≥4 conditions, respectively. This means that individuals with four or more chronic conditions who have a certain rate of dying would be expected to have had the same mortality rate at a later age (+11.13 years) had they been disease-free. Among combinations with the same number of conditions there was substantial variability in RAPs.
Conclusion: In people aged 65 years and older, the period by which the rate of dying is advanced increases with each additional chronic condition, but discordant effects were observed across disease combinations with the same number of conditions.
Funding source: On behalf of the CHANCES project consortium; CHANCES received funding by the FP7 framework programme of DG-RESEARCH in the European Commission (grant agreement no. HEALTH-F3-2010-242244).

O-430 - Exploring Patterns Of Deprivation For People Living With Cancer: 20-Year Cancer Prevalence In The UK

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Purpose

An estimated 2.5 million people are living with cancer in the UK and this is predicted to increase to 4 million by 20301. The Macmillan-NCIN UK Cancer Prevalence Project aims to provide the most granular understanding of the cancer population.

Patient needs and experiences vary over time and space. We explore patterns of deprivation for short and long term survivors by cancer type within each nation to ensure future services are better tailored to suit their needs.

Methods

We used Public Health England's National Cancer Data Repository to link UK cancer registrations to mortality records, in order to identify people diagnosed with cancer between 1991 and 2010 and who were still alive on 31st December 2010.

We analysed the data to explore variations in deprivation groups for people living with cancer by common cancer type, time since diagnosis and sex. Counts are based on the first diagnosis of a specific cancer within the 20-year period2. Deprivation groups are population-based quintiles, based on residence at time of diagnosis.

Results

Overall the least deprived account for the highest proportion of cancer survivors for the 20-year period across most cancer types. This is likely due to the least deprived having a higher incidence in the better prognosis cancers such as breast and melanomas, and the most deprived groups having higher incidence in the poor prognosis cancers.

Patterns of how deprivation distributions vary according to time since diagnosis for different cancer types for each nation will be presented.

Conclusions

Our analysis provides a more granular understanding of the UK cancer population by deprivation for each UK nation. Segmenting the cancer population in this way can help inform better planning and tailoring of health and social care.

Funding source

Macmillan Cancer Support

O-431 - How Many People Are Living With Cancer In The UK At The End Of 2013?

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Purpose

Maddams et al (2009)[1] estimated that there were 2 million people living with cancer in the UK at the end of 2008. As part of the Macmillan-National Cancer Intelligence Network (NCIN) UK Cancer Prevalence project, we extended this work to incorporate more recent data and to estimate complete prevalence in the UK at the end of 2013.

Methods

Cancer registrations of people diagnosed with cancer and alive at the end of 2013 were extracted from the registrations systems for England, Northern Ireland, Scotland and Wales by each registry and provided to NCIN. NCIN continues to collaborate with these registries and Macmillan Cancer Support.
Cancer registrations were categorised into female breast, colorectal, lung, prostate and all other cancers excluding non-melanoma skin cancers. Data on age, sex, nation and year of diagnosis were also used.

A negative binomial regression model was used to estimate the number of people living with cancer before cancer registries were established in the respective countries.

Results

Initial estimates for England are in line with previous work[2] for the number of people living with cancer by tumour type up to the end of 2013. This is being extended to include the estimates for the other nations.

Conclusions

The inclusion of more recent cancer registration data has provided an updated picture of complete prevalence in the UK. Understanding the total burden of cancer will enable the provision of cancer services to be targeted accordingly and provide a new baseline to articulate specific needs within the cancer population.

Funding source
Macmillan Cancer Support

1. Maddams, J., et al., Cancer prevalence in the United Kingdom: estimates for 2008. Br J Cancer, 2009. 101(3): p. 541-7.
2. Maddams, J., M. Utley, and H. Moller, Projections of cancer prevalence in the United Kingdom, 2010-2040. Br J Cancer, 2012. 107(7): p. 1195-202.

O-432 - Influence Of A Cancer Diagnosis On The Evolution Of Diet, By Socioeconomic Status: Evidence From The E3N-EPIC Cohort Study

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Purpose
The World Cancer Research Fund has established nutritional recommendations for cancer prevention and for people who had a cancer diagnosis. But little is known on how individuals with a cancer diagnosis follow these recommendations.

Methods
Using data from 55,223 participants of the large French E3N-EPIC cohort study, we studied the influence of a cancer diagnosis on the evolution of diet between 1993 and 2005, according to the socioeconomic status (SES). Models were adjusted for age, body mass index, physical activity and the duration between the baseline questionnaire and the cancer diagnosis.

Results
We identified only one specific socioeconomic group where women changed their dietary habits after a cancer diagnosis between 1993 and 2005. Indeed, women who used to live more frequently in rural and quasi-rural areas with a high deprivation index, had a higher increase in their fruits intakes after their cancer diagnosis than similar women free of cancer during this period (+1.07 standard portions *vs*. +0.76 standard portions, p=0.001).They had a lower increase in their alcohol consumption when compared to cancer-free women in the same SES group (+0.39 g/d *vs*. +0.82 g/d, $p<0.05$). Otherwise, no significant evolutions were found for the other food groups such as meat, fish, cereals, seafood and dairy products, whatever the SES.

Conclusions
We have shown that all the participants, except those in a “Rural” SES pattern, did not significantly change their dietary habits after a cancer diagnosis. For a greater penetrance, public health and nutritional strategies for cancer could be modulated according to the SES.

Funding source:
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O-433 - Socioeconomic Disparities In Childhood Cancer Survival In Switzerland

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Purpose: In this study, we investigated whether childhood cancer survival in Switzerland is influenced by socioeconomic status (SES), and if disparities vary by type of cancer and definition of SES (parental education, living condition, area-based SES).

Methods: Using Cox proportional hazards models, we analyzed 5-year cumulative mortality in all patients registered in the Swiss Childhood Cancer Registry diagnosed 1991-2006 below 16 years. Information on SES was extracted from the Swiss census by probabilistic record linkage.

Results: The study included 1602 children (33% with leukemia, 20% with lymphoma, 22% with central nervous system (CNS) tumors); with an overall 5-year survival of 77% (95%CI 75-79%). Higher SES, particularly parents' education, was associated with a lower 5-year cumulative mortality. Results varied by type of cancer with no association for leukemia and particularly strong effects for CNS tumor patients, where mortality hazard ratios for the different SES indicators, comparing the highest with the lowest group, ranged from 0.48 (95%CI: 0.28–0.81) to 0.71 (95%CI: 0.44–1.15).

Conclusions: Even in Switzerland with a high quality health care system and mandatory health insurance, socioeconomic differences in childhood cancer survival persist. This study showed a socioeconomic deprivation gap in 5-year mortality of Swiss children with CNS tumors, with mortality being almost twice as high in children from not well-educated fathers. Factors causing these survival differences have to be further explored, to facilitate universal access to optimal treatment and finally eliminate social inequalities in childhood cancer survival.

Ref: Adam M*, Rueegg CS*, Schmidlin K, et al. Socioeconomic Disparities in Childhood Cancer Survival in Switzerland. *International Journal of Cancer*; 2016: *in press*
*both authors contributed equally

Funding sources: This work was supported by Oncosuisse (OCS – 01869 – 02 – 2006, KLS 01869-02-2006) and the Swiss National Science Foundation (Prosper 3233-069348 to CK, and SNC (3347CO-108806, 33CS30_134273 and 33CS30_148415)).

O-434 - Identifying Progressive Cancers In Head And Neck Cancer Patients Using Routine Health Datasets In England

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Purpose

Historically there has been limited national information on progressive cancers (recurrence, second cancers and metastatic disease). Macmillan Cancer Support and the National Cancer Intelligence Network are collaborating with academics and clinicians by using patient-level national cancer datasets to build our understanding of progressive cancer at a population level.

We have developed an algorithm to identify patients with primary head & neck cancers who have subsequently developed progressive cancer, in England, using routinely collected electronic healthcare data.

Methods

Records of patients diagnosed with head and neck cancer in 2013 with no previous history of cancer diagnosis were extracted from Public Health England's Cancer Analysis System (CAS). These records were linked to the Hospital Episode Statistics (HES) data, Systemic Anti-Cancer Therapy (SACT) data and the Radiotherapy Dataset (RTDS).
The results from the algorithm will be validated using data in selected Trusts and also national head and neck audit (DAHNO).

Results

Preliminary results from linking to the HES dataset based on time between events are promising. Further work is underway to incorporate chemotherapy and radiotherapy data.

Conclusions

Initial results have shown that it is possible to identify head and neck cancer patients with progressive cancers using an algorithmic approach; however, further work will determine how accurate this method is. To meet the needs of people living with cancer beyond their initial treatment and to facilitate timely re-introduction to the healthcare system we need to understand how many people have progressive cancers and their touch points on the health system. This is particularly key for many people with a head and neck cancer as progression can occur in a relatively short time frame after initial diagnosis.

Funding Source

Macmillan Cancer Support

O-435 - Exploring The Relationship Between Patient Experience And Outcomes; How Well Represented Are The Cancer Population In The English Cancer Patient Experience Survey?

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Purpose

We aimed to link the English Cancer Patient Experience Survey (CPES) to cancer registration records to allow new exploration of the association between patient experience and outcomes in order to identify areas of future focus in improving service provision and patient outcomes.

Methods

Patients' responses from the first 3 waves (2010, 2011/12 and 2013) of the CPES were initially linked to Public Health England's tumour level cancer registration records. An assessment was made to determine how well represented the CPES patients are when compared with the general cancer population.
The characteristics of a comparative population of cancer patients, defined as patients who were diagnosed within a year before and up to the end of each survey period, and alive at the end of each period were then compared with those in CPES.

Results

Over 75% of records were able to be linked for all of the survey waves. Analysis based on concordance between data items in both CPES and cancer registrations showed relatively little difference in the information about patients collected in the two datasets.

The 2nd wave of CPES had more responses from patients diagnosed with breast or haematological malignancies, those aged 50 to 75 at diagnosis and from females compared to the comparator cancer population.

Conclusions

This is the first time the CPES has been linked to cancer registrations. The new linkage provides new and unique insight into how well represented the overall cancer patient population is within CPES and also assess concordance of data between them. This initial work is essential to support a programme of further analysis being spearheaded by NCIN partnerships with Macmillan Cancer Support and Cancer Research UK.
Funding source
Macmillan Cancer Support and Cancer Research UK

O-436 - Life After Prostate Cancer Diagnosis (LAPCD)

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Prostate cancer may impact physically, psychologically and socially affecting health-related quality of life (HRQL) of men and their partners/spouses. The LAPCD study aims to:

describe HRQL of men with prostate cancer using qualitative and quantitative methods;
explore if and how HRQL is associated with or predicted by disease, treatment and/or patient characteristics with a view to informing healthcare policy and service
delivery;
describe levels of patient empowerment and explore the interaction between patient empowerment and HRQL;
undertake a study of men without prostate cancer to determine community levels of symptoms for comparison.

Methods: We will survey prostate cancer survivors in all four UK countries diagnosed between 18–42 months post-diagnosis, identified through cancer registration systems (~100,000). Men will be surveyed twice, 12 months apart, to determine changes in outcomes over time. We plan to survey second de novo cohorts once and will investigate the acceptability of online survey tools. To ensure detailed understanding of issues of importance, we will interview a sample of men who complete the survey (~150) along with a small number of partners/spouses (~30). We have developed a comprehensive Patient Reported Outcome Measure (PROM) using generic and specific instruments
with proven psychometric properties and relevance in national and international studies. The outcome data will be linked with administrative health data (e.g. treatment information
from hospital data).

Reporting plans: The first surveys are underway with preliminary results available June 2016. Aggregated results will be available to men and their partners/spouses, the funders, the health service, social care, voluntary sector organisations and other researchers. This 3-year study will provide data to steer service improvements, produce information to help men when making treatment decisions, and inform future research. This study is funded by Prostate Cancer UK and the Movember Foundation and linked closely with national cancer registries.

O-437 - Ethnicity And The Tumour Characteristics Of Breast Cancer In A Large Nationally Representative Sample Of Women In England

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Background
Some studies have suggested that ethnic minority women have more aggressive breast cancer compared to White women. However the evidence is limited and inconsistent, and generally has not accounted for sociodemographic differences. Complete data on tumour characteristics by ethnicity are available for over 68000 breast cancers registered in England between 2006 and 2013 and are reported here.
Methods
The data analysed includes patient characteristics (age/ deprivation/ethnicity) and tumour characteristics (size/grade/ nodal status/receptor profile). For each tumour characteristic logistic regression yielded odds ratios (OR) by ethnicity adjusting for age, region, deprivation, and all other tumour characteristics.
Results
There were 66,192 breast cancers in White women, 1233 in South Asian women and 641 in Black women. The mean age at diagnosis was on average five years younger in South Asians and Blacks compared to Whites (55 versus 60 years). In unadjusted analyses, both South Asian and Black women were more likely than White women to have higher risks of more biologically aggressive tumour factors including higher grade, larger size, ER negativity and node positive tumours. However after adjustment for age in particular, and other factors, these differences between the ethnic groups were reduced substantially. For example, compared to White women, the unadjusted and adjusted OR for tumours >5cm was 1.23 and 1.03 (NS) for South Asian women, and 2.05 and 1.44 (NS) for Black women. Similarly, compared to White women, the unadjusted and adjusted OR for node positive cancers was 1.23 and 1.03 (NS) for South Asian women and 1.6 to 1.2 (NS) for Black women.
Conclusions
This study provides large scale nationally reliable data on the association between ethnicity and different tumour characteristics of breast cancer. Much of the apparent differences in tumour characteristics by ethnicity are due to differences in age at presentation.
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