International Agency for Research on Cancer

World Health Organization

Scientific Council **SC/57/5**
Fifty-seventh Session 05/01/2021

Lyon, 10–12 February 2021
By web conference

Book of Abstracts – Poster session

Watch video presentations available on: https://events.iarc.who.int/e/SC57
(Select "Poster session and comments")

One MASTER poster describing the overall work of the Section/Group in the context of the new Medium-Term Strategy (MTS) is available. In addition, SUPPORTING posters were prepared by scientists in the Sections (maximum 7 posters, except the Section being reviewed [GEN] that has 12 posters), along with an abstract to illustrate either the fundamental activities or the emerging priorities (or both) and present them through short recorded videos.

Action by the Scientific Council

The Secretariat has assigned posters for review by each Scientific Council member (see distribution below), who is kindly requested to view the recordings in their own time and leave their comments/recommendations to scientists on what they can do to help strengthen their work.

Zoom meetings to encourage interaction with IARC junior scientists can be organized during the month of January 2021 (by the respective Sections upon request by the SC members).

Please make your recommendations under the comments text box. Comments on the abstracts and presentations will be closed on **1 February 2021.**

Proposed assignments

SC members	Sections	Tasks
Marc ARBYN	**INF, EDP**	Review all posters in these 2 Sections
Karima BENDAHHOU	**ENV, INF**	Review all posters in these 2 Sections
Tone BJØRGE	**INF, ENV**	Review all posters in these 2 Sections
Hendriek BOSHUIZEN	**NME, CSU**	Review all posters in these 2 Sections
Salha M. BUJASSOUM Al BADER	**ESC, LSB**	Review all posters in these 2 Sections
Ferrán CATALÁ LÓPEZ	**INF, ETR**	Review all posters in these 2 Sections
James Robert CERHAN	**GEN**	Review all posters in GEN
Kalipso CHALKIDOU	**ETR**	Review all posters in ETR
Jacqueline CLAVEL	**ENV, CSU**	Review all posters in these 2 Sections
Gunilla ENBLAD	**LSB**	Review all posters in LSB
Christine FRIEDENREICH	**NME**	Review all posters in NME
William GALLAGHER	**ESC, MCA**	Review all posters in these 2 Sections
Louisa GORDON	**ETR, EDP**	Review all posters in these 2 Sections
Ulrike HAUG	**GEN, EDP**	Review all posters in these 2 Sections
Manami INOUE	**ETR, CSU**	Review all posters in these 2 Sections
Sergey A. IVANOV	**ESC, LSB**	Review all posters in these 2 Sections
Ravi MEHROTRA	**ESC**	Review all posters in ESC
Péter NAGY	**MCA**	Review all posters in MCA
Jong Bae PARK	**GEN**	Review all posters in GEN
Pietro PICHIERRI	**MCA, LSB**	Review all posters in these 2 Sections
Janne Mikael PITKÄNIEMI	**GEN, CSU**	Review all posters in these 2 Sections
Sabine ROHRMANN	**NME**	Review all posters in NME
Maria SIBILIA	**GEN**	Review all posters in GEN
Anne TJØNNELAND	**NME**	Review all posters in NME
João P.B. VIOLA	**GEN, MCA**	Review all posters in these 2 Sections
Kazem ZENDEHDEL	**EDP, ENV**	Review all posters in these 2 Sections

Proposed assignments by Section

Section	Name of SC members
CSU	Janne Pitkäniemi; Jacqueline Clavel; Manami Inoue; Hendriek Boshuizen
EDP	Louisa Gordon; Marc Arbyn; Ulrike Haug; Kazem Zendehdel
ENV	Jacqueline Clavel; Kazem Zendehdel; Karima Bendahhou; Tone Bjørge
ESC	Ravi Mehrotra; William Gallagher; Salha Bujassoum; Sergey Ivanov
ETR	Ferran Catala Lopez; Kalipso Chalkidou; Louisa Gordon; Manami Inoue
INF	Marc Arbyn; Karima Bendahhou; Tone Bjørge; Ferran Catala Lopez
LSB	Sergey Ivanov; Gunilla Enblad; Pietro Pichierri; Salha Bujassoum
MCA	João Viola; Péter Nagy; William Gallagher; Pietro Pichierri
NME	Christine Friedenreich; Anne Tjønneland; Hendriek Boshuizen; Sabine Rohrmann
GEN (review)	Maria Sibilia; Janne Pitkäniemi; Jong Bae Park; James Cerhan; João Viola; Ulrike Haug

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Abstract ID: **5**

CSU1 - Occupational cancer in under-researched settings

Content

One of the remits of the Section of Cancer Surveillance is the regular provision of global estimate of the cancer burden. GLOBOCAN 2020 updates the previously published estimates of cancer incidence and mortality in the year 2018. The basic units for estimation are countries, together with aggregated results globally and in 20 world regions, as defined by the United Nations. 36 cancer sites and all cancers combined were estimated by sex and for eighteen age groups. The methods of estimation still rely upon the best available data on cancer incidence and mortality at the country level. Facilities for the tabulation and graphical visualisation of the full dataset of 185 countries and world regions can be accessed via the Global Cancer Observatory (GCO) homepage (https://gco.iarc.fr).
Worldwide, an estimated 19.3 million new cancer cases (18.1 million excluding nonmelanoma skin cancer) and almost 10.0 million cancer deaths (9.9 million excluding nonmelanoma skin cancer) occurred in 2020. Female breast cancer is now the leading cause of global cancer incidence, with an estimated 2.3 million new cases (11.7% of the total cases), followed by lung (11.4%), colorectal (10.1 %), prostate (7.3%), and stomach (5.7%) cancer. Lung cancer remains the leading cause of cancer death, with an estimated 1.8 million deaths (18% of the total deaths), followed by colorectal (9.4%), liver (8.3%), stomach (7.7%), and female breast (6.9%) cancer.
The global burden of cancer is expected to be 28.4 million in 2040, a 47% rise from 2020 due to projected demographic changes and assuming rates stay the same. Biggest increases in cancer incidence will occur in less developed countries, countries that are least equipped at present to deal with the rapidly rising burden.

Primary author: FERLAY, Jacques (IARC)

Presenter: FERLAY, Jacques (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Wednesday 09 December 2020**

Abstract ID: **36**

CSU2 - The GICR in 2021 - 2025: Innovations to support capacity building in LMICs

Content

High quality cancer data is essential in cancer control yet is lacking in many parts of the world. In response, the Global Initiative for Cancer Registry Development (GICR) was launched to improve the coverage, quality and accelerate the availability of population-based cancer registries (PBCRs). A core priority will be to continue to expand regional partnerships through the six IARC GICR Hubs and associated Collaborating Centres to better coordinate support to countries. In addition, implementation in 2021 – 2025 will be focused on three main areas:
Targeted assistance to intensify training, mentorship, and twinning opportunities with GICR Partner countries, a designation in recognition of local commitments to address needs through a measured action plan.
Increased educational resources, particularly through investments in the GICRNet, a global network of regional trainers who support in-country capacity building. Mutual development of e-learning modules with GICRNet trainers and other partners will be made available to reach a wider audience of users.
Electronic Innovation, in the form of linkages with electronic medical health records and new tools to assist with dissemination of information. Specifically, CanReg5, a free, open-sourced software for registries developed by IARC, will be enhanced to integrate with e-health systems and improve on its analytic functions.
A knowledge translation framework applied to cancer registration will be created to assist with applying models to generate, share and utilize knowledge for cancer control. A Monitoring and Evaluation framework will be implemented to help guide and assess the progress of registries through different phases of development.

Primary authors: MERY, Les (IARC); PINEROS, Marion (IARC); STELIAROVA-FOUCHER, Eva (IARC); ZNAOR, Ariana; BRAY, Freddie (IARC)

Presenter: MERY, Les (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **6**

CSU3 - ChildGICR: a St Jude-IARC collaboration to support the Global Initiative for Childhood Cancer

Content

St. Jude Children's Research Hospital and the International Agency for Research on Cancer (IARC) launched a bilateral collaborative agreement "Targeting Childhood Cancer through the Global Initiative for Cancer Registry development (GICR)" in May 2020, as an expression of the shared interest in the reduction of cancer burden in childhood. This collaboration is established in the framework and in support of the WHO Global Initiative for Childhood Cancer (GICC).

ChildGICR has three main objectives, focused on childhood cancer.

Implementation of cancer registration in countries will start with involvement of stakeholders. A country profile will be prepared to help set up site visits and a national workshop. Country- specific guidelines will be developed for the target countries, initially including Mexico, Georgia, South Africa, and Vietnam.

Education strategy will be based on assessment of needs and identification of the trainers within the existing GICR Network. Using the train-the-trainers methodology, an online learning module will be developed.

Research studies will support the other parts of the project. The barriers in data sharing will be assessed. A classification of childhood CNS tumours and recommendations for registration of non- malignant CNS tumours will be reviewed. The financial burden born by families affected by cancer in a child will be analysed. A tool quantifying the cost of registration of cancer in children will be developed.

Each objective is addressed in a working group lead jointly by the IARC and St Jude. ChildGICR has a potential to develop into a multi-annual programme, with annual reviews and extensions.

St Jude collaborators:

Nickhill Bhakta, Catherine Lam, Paola Friedrich, Victor Santana, Daniel Moreira, Mini Devidas, Carlos Rodriguez-Galindo.

Primary authors: STELIAROVA-FOUCHER, Eva (IARC); MERY, Les (IARC); PINEROS, Marion (IARC); ZNAOR, Ariana; DOLYA, Anastasia (IARC); MEHEUS, Filip (IARC); BRAY, Freddie (IARC)

Presenter: STELIAROVA-FOUCHER, Eva (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **7**

CSU4 - Benchmarking International Cancer Survival: In-depth analyses to drive action

Content

Background: International benchmarking studies on cancer survival is an important aspect in cancer surveillance and plays a key role to develop and assess early-detection strategies, the quality of clinical care, and the management of cancer patients.
The International Cancer Benchmarking Partnership (ICBP) SURVMARK-2 is a global, multidisciplinary partnership of clinicians, academics, and policy makers seeking to understand how and why cancer survival differs across countries that have high-quality cancer registries and universal access to, and comparable expenditure on, health care. The SURVCAN expands the work on SURV- MARK to provide benchmarking of survival estimates in low- and middle-income countries (LMICs). Methods: Under the ICBP SURVMARK-2 and SURVCAN projects, we collated and validated patient- level data from population-based cancer registries. For SURVMARK-2, data was collected on 3.9 million patients spanning seven countries on seven different cancer sites (esophagus, stomach, colon, rectum, pancreas, lung, and ovary). For SURVCAN-3, data on over 30 LMICs were collected for all cancer sites.
Results: The SURVMARK-2 study showed marked improvements in cancer survival over time and across countries. For example, 5-year survival of rectal cancer increased by more than 13 percentage points during the 20-year study period in Denmark, Ireland and the U.K. Most of the international variations in survival were due to stage and age at diagnosis. In-depth studies also highlighted differences in survival by histological subtypes.
Using SURVCAN data, in Thailand for example, regional differences in survival were also noted for three preventable cancer sites (cervical, breast and colorectal). Of the three, colorectal cancer had the lowest 5-year survival (47.6%) compared to breast (75.1%) and cervical (59.5%) during 2008-2012.

Primary authors: MORGAN, Eileen (IARC); CABASAG, Citadel (IARC); MIRANDA, Adalberto (IARC); SOERJOMATARAM, Isabelle (IARC)

Presenter: MORGAN, Eileen (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **8**

CSU5 - Burden of cancer related to tobacco smoking and impact of tobacco control policies on predicated cancer incidence in Europe

Content

Background: Tobacco smoking is the single largest cause of cancer, yet despite recent national declines in smoking rates in both sexes, smoking remains the most preventable cause of cancer in Europe. With lung cancer being the most common cancer type associated with tobacco smoking, the disease provides a case study in showing the potential impact of smoking prevention if European countries attained comprehensive implementation of tobacco control policies.
Methods: We estimated the population attributable fraction (PAF) using Levin's formula based on GLOBOCAN 2018 data by country, cancer type, sex and age. In addition, long-term incidence data from population-based cancer registries were used to predict sex-specific lung cancer incidence for 30 European countries over the following 20 years, up to 2037. Country-specific numbers and proportions of potentially preventable lung cancer cases were estimated using national smoking prevalence data and the national scale of MPOWER implementation (Tobacco Control Scale) data. Results: In Europe in 2018, in total 758,000 new cancer cases were attributable to tobacco smoking, accounting for 20% of all cancer cases. By region, the highest and the lowest PAF due to smoking in males were estimated in Eastern Europe (35% of all cancer cases) and Northern Europe (21%), respectively. Among women, this pattern was reversed (16% in Northern Europe and 6% in East- ern Europe). Lung cancer accounted for more than half of the total cancer burden attributable to smoking (382,000 cases). If tobacco control policies were implemented at the highest level as recommended by the MPOWER, an estimated 1·65 million lung cancer cases (21·2%, 19·8% in men and 23·2% in women) could be prevented over a 20-year period. In women, where lung cancer incidence rates are still on the rise in some countries, we estimated large proportions of preventable lung cancer cases ranging from 10-34%, with similar preventable cases in men (9-29%).
Conclusion: Tobacco smoking was responsible for one in five cancer cases in Europe in 2018. Com- prehensive implementation of evidence-based tobacco control policies is critical in reducing the future lung and smoking-related cancer burden across Europe.

Primary authors: SOERJOMATARAM, Isabelle (IARC); RUMGAY, Harriet (IARC); VIGNAT, Jerome; KULHANOVA, Ivana; GREDNER, Thomas; ESPINA GARCIA, Carolina (IARC); BRAY, Freddie (IARC)

Presenter: SOERJOMATARAM, Isabelle (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **75**

CSU6 - Global trends in thyroid cancer incidence and the impact of overdiagnosis

Content

Thyroid cancer (TC) incidence increased dramatically in the past decades in many high-resource countries, but corresponding mortality remained constant or declining. Incidence increases appear largely restricted to small papillary TC and affecting predominantly young women. The same phenomenon is now expanding in several countries undergoing fast socioeconomic transition, such as China, Brazil, Turkey and India. The TC epidemic is estimated to be largely due to overdiagnosis, i.e., diagnosis of thyroid tumors that would not progress to cause symptoms or death in an individual's lifetime. Over 1 million adult people (830,000 women and 220,000 men) might have been overdiagnosed with TC, in only 5 years (2008–2012) in 26 countries (up to 60-90% of the diagnosed TC cases). Overdiagnosis may also account for substantial number of TC diagnosed in adolescents worldwide, particularly girls. The organization of the health systems, local medical practices, the number and attitude of physicians and the penetration of new diagnostic and screening practices have a major role in the detection and diagnosis of the large reservoir of subclinical diseases known to exist in the thyroid gland. The clinical and human burden of TC overdiagnosis is heavy, especially on young women. Over 90% of patients receiving a TC diagnosis undergo total thyroidectomy and often other harmful and lifelong treatments. Besides, TC overdiagnosis is associated with large and unnecessary financial costs for the health systems and for the society. In summary, TC overdiagnosis has become a major public health challenge that needs to be closely monitored worldwide.

Primary authors: VACCARELLA, Salvatore (IARC); MENGMENG, Li (Former IARC Fellows); MI- RANDA, Adalberto (IARC); BRAY, Freddie (IARC); DAL MASO, L (IRCCS)

Presenter: VACCARELLA, Salvatore (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Wednesday 16 December 2020**

Abstract ID: **37**

CSU7 - The role of economics in global cancer prevention and control

Content

Countries at all income levels face significant challenges in implementing an efficient response to the growing burden of cancer and inequities in cancer outcomes are widespread between and within countries, leading to avoidable and premature deaths, but also threatening health budgets and economies, and causing financial catastrophe and impoverishment for individuals and families.

CSU is expanding its portfolio of research to examine the societal and economic impact of cancer, as part of IARC's mandate as a reference source in the provision of global cancer data. With governments committing to improve equitable and affordable access to high-quality, cost-effective cancer services in line with the UN Agenda for Sustainable Development and Universal Health Coverage in response to the growing burden of cancer, there is an increasing need for a systematic and ongoing collection of economic data: from understanding and assessing the societal and economic impact of cancers, at all levels, to examining the impact of cancer control interventions.

In the medium-term strategy 2021-2025 the economics of cancer prevention and control was recognized as a priority research area to the Agency. CSU will coordinate with external partners, including the World Health Organization headquarters, research activities in the following areas: (1) describe and understand the economic burden and socioeconomic inequalities of cancer including projects related to the estimation of productivity losses and disability-adjusted life-years; (2) priority setting and the development of investment cases in cancer prevention and control; and (3) provide technical support to cancer registries including the development of a registry costing tool.

Primary authors: MEHEUS, Filip (IARC); SOERJOMATARAM, Isabelle (IARC); BRAY, Freddie (IARC); ILBAWI, André (World Health Organization)

Presenter: MEHEUS, Filip (IARC)

Track Classification: CSU - CSU

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **9**

EDP1 - Cytology-based techniques for triage HPV positivewomen: fromPaptop16/ki67(CINtec®PLUS)

Content

In HPV cervical screening followed by Pap triage, the high sensitivity of HPV testing for CIN3+ detection may be hampered by Pap's limited sensitivity, which may be improved when Pap interpretation is done knowing HPV status. Dual-stain cytology with p16/Ki-67 proteins (CINtec®PLUS), a more objective technique, may be an alternative triage for HPV positive women (HPV+).
In the ESTAMPA study, Paps are processed/read in 10 laboratories (6 public, 4 private; in 4 pathologists read all smears, in 5 only ASCUS+, in 1 only Paps from HPV+ are processed/read). Re-reading of Paps knowing HPV status is undergoing in 6 laboratories. Pap performance for CIN3+ detection among HPV+ by laboratory characteristics and HPV status knowledge is being evaluated.
After technique standardization, dual-stain cytology is being prepared/interpreted on samples from HPV+ in Costa Rica.
Overall Pap sensitivity not knowing HPV status for CIN3+ detection was 53.9% (95%CI:49.3-58.3). The highest sensitivity: 70% (95%CI:60.9-77.8) was observed in the laboratory where only smears of HPV+ were interpreted. To date, 187 of 2,858 Paps have been re-read knowing they are from HPV+.
The percentage of dual-stained slides satisfactory for interpretation increased from 77.7% (95%CI:
68.6 -84.8) in the first run to 93.4% (CI: 91.4-95) after technique standardization. Of 981 dual-stained slides of HPV+, 25.7% (95CI%:23.1-28.5) were positive.
Pap performance may be improved when HPV status is known. Dual-stain cytology for CIN3+ detection among HPV+ may be an alternative to Pap, however, standardization of the technique may be required before implementation according to local context in different settings.

Primary authors: RAMIREZ, Tatiana (IARC); BAENA, Armando (IARC); ROL, Maryluz (IARC); GON- ZALEZ, Emmanuel (2. Hospital Dr. Enrique Baltodano Briceño, CCSS, Liberia, Costa Rica); BROUTET, Nathalie (3. HRP (the UNDP / UNFPA / UNICEF / WHO / World Bank Special programme of research, development and research training in human reproduction), WHO, Geneva, Switzerland); HERRERO, Rolando (IARC, Lyon, France and 4. Agencia Costarricense de Investigaciones Biomédicas, Guanacaste, Costa Rica); ALMONTE, Maribel (IARC); ON BEHALF OF THE ESTAMPA STUDY (5. ESTAMPA
study collaborators from Argentina, Bolivia, Colombia, Costa Rica, Honduras, Mexico, Paraguay, Peru, Uruguay and the USA)

Presenter: RAMIREZ, Tatiana (IARC)

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **10**

EDP2 - Implementation of HPV screen-and-treat strategies in high-risk populations to accelerate cervical cancer elimination

Content

Cervical cancer Screen-and-Treat strategies could accelerate cervical cancer elimination if they proved to be efficient and scalable. We are evaluating those strategies in high-risk populations in Africa.

The CESTA study is a RCT among underscreened HIV-negative women (Senegal) and Women Living with HIV (WLHIV, South Africa [SA]) comparing the efficacy of two HPV Screen-and-Treat strategies: 1) HPV with Visual Inspection with Acetic Acid (VIA) triage and Ablative Treatment (AT) of HPV/VIA positives; 2) immediate AT of all HPV-positives. Self- and clinician-samples are collected on all women and tested using a PCR-based test (Xpert). Women are referred to colposcopy after inadequate VIA, when the squamous columnar junction (SCJ) is not visible, or when ineligible for AT. HPV prevalence, number of women treated with AT, %ineligible for AT,

%VIA inadequate or with suspected cancer result (Arm1), %SCJ not visible are estimated by arm, age, and population.

The HPV prevalence among 350 women recruited in Senegal was 18% (95%CI:14-23). Of 49 HPV- positives with VIA triage, 17 were treated with AT, while of 14 HPV-positive without triage, 12 were treated with AT. The prevalence of HPV among 400 WLHIV recruited in SA was 62% (95%CI:57-67). Of 185 HPV-positives with VIA triage, 130 were treated (86 AT, 44 LLETZ); while of 44 HPV-positive without triage 34 were treated (28 AT, 6 LLETZ).

HPV Screen-and-Treat is feasible, can be performed by nurses or midwives. However, the observed high colposcopy referral deserves further evaluation. Recruitment of WLHIV will continue to reach statistical power for comparing the strategies.

Primary authors: FORESTIER, Mathilde; SEBITLOANE, M; DIOP, M; DE VUYST, Hugo (IARC); BAENA,
Armando (IARC); RAMIREZ, Tatiana (IARC); ROL, Maryluz (IARC); HERRERO, Rolando (IARC, Lyon, France and 4. Agencia Costarricense de Investigaciones Biomédicas, Guanacaste, Costa Rica); BROUTET, Nathalie (3. HRP (the UNDP / UNFPA / UNICEF / WHO / World Bank Special programme of research, development and research training in human reproduction), WHO, Geneva, Switzerland); ALMONTE, Maribel (IARC)

Presenter: FORESTIER, Mathilde

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **11**

EDP3 - Integrating HPV vaccine into HPV screen-and-treat approaches to boost cervical cancer elimination: a potential alternative for women living with HIV (WLHIV)

Content

Cervical cancer (CC) is a major problem worldwide with highest rates in sub-Saharan Africa where HIV is highly prevalent and up to 65% of CC is diagnosed in WLHIV.1, 2 WHO CC elimination goals for 2030 include achieving 90% HPV vaccination of young girls, 70% of HPV-based cervical screening of adult women, and 90% of cervical lesions treated and cervical cancers managed. Resource-limited countries usually with the highest CC and HIV prevalence rates may experience greater challenges to achieve these goals, therefore, combination of HPV vaccination and HPV- based screening among adult WLHIV needs strong consideration. HPV vaccination is highly effective to prevent CC, especially of young girls.3 Furthermore, efficacy against pre-cancer in adult women (≤45 years), presumably pre-exposed to HPV, has been also shown, but there is limited evidence on efficacy among WLHIV, especially adults.3-8 HPV vaccination in HPV pre-exposed women has been postulated to reduce HPV infections transmission, viral load and persistent infections, and recurrence of treated lesions.9-14 Access to HIV therapy in sub-Saharan Africa has improved over time through HIV Care Clinics (HCC).15 We propose to integrate HPV vaccination and HPV-based screening approaches into HCC services to accelerate CC elimination. We aim to use hybrid effectiveness-implementation designs16 to fill in research gaps on the effectiveness of different vaccine dosing schedules in a broad range age group of WLHIV while studying the barriers and facilitators of adding HPV vaccination to HPV-based screening among WLHIV attending HCC in sub-Saharan African countries, where the need is highest.

Primary authors: BAENA, Armando (IARC); FORESTIER, Mathilde (IARC (Lyon, France) and HRP (The UNDP / UNFPA / UNICEF / WHO / World Bank Special programme of research, develop- ment, and research training in human reproduction), WHO, Geneva, Switzerland); RAMIREZ, Tatiana (IARC); ROL, Maryluz (IARC); DE VUYST, Hugo (IARC); HERRERO, Rolando (IARC, Lyon, France and Agencia Costarricense de Investigaciones Biomédicas, Guanacaste, Costa Rica); BROUTET, Nathalie (HRP (the UNDP / UNFPA / UNICEF / WHO / World Bank Special programme of research, development and research training in human reproduction), WHO, Geneva, Switzerland); ALMONTE, Maribel (IARC)

Presenter: BAENA, Armando (IARC)

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **12**

EDP4 - Evaluating long-term efficacy of a single dose of quadrivalent HPV vaccine compared to two and three doses

Content

Background: High cost and complex logistics of administering two doses of HPV vaccine to pre- adolescent girls have prevented introduction of the vaccine in more than three-fourth of the low- and middle-income countries. In a multi-centric Indian cohort study, unmarried girls aged 10–18 years received three doses, two doses or a single dose of the quadrivalent vaccine. We present the 11-year follow-up findings on the efficacy of a single-dose compared to other doses in preventing persistent HPV infection and high grade cervical precancers for the vaccinated and age-matched unvaccinated cohorts.
Design: Around 17,000 vaccinated (evenly distributed across different dose groups) and 1,450 un- vaccinated women are being followed up yearly. Cervical samples are collected initially at 18- months after marriage and yearly thereafter for at least four consecutive samples. E7-PCR multiplex genotyping is performed on the samples to detect 19 high-risk or probable high-risk types and two low-risk types. Married participants are screened for cervical cancer starting at 25 years with Hybrid Capture-II HPV test.
Summary findings: Persistent HP16/18 infections were detected only in 0.05% of 2,136 single-dose, 0.1% of 1,451 two-dose and 0.1% of 1,460 three-dose groups, compared to 2.5% of 1,265 unvaccinated participants assessed. No HPV16/18-related CIN2/3 were detected in vaccinated women.
Conclusions: These encouraging results on single-dose efficacy have been reviewed by WHO- SAGE and national vaccine advisory committees. In 2-3 years, we expect to provide conclusive evidence to inform WHO policies on a potential reduction in HPV vaccine doses.

Primary authors: MUWONGE, Richard (IARC); BASU, Partha; LUCAS, Eric (IARC); SAUVAGET, Catherine (IARC); SANKARANARAYAN, Rengaswamy (IARC)

Presenter: MUWONGE, Richard (IARC)

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **13**

EDP5 - Working collaboratively with vulnerable women to identify the best implementation gains by screening cervical cancer more effectively in European countries (CBIG-SCREEN Study)

Content

Other authors (with affiliations): Basu P, Carvalho AL, Muwonge R, Lucas E, Villain P - Screening Group, Section of Early Detection and Prevention, International Agency for Research on Cancer, Lyon, France

Background: Though cervical cancer screening (CCS) programmes drastically reduce cervical cancer mortality, they remain largely inaccessible and underused by subpopulations of vulnerable women, creating inequality in the European healthcare system. Our multi-centric implementation research study aims to tackle inequality in CCS continuum in Estonia, Portugal and Romania. These 'focus countries' have been identified to represent different healthcare settings within Eu- rope.

Methods: CBIG-SCREEN will create a Europe-wide knowledge framework around barriers to CCS and generate policies, programmes, communications and other required services to meet the needs of underserved women with inherent high-risk of cervical cancer and low access to proper health- care routes. CBIG-SCREEN will be working collaboratively with vulnerable and underserved women to identify the interventions that will more effectively engage and retain them in CCS programmes in the three countries. We will design a protocol of providing CCS services to the vulnerable women through stakeholder engagement and structured reviews of current policies. We will implement CCS with new protocol in real programmatic settings in the focus countries and measure the outcomes using the 'logic model', A comparison with the existing 'standard-of-care' will allow us to objectively document the improvement in participation of the vulnerable women to the entire CCS care continuum, starting from screening to treatment. Our interventions aim to increase screening participation among vulnerable women from current 26% to 45% and intend to offer support to policymakers and national programmes to help Europe reach the WHO 2030 target of screening >70% of women for cervical cancer.

Primary authors: LUCAS, Eric (IARC); BASU, Partha; CARVALHO, Andre (IARC); MUWONGE, Richard (IARC); VILLAIN, Patricia (IARC)

Presenter: LUCAS, Eric (IARC)

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **14**

EDP6 - Cancer Screening in 5 continents (CanScreen5) – Improving data collection for monitoring and quality assurance of cancer screening programmes worldwide

Content

Background: Cancer screening programmes are complex and resource-intensive but can have huge benefits when implemented with appropriate quality and equity. The CanScreen5 project (http://canscreen5.iarc.fr/) aims to encourage and support countries to collect and use cancer screening data for programme evaluation and quality improvement. The initiative will also motivate and support programme managers to improve health information systems and assess cancer screening programmes for better overall management, quality assurance and informed policy-making. Moreover, training is a cornerstone of the development and maintenance of this global network. Methods: We are implementing different and tailored strategies to assist countries while collecting data. In the Community of Caribbean and Latin American states (CELAC) we are focused on understanding social inequality on cancer screening, by conducting a situational analysis in which the qualitative and quantitative information from the cancer sites is complemented with the examination of the barriers to a successful screening programme. Additionally, evidence-based interventions to tackle those barriers will be presented enabling countries to design a country-tailored road map to achieve an improvement and equality in cancer screening. Regarding capacity building, CanScreen5 is organizing training programmes in partnership with WHO regional offices to allow the development of regional quality indicators and standards, and ultimately regional implementation guidelines in line with international standards. The first training happened with 17 African countries, and the second (in Spanish) and third training (in English) will focus on CELAC. We will replicate this model in other WHO-regions. Regarding the CanScreen5 platform as a global repository designed to collect, analyse, and disseminate standardized information on cancer screening programmes, we have received data from 14 countries.

Primary authors: CARVALHO, Andre (IARC); ZHANG, Li (IARC); MOSQUERA METCALFE, Isabel Maria (IARC); MUWONGE, Richard (IARC); LUCAS, Eric (IARC); BASU, Partha

Presenter: CARVALHO, Andre (IARC)

Track Classification: EDP - EDP

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **15**

ENV1 - Identifying pathways to improve breast cancer survival in sub-Saharan Africa in the ABC-DO cohort

Content

Introduction: Breast cancer is a potentially curable cancer but its survival in Sub-Saharan Africa is low. The African Breast Cancer Disparities in Outcomes (ABC-DO) is studying factors that need to be targeted to avert breast cancer deaths.
Design: ABC-DO is a cohort of over 2100 women diagnosed with breast cancer during 2014-17 across Namibia, Nigeria, South Africa, Uganda and Zambia. The present work examines (i) the geospatial barriers to early diagnosis and (ii) survival and scenarios of how to improve it.
Results: (i) In the help-seeking journey to diagnosis, distance to first provider was not associated with late stage at diagnosis, but distance to the diagnostic/treatment facility was associated with time delays to diagnosis (highest vs lowest quartile: Odds Ratio (OR)=1.56, 95% CI=1.08-2.27) and late stage (OR=1.73, 95% CI=1.18-2.54).
(ii) Three-year survival was 50% overall, but varied between races in Namibia (90% white, 69% mixed-race and 56% in black women) and South Africa (76% mixed-race, 59% black) and between countries: 44 to 47% in Uganda and Zambia and 36% in Nigeria. Improvements in early diagnosis and treatment were predicted to result in the largest survival gains of up to a combined 22% absolute increase, compared to the contributions of social inequalities (up to 5%), non-receptor positive tumours (up to 4%) and young age or HIV positivity (<2% each).
Discussion: Special attention needs to be made to women residing far from treatment centres to achieve earlier diagnosis. Improving access to complete quality treatment needs to be strengthened alongside downstaging efforts

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Presenters: TOGAWA, Kayo (IARC); MCCORMACK, Valerie

Track Classification: ENV - ENV

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **16**

ENV2 - Alcohol and geophagia in relation to esophageal cancer in East Africa: ESCCAPE case-control study

Content

Introduction: The ESCCAPE project investigates the aetiology of unusually high incidence rates of esophageal squamous cell carcinoma (ESSC) in East Africa. Putative risk factors under investigation during 2020 were geophagia and alcohol consumption. Geophagia is the intentional practice of eating earth or soil and is often, but not exclusively, practised during pregnancy. Alcohol consumption includes diverse local brews/distillations.
Design: A multi-country ESCC case-control study across Malawi, Tanzania and Kenya, with 1200 cases and the same number of age-sex frequency matched controls. Exposure data were self-reported. Odds ratios (OR) are adjusted for design and sociodemographic factors, tobacco and (for geophagia) alcohol.
Results: (i) Among controls, geophagia was most common in women in Malawi (49%), Kenya (43%) and Tanzania (29%), and less common in men. Geophagia was not associated with ESCC overall (OR 0.96 (95% CI: 0.76, 1.22)), however there was a suggestion of a positive association in women under age 50 (OR 1.18 (0.69, 2.00).
(ii) Ever-consumption of alcohol was strongly associated with ESCC in men in Kenya (OR 4.2 95% CI (2.6, 6.9)) and Tanzania (3.0 95% CI (1.6, 5.7) and in each setting, ORs were approximately half in women. In Malawi, the country with the world's highest ESCC incidence rates, alcohol consumption was also associated with increased risks in women but with a protective effect in men. The latter was due to differential underreporting in male cases.
Discussion: The impact of geophagia on the oesophagus in young women needs further investigation. Under-reporting of alcohol consumption should be considered in cancer case-control studies in East Africa.

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Presenters: NARH, Clement (IARC); MCCORMACK, Valerie

Track Classification: ENV - ENV

Status: SUBMITTED

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Abstract ID: **17**

ENV3 - Cancer risks after exposures to low-dose ionising radiation

Content

ENV radiation team researches cancer risk in various populations across the world exposed to ionizing radiation (IR) from environmental (Chernobyl accident, Ukraine; Semipalatinsk nuclear testing, Kazakhstan; Techa River radioactive contamination, Russia; uranium-rich gold mine tailings, South Africa), occupational (nuclear workers), and medical diagnostic sources. The main focus is on overall and site-specific cancer risks in populations exposed to low-doses of IR at various life periods (before conception, in utero, early childhood, adolescence, young adulthood etc.) taking into account potential confounding as well as radiation-related risk modifying factors (sex, age at first exposure, time since exposure etc.). Radiation risk assessment is typically based on individually reconstructed doses to the target organs, e.g. thyroid, breast, bone marrow etc. with estimation of dose uncertainties. Recently, incorporating stochastic thyroid dose estimates, we published on the elevated thyroid cancer risk after exposure to radioiodine in childhood from Chernobyl fallout, especially in the study subjects who did not received stable iodine supplementation in the years after the accident. Next is to finalize the thyroid cancer geneXIR interaction analysis in this population. Using ecological study design, we found no increase in breast cancer incidence in relation to district-average accumulated breast dose in female residents of the most contaminated areas in Ukraine and Belarus after Chernobyl accident (1986-2016), however due to potential dose mis-classification a detailed analytical study is highly warranted. An observed increased risk of some solid cancers after paediatric computed tomography procedures has societal importance to ensure adequate protection of patients.

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Presenter: OSTROUMOVA, Evgenia (IARC)

Track Classification: ENV - ENV

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **18**

ENV4 - Glioma incidence in the Nordic countries from the perspective of possible mobile phone-associated risks

Content

Introduction: In all countries, the use of mobile phones increased sharply. In the Nordic countries, this increase occurred in the mid-1990s, earlier than in other countries; thus, the evolution of brain tumour incidence over time may provide information about a possible risk associated with mobile phone use.
Design: We investigated time trends in the incidence rates of glioma between 1979 and 2016 in Denmark, Finland, Norway, and Sweden, using data from national cancer registries, among adults. Linear models allowing for up to 3 join-points were fitted to the incidence rates. The power of this study was evaluated assuming a hypothetical risk increase of glioma from mobile phone use of 1.5 after an induction and latent period of up to 20 years.
Results: Among men and women below 60 years old, no join-point was detected, and the rates hardly changed over the period (annual percent change in men 40-59 years old = 0.1 95%CI 0.0-0.3). Among people aged 60-69 years old, the rates increased regularly, in all countries. The patterns in the rates in men and women aged 70-84 years old varied. Under this hypothetical risk scenario, calculations demonstrated that the power of our data to detect this risk increase is 100%, thereby this hypothetical risk scenario can be safely excluded.
Discussion: If mobile phone were to increase the risk of glioma, their widespread use would ultimately increase the number of glioma cases globally. In the period 1979-2016, incidence rates have remained stable among adult men and women below age 60 in the Nordic countries, showing no detectable impact of the widespread and long term use of mobile phones in these age groups.

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Track Classification: ENV - ENV

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **19**

ENV5 - Roadmap European Code Against Cancer

Content

As part of the third European Commission's Joint Action on Cancer (Innovative Partnership for Action Against Cancer - iPAAC), IARC, as coordinator of the update of the 4th edition of the European Code Against Cancer (ECAC), has been responsible for providing guidance, involvement of scientific experts and introducing a plan for a monitoring and sustainable follow-up of the ECAC. This plan has been drafted in the report "Recommendations for the Sustainability and Monitoring of the European Code Against Cancer" containing eight recommendations and four identified re- search needs, overarching and complementary to the sustainability and optimisation of the ECAC in the context of implementing cancer prevention, dissemination to various target audiences and continued aetiological research. The plan focuses specifically on the scope of a future 5th edition of the ECAC, including updating the scientific evidence and its maintenance, and on the strategies to further expanding its scope, implementation and dissemination across Europe. The methodology followed included a co-creational consultation process, including a virtual workshop, coordinated by IARC, the Association of European Cancer Leagues (ECL) and the Cancer Society of Finland (CSF). Input on cancer prevention from more than 100 participants, from scientists and experts in cancer prevention and/or public health to dissemination and communication advisors and representatives of European authorities, was collected and discussed to assess the needs and pave the way for the future of the ECAC. Overwhelming support for the need of the ECAC and its continuous updating, optimization and wider dissemination was expressed by all the stakeholders.

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Presenter: ESPINA GARCIA, Carolina (IARC)

Track Classification: ENV - ENV

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **20**

ENV6 - Parental domestic use of pesticides during early periods of child development and risk of testicular germ cell tumors in adulthood: a French nationwide case-control study

Content

Introduction: In ENV, several projects are ongoing to investigate the role of exposure to pesticides in cancer risks. We present a French nationwide case-control study where we assessed adult TGCT risk associated with parental domestic use of pesticides during early periods of child development. Design: The study included 304 TGCT cases, aged 18-45 years, recruited at 20 French university hospitals, and 274 controls frequency-matched on hospital and birth year. Participants' mothers provided information on their domestic use of pesticides from one year before start of pregnancy to one year after their son's birth. Odds ratios (OR) for TGCT and 95% confidence intervals (CI) were estimated using conditional logistic regression.
Results: Overall, 78.9% of the participants reported domestic use of pesticides (insecticides: 77.3%, fungicides: 15.9%, herbicides: 12.1%). While no association was found for any use of insecticides (OR=1.27, CI=0.80-2.01) or herbicides (OR=1.15, CI=0.67-2.00), increased risks of TGCT overall (OR=1.73, CI=1.04-2.87) and non-seminoma subtype (OR=2.44, CI=1.26-4.74) were observed for any use of fungicides. When specific purposes of use were examined, using fungicides and/or insecticides for woodwork (OR=2.35, CI=1.06-5.20) and using insecticides on cats and dogs (OR=1.95, CI=1.12-3.40) were associated with an increased risk of non-seminoma subtype. We found no as- sociation for seminoma.
Discussion: Although recall bias may partially explain the elevated ORs, our study provides some evidence of a positive association between domestic use of pesticides, particularly fungicides and risk of TGCT and non-seminoma.
Conclusion: Given the common domestic use of pesticides in France, further research on TGCT risk is warranted.

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Track Classification: ENV -

ENV **Comments:**

for the TESTIS study group

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **21**

ENV7 - Occupational cancer in under-researched settings

Content

Background: Many human carcinogenic agents (IARC group 1) are found primarily in the occupational settings. Still, most epidemiological studies on occupational cancers have been mainly conducted in high-income countries. Because we commonly "act on what we see" we need to expand the knowledge base on occupational cancer epidemiology to under-researched settings. Once identified, most occupational carcinogens can be regulated. Conducting research highlights local conditions, which can result in measures to control or reduce exposures in workplaces.
Design: ENV is involved in epidemiological studies on occupational cancers in: 1) the Russian Federation via the Asbest Chrysotile Cohort Study - a large retrospective industrial cohort study of workers in the world's largest chrysotile mine and nearby processing factories; 2) the Islamic Republic of Iran by hosting and supervising Bayan Hosseini - a PhD student – working on occupational data from a nationwide case-control study and will guide forthcoming studies in Iran; and 3) Ogoniland in the south of Nigeria, severely polluted from the petroleum industry. ENV is hosting and supervising Felix Onyije an IARC post-doctoral fellow from Port Harcourt. We foresee to set up epidemiological studies to investigate workers' and residents' health, in collaboration with UNEP in 2021.
Conclusion: As occupational cancers are preventable it is an important field of research to expand further. Our projects contribute to strengthening research capacity of conducting epidemiological studies in under-researched settings.

Primary authors: OLSSON, Ann (IARC); ONYIJE, Felix (IARC); HOSSEINI, Bayan (IARC); BOUAOUN, Liacine (IARC); SCHUZ, Joachim (IARC)

Presenter: OLSSON, Ann (IARC)

Track Classification: ENV - ENV

Status: SUBMITTED

Submitted on **Thursday 10 December 2020**

Abstract ID: **22**

ESC1 - Adapting IARC Monographs meetings to the COVID-19 era

Content

The IARC Monographs on the Identification of Carcinogenic Hazards to Humans has been described as the WHO's "encyclopaedia of carcinogens". Since 1971, the Programme has identified preventable causes of cancer by conducting authoritative evaluations of chemical, biological, and physical agents, as well as complex exposures, occupations, and exposures of everyday life. Each year, for nearly 50 years, the Monographs Programme has convened two or three meetings in Lyon, France, of Working Groups of independent global experts in cancer epidemiology, cancer bioassays, carcinogen mechanisms, and exposure characterization to review the evidence on carcinogenicity and develop consensus evaluations for an agent or group of related agents. More than 1000 evaluations have been conducted through the history of the Programme. During the COVID-19 global pandemic, the Monographs Programme has adapted its meetings of these global cancer experts to an online format, achieving robust evaluations that will be published in high- quality Monographs volumes for which IARC is widely known. This presentation will describe the adaptations made to hold three Monographs meetings (for Volumes 126–128) fully remotely in 2020, including lessons learned, feedback garnered from surveys of Working Group members, and adaptations that are likely to persist moving forward into the post-COVID-19 era.

Primary authors: SCHUBAUER-BERIGAN, Mary (IARC); GROSSE, Yann (IARC); GUYTON, Kathryn (IARC); ON BEHALF OF THE IARC MONOGRAPHS GROUP, IARC, LYON, FRANCE

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Track Classification: ESC - ESC

Comments:

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Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **23**

ESC2 - IARC Monographs evaluations using the newly adopted Preamble: summary of vols. 124–128

Content

The IARC Monographs Programme identifies the preventable causes of human cancer. In 2019, IARC updated its procedures for carcinogen identification through amendments to the Mono- graphs Preamble. This presentation will review the carcinogens identified since the 2019 Preamble was adopted. In five meetings, the Monographs Programme convened independent global experts in cancer epidemiology, cancer bioassays, and carcinogen mechanisms to review evidence on carcinogenicity and develop consensus classifications for a range of agents. These included: opium consumption (Group 1) and night shift work (Group 2A), with sufficient or limited evidence noted for cancers of larynx, lung, bladder, oesophagus, stomach, pancreas, pharynx, breast, prostate, and/or colorectum; various industrial chemical intermediates and solvents, including glycidyl methacrylate (Group 2A); some aromatic amines, including aniline, ortho-anisidine and ortho-nitroanisole (Group 2A); acrolein (Group 2A), crotonaldehyde (Group 2B) and arecoline (Group 2B). Exposures to these carcinogens can occur in various settings, including in the workplace, from cigarette smoking and air pollution, from consumer products, or through consumption of drugs commonly used in in low- and middle-income countries. These evaluations revealed several strengths of the amended Preamble, including enhanced clarity and rigor of the systematic review process and strengthened evidence integration procedures. Additionally, a structured review based on the key characteristics of carcinogens facilitated a comprehensive and systematic consideration of a range of informative mechanistic data. The classifications of several carcinogens relied partly or wholly on mechanistic evidence, highlighting opportunities to apply novel molecular research findings to identify new causes of human cancer, the first step in cancer prevention.

Primary authors: GUYTON, Kathryn (IARC); GROSSE, Yann (IARC); BOUVARD, Véronique (IARC); SCHUBAUER-BERIGAN, Mary (IARC)

Presenter: GUYTON, Kathryn (IARC)

Track Classification: ESC - ESC

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **24**

ESC3 - Handbook 18 – Cervical cancer screening

Content

The IARC Handbooks of Cancer Prevention provide definitive evaluations about which interventions or strategies can prevent cancer, detect precancerous lesions, or detect cancer at an early stage.
Following the WHO call for a global Cervical Cancer Elimination Initiative in May 2018, the Handbooks programme has undertaken an update of Vol. 10 on cervical cancer screening.
The following cervical cancer screening tests were evaluated for their efficacy and/or effectiveness in population-based programmes: conventional cytology; liquid-based cytology; HPV-nucleic acid tests; visual inspection with acetic acid; and Romanovski Giemsa stain. In addition, the Working Group provided statements on the comparative effectiveness of HPV test against cytology (conventional or liquid-based) and against VIA. The evaluations and comparative statements have been directly used by WHO for the update of their recommendations.
The Handbooks also contains reviews of the literature on other topics related to cervical cancer screening: cervical cancer burden and screening practices worldwide, screening in populations at differential risk, the screen-and-treat approach in low-resource settings, and promising emerging techniques, amongst others.

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Track Classification: ESC - ESC

Comments:

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Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **25**

ESC4 - BBEST, an expert selection tool for the Blue Books

Content

he World Health Organization Classification Tumours (published as the WHO Blue Books) provides the international standards which underpin cancer diagnosis and research. Its production requires frequent selection of representative experts worldwide. Editors and authors are usually selected from the personal network of individuals, with high risk of bias. Our aim was to develop a tool to assist the selection of experts using scientometric analysis of bibliometric data. A web-based interface, the Blue Books Expert Selection Tool (BBEST) allows structured searches to retrieve and evaluate a set of potential experts based on their publications. Bibliometric variables from Medline, Web of Science and Altmetrics are analysed to produce Summary tables, rankings, descriptive plots as co-authorship networks and co-citation analysis, to assess publication records of experts and allow a more evidence-based suggestion of experts. This informed bibliometric approach is able to produce more internationally balanced groups of experts current in the field.

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Presenter: CIERCO JIMENEZ, Ramon (IARC)

Track Classification: ESC - ESC

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **26**

ESC5 - WHO Classification of Tumours: 2020 Highlights

Content

2020 was a successful year for the WHO classification of tumours, despite the need for considerable agility from the team to meet the demands of teleworking, and remote meetings, the first of which was in March. We have published two books in the year, and the thoracic book is now in final proof, and expected to go to the printers before the scientific council meeting. The volume on Female Genital Tract tumours was particularly important, as it included a revision of the classification of cervical cancer, which now underpins the WHO program for the elimination of the cancers caused by HPV.

The Histopathology laboratory continues its work with numerous groups within IARC, which depend on it for processing samples from all over the world for their projects. It is increasingly focused on the whole slide imaging of the preparations prepared in the laboratory, as well as those from outside sent to us. Images from the Histopathology laboratory have made their appearance within the Blue Books Online website, and are much appreciated by users and the larger scientific community.

We have developed a new computational tool for the systematic identification of expert editors and authors, and are now beginning to use this widely. This is an example of the work of the IARC international collaboration for cancer classification research (IC3R), which has 11 core and full members, and is proving successful in stimulating evidence-based pathology.

Primary authors: CREE, Ian (IARC); WHITE, Valerie (IARC); INDAVE, Iciar (IARC)

Presenter: CREE, Ian (IARC)

Track Classification: ESC - ESC

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Abstract ID: **27**

ESC6 - Systematic review for tumour classification

Content

Background & Objective: New methods of evidence synthesis are necessary to classify/reclassify histologically similar tumours. Our objective was to assess the distinction between adenosquamous (ADSQ) and mucoepidermoid carcinomas (MEC) using systematic review methodology to synthesize published molecular information on these two tumours.
Methods: We performed a systematic literature search of Medline, Embase and Web of Science from 1990-2019 for articles studying molecular alterations in MEC and ADSQ from any site. Retrieved citations were screened and reviewed for eligibility by two independent reviewers. A third reviewer arbitrated. Two reviewers independently extracted data and conducted a Risk of Bias assessment of included studies.
Results: Of 6688 references, 95 met the criteria for further review. Only 5 articles directly compared these two tumour types. These found that MAML2 rearrangement was present in 52/88 (59%) MEC and in none of 110 (0%) ADSQ. 34/94 articles studied MAML2 rearrangement in MEC only showing that 852/1382 (62%) were positive for the fusion. One paper studied 20ADSQ for MAML2 rearrangement finding that all were negative. In 55/94 articles that studied other commonly mutated genes, EGFR mutations were reported in 34.4% (517/1501) of ADSQ versus 7% (8/115) MEC. Mutations in KRAS were found in 19.1% (100/523) ADSQ versus 2.2% (3/139) MEC. 100% (51) pancreatic ADSQ had mutations in KRAS.
Conclusions: We found no published molecular evidence to support similarities between ADSQ and MEC, supporting the separation of these neoplasms. Systematic review methodology provides a tool for assessing molecular data accruing on all tumours and may assist in their classification or reclassification.

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Track Classification: ESC - ESC

Status: SUBMITTED

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Abstract ID: **28**

GEN1 - GEM 4.2.1 IARC Analytical Hub to facilitate data sharing

Content

Introduction: The success of modern genomic and epidemiological projects relies on the availability of state-of-the-art omics data on large numbers of study samples. IARC has a role in facilitating the collaborations that brings together these multi-centric studies, but also engages our expertise in epidemiology and bioinformatics to harmonize the multiple forms of molecular and epidemiological data into a usable format. This project aims to improve access for external investigators to the harmonized databases that are created and organized by IARC.
Design: This project aims to establish a user-friendly, accessible, centralized platform of genetic and epidemiological data for various IARC projects. This analytical hub will then be used to maintain and provide access to our various datasets. There are four key objectives: 1. Organize relevant consortium databases on the IARC Analytical Hub. 2. Establish a pipeline for external investigators to access data on the IARC Analytical Hub that adheres to the governing and legal requirements for the respective databases. 3. Leverage the analytical hub to facilitate ongoing data curation and harmonization processes. 4. Leverage the analytical hub to provide data, along with appropriate analytical software, to scientific users outside of IARC.
Expected Results: This platform will develop the infrastructure, operating protocols and administrative structures to support this type of analytical processes. We envisage four consortia based projects to be used within the analytical hub in the near term; The Lung Cancer Cohort Consortium (LC3), The InterLymph Consortium, The HPV Cancer Cohort Consortium (HPVC3), and Translational Studies of Head and Neck Cancer in South America and Europe (HEADSpAcE). While these projects on lung, head and neck cancers and lymphomas will be the first use, we expect that similar projects will subsequently use these analytical processes.
Impact: We aim to facilitate access to these datasets so that the scientific community can address pertinent research questions in a timely manner, but at the same time, ensuring that the data is stored in a manner consistent with international data security laws. This is a capacity building project that we believe will strengthen IARC in our stated objective to promote international collaboration in cancer research in general, and specifically our ability to effectively lead consortium projects.

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Presenter: MCKAY, James (IARC)

Track Classification: GEN - GEN

Status: SUBMITTED

Abstract ID: **29**

GEN2 - GEM 4.2.3 Identifying mutation signatures for specific exposures including opium, alcohol and aristolochic acid

Content

Introduction: Many common cancers exhibit major differences in incidence between geographical areas and trends over time for which we do not understand the reasons. We have initiated several additional studies to the Mutographs project that seek to understand how potential carcinogens cause specific cancers and striking incidence distribution. Prioritization of these cancer sites was carefully considered based on the scientific relevance of the associated exposures and our strong external collaborations to optimize probability of success. These are: aristolochic acid as a cause of kidney and urothelial tract cancers, alcohol as a cause of head and neck cancers, opium as a cause of bladder cancer in Iran, and gallbladder cancer in India.

Design: As for main Mutographs project, materials and associated data are collected through a net- work of local contributing centres coordinated by IARC, following detailed procedures described in the adapted Mutographs Standard Operating Procedures to the specificities of these proposals. Tumour and germline sequence data will be used to extract mutational signatures that will be correlated with demographic, histological, clinical and questionnaire data. We will recruit 300 kidney and urinary tract cancer cases across the Balkans and complement with the collection of multiple tumour biopsies, urine samples and an additional validated questionnaire on use of herbal remedies and residential history together with questionnaire data from 550 controls. We will use a series of 500 head and neck cancer cases (HNSCC) collected from existing large biorepositories from North America: (TAP-WUSM), South America (InterCHANGE) and Europe (ARCAGE). This will allow for identification of mutation signatures associated to HPV infection and those specific for both alcohol and tobacco, as well as for their combined effect. We have also initiated two pilot studies on gallbladder cancer in India and bladder cancer in Iran for which we will recruit 30 and 100 cases, respectively.

Expected results and impact: We anticipate that these projects will fill in knowledge gaps in our understanding of the proposed cancers, which is essential to design effective prevention measures. Through understanding the causes specific mutational signature, evolutionary histories of the pat- tern of mutations over time and its correlation with possible exposures, this unprecedented effort may lead to new approaches to prevent cancer and may provide opportunities to empower early detection, refine high-risk groups for which screening strategies would be most beneficial, con- tribute to further therapeutic development and outline modifiable risk factors that could contribute to prevent cancer occurrence.

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Presenter: FERREIRO, Aida (IARC)

Track Classification: GEN - GEN

Status: SUBMITTED

Abstract ID: **30**

GEN3 - GEM 4.2.4 Mendelian randomization and direct exposure measurements in large cohorts

Content

Background: Traditional longitudinal cohort-studies studies offer a powerful approach to assess the relation between putative risk factors and disease risk without imposing interventions – but the results may be subject to bias or to unmeasured or residual confounding. Insights into the potential causality of exposure-disease associations should ideally come from a variety of complementary study designs with different limitations and biases. An example of such an approach is Mendelian randomization (MR), whereby germline genetic markers are used as proxies – or instrumental variables – for putative risk factors. These genetic markers cannot be influenced by reverse causation, and assuming an absence of pleiotropy, can provide un-confounded estimates of disease risk. This project aims to systematically evaluate the etiological relevance for broader panel of putative risk factors in multiple cancers using two complementary observational epidemiological approaches; two-sample Mendelian randomization (MR) and direct risk factor analysis in longitudinal cohort studies.
Design: Two types of data will be used in this project; i) large-scale genome-wide-association study data that will be used to 'look-up' risk-factor associated SNPs (i.e. instrumental variables) for MR analyses of putative risk factors, and ii) directly measured risk factors data in large population cohorts with long-term follow-up for incident cancers that will be used to evaluate cancer risk associations using standard methods for analyzing longitudinal data. Cancers of interest for which we have data on include pancreatic, kidney, lung, and head & neck cancers. We intend to interrogate both a) a pre-defined list of putative risk factors, including obesity-related anthropo- metric measures and related biomarkers (e.g. insulin and inflammation biomarkers), as well as b) a broader panels of biomarkers measured through state-of-the-arts Omics platforms (e.g. proteomics) that will allow for a hypothesis-free approach to identify novel risk factors.
Expected results and impact: We believe that adopting two complementary observational approaches in tandem has a strong potential to conclusively establish (or reject) the causal role of putative risk factors. We hope to answer important questions regarding the etiological relevance of several pre-defined risk factors, as well as to identify novel causal biomarkers that might be targeted for preventive measures.

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **31**

GEN4 - GEM 4.2.6 Cross-agency Collaborations on Lung Cancer Screening

Content

Introduction: Multiple randomized trials have demonstrated that low-dose CT lung cancer screening can reduce lung cancer mortality among people with a heavy smoking history. In 2019, GEP scientist Dr. Robbins co-founded the IARC Lung Cancer Screening Working Group with SCR scientist Dr. Andre Carvalho. The group is well-positioned to contribute to its mission of advancing scientific collaboration in lung cancer screening research. Thus far, WHO has not endorsed population-based lung screening, but there is rapid movement toward implementation in many countries around the world.
Design: In the context of this working group, GEM will lead and contribute to projects for which its expertise and resources are specifically relevant. These projects include: (1) development and validation of lung cancer risk prediction models in the Lung Cancer Cohort Consortium; (2) modeling benefits, harms, and cost-effectiveness of lung screening in France; (3) identifying sources of variation in overdiagnosis estimates from lung cancer screening trials; and (4) implementation study of lung screening in Belarus. Funding has been successfully acquired from the US NCI (R03, PI Robbins and U19 supplement, PI Robbins/Johansson/Brennan), the French National Cancer Institute (DEPREV, PI Robbins), and the Lung Cancer Research Foundation (PI Robbins).
Expected results and impact: These projects will clarify various aspects of lung screening including the role of risk prediction, the international landscape for implementation, and potential harms of the screening process. They address IARC's emerging priorities including implementation re- search, cancer disparities, and economic evaluations.

Primary authors: ROBBINS, Hilary (IARC); CARVALHO, Andre (IARC); CHARVAT, Hadrien (Formerly Section of Cancer Surveillance, IARC, France); VACCARELLA, Salvatore (IARC); LI, MengMeng (IARC); JOHANSSON, Mattias (IARC)

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **33**

GEN5 - GEM 4.2.10 Integrated Omics analysis into Renal Cancer Incidence and Survival – the KidOmics project

Content

Introduction: In 2014, we identified a novel risk factor of RCC onset and survival, namely circulating pyridoxal 5'phosphate (PLP) – the active form of vitamin B6. This initial study was based on pre-diagnostic case-control pairs from two large population cohorts and identified strong inverse associations between pre-diagnostic blood PLP concentrations and RCC risk, as well as survival following renal cancer diagnosis. We subsequently followed-up on the survival signal using pre- treatment blood from 630 newly diagnosed RCC cases from two case-series. Between the top and bottom PLP quartiles, we saw 3-fold survival differences for all cause-mortality (HR: 0.33, 95%CI: 0.18-0.60) and 5-fold survival differences for renal cancer-specific death (HR: 0.22, 95%CI: 0.11-0.46)
– after accounting for disease stage. These results suggested that PLP may prove to be the most informative circulating biomarker for renal cancer prognostics identified to date. However, fully understanding the mechanistic background to these observations warrant large-scale integrative Omics studies on RCC tumors with matched blood samples.
Design: The foundation of the KidOmics project is the Mutographs renal cancer case-series with whole-genome sequencing data on 1,000 renal cancer cases. We will initially enrich the study sample by generating RNA sequencing and blood proteomics data on all 1,000 renal cancer Mutographs cases. These data will subsequently be used to identify genes and circulating proteins associated with RCC survival through a series of integrative bioinformatical analyses, both agnostically and with a focus on already identified renal cancer genes. This data will also allow us to evaluate if identified renal cancer genes/proteins can account for and/or improve upon the RCC prognostic information of circulating PLP. Finally, we will evaluate if RCC proteins also pre-dispose incident disease using pre-diagnostic blood samples from two US population cohorts.
Expected results: We believe that this project has a strong potential to clarify our specific research questions related to PLP in renal cancer etiology, and specifically identify novel minimally invasive biomarkers that may be used for RCC prognosis in the clinic. In support of this, preliminary pilot blood proteomics data on a case-cohort of 149 newly diagnosed renal cancer cases identified 20 individual proteins associated with renal cancer survival after accounting for multiple testing. In addition, the project will also establish a rich infrastructure for molecular studies of RCC that will allow for a wide variety of integrative tumor genomics analyses across three layers of Omics data on 1,000 RCC cases, including WGS, RNAseq and blood proteomics data.

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Track Classification: GEN - GEN

Status: SUBMITTED

Abstract ID: **34**

GEN6 - GEM 4.2.13 MESOMICS: French project of multi-omic characterization of malignant pleural mesothelioma

Content

Introduction: Malignant pleural mesothelioma (MPM) is a rare, aggressive cancer associated with asbestos exposure. Despite considerable progress in recent years in the molecular characterization of MPM, most genomic studies focused on a single 'omic technique resulting in a lack of deep and comprehensive characterizations. The MESOMICS project (http://rarecancersgenomics.com/mesomics/) aims to fill this gap and to help the discovery of predictive markers for etiology, early detection, classification, and treatment response.
Design: We have generated whole-genome sequencing, RNA-sequencing, and EPIC 850k methylation arrays data for 120 MPM of the three main histological types and subtypes. In addition, we have generated multi-regional multi-omic data for 12 MPM samples.
Expected results: We provide the first integrative multi-omic characterization of MPM. Our preliminary data reveal novel molecular profiles associated with histological types, etiology, and particular genomic features. We also identified a group of samples that might be candidates for immunotherapy, based on their molecular characteristics. Thus, we expect to provide an integrative molecular cartography with an informative value for classification, evolutionary trajectories, therapeutic response, as well as, clinical management. To translate the molecular insights directly to the clinic, we will integrate whole-slide image Artificial Intelligence (AI) data to assess its role in clinical management of MPM.
Impact: We expect to provide insights into the key molecular alterations and pathways in MPM, that can be integrated with clinical, epidemiological data and prognostic morphological features identified by AI, in order to improve MPM early detection, diagnosis, classification, and clinical management.

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Presenter: MANGIANTE, Lise (IARC)

Track Classification: GEN - GEN

Status: SUBMITTED

Abstract ID: **35**

GEN7 - GEM 4.2.15 Unveiling the molecular pathways underlying tumor evolution through mechanistic and computational model

Content

Introduction: Genomic studies have generated a plethora of hypotheses about the impact of somatic alterations on tumorigenesis which have yet to be tested. Organoids are revolutionary experimental models summarizing the anatomy and function of an organ. Patient-derived tumor organoids (PDTOs) have been derived for many common cancers, shedding light on disease progression and providing preclinical models for personalized treatments. Nevertheless, few models are available for rare cancers, and the analytical tools to infer biological processes from such data are scarce.
Design: (i) We will model disease initiation and progression using neuroendocrine PDTOs from multiple body sites and organoids of progenitor cells. We will use CRISPR/Cas9-mediated genome editing to introduce candidate alterations and monitor their molecular impact using multi-omic profiling (WGS, RNA-seq, and methylation arrays), projecting the organoids into the tumor maps generated in the lungNENomics project (http://rarecancersgenomics.com/lungnenomics). (ii) We will develop analytical frameworks to monitor intra-tumor heterogeneity (ITH) through time using robust descriptive statistics of molecular diversity spanning multiple 'omic layers. We will also develop methods to infer tumor growth patterns and natural selection from time-sampled data using large reconstructed genealogies.
Results: We have generated and analyzed data for 14 PDTOs: 6 lung carcinoids, 3 LCNEC, 4 small intestine NETs, and 1 pancreatic NEC. These data confirmed that the PDTOs faithfully summarize the ITH. We are now testing the genome-editing process.
Impact: The project will advance our understanding of the causes of the development of under- studied rare cancers, and help refine the classification of tumors.

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Presenter: ALCALA, Nicolas (IARC)

Track Classification: GEN – GEN

Abstract ID: **38**

GEN8 - GEM 4.2.16 Genomic basis of hereditary breast and ovarian cancer in admixed populations

Content

Introduction: Hereditary Breast and Ovarian Cancer syndrome (HBOC) is a genetic condition associated with an increased risk of breast and/or ovarian cancer with cancers being also diagnosed at a younger age. The genomic bases of HBOC have been studied almost exclusively in people of European ancestry. Additional research is needed to identify both genetic and non-genetic determinants of HBOC among women with admixed ancestry. Latin America (LA) is a representative region of a current epidemiological transition and the presence of admixed ethnicity. Additional germline alterations in cancer related genes not yet described could contribute to HBOC development in admixed populations. The effect of lifestyle modifying risk factors might differ in these cases compared to cases of European origin.

Design: The Latin American consortium for HBOC-LACAM aims to recruit a large series of 3000 cases in 6 LA countries with biological samples and epidemiological and clinical questionnaires. Genomic techniques (targeted sequencing and genotyping arrays) will be used to characterize genomic alterations in cancer susceptibility genes in particular for genes not previously associated with HBOC. An extended lifestyle and clinical questionnaire will allow us to identify non-genetic modifying risk factors that could be potentially relevant for preventive interventions and improve the selection of high-risk individuals with tailored risk prediction models.

Expected results and impact: To improve our understanding of the underlying genetic architecture of breast cancer in young and high-risk women accounting for the admixture component. These results will establish the foundation for translational studies in stratified prevention through com- prehensive breast cancer risk models.

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **39**

GEN9 - GEM 4.2.17 Understanding the causes of late diagnosis of head and neck cancer

Content

Introduction: Most individuals with head and neck cancer (HNC) present with advanced disease. Stage at diagnosis is the major driver in poor survival from HNC. Within the European ARCAGE study 35% of cases presented with advanced metastatic stage IV disease, whereas 57% of cases did in the South American InterCHANGE study. Stage at diagnosis is a primary reason for poor survival from HNC, especially in South America. The objectives here are to 1) identify main factors associated with time between first symptoms and time of diagnosis, including patient-related and medical infrastructure-related factors; 2) assess inequalities in late stage of presentation of HNC – focusing on socioeconomic, logistical (healthcare system), and biological (tumour) factors.
Design: Interviews with targeted questions on aspects affecting patient delay will be conducted with 1100 patients across 12 recruitment centers. In-depth semi-structured interviews will be con- ducted in 2 centers with HNC survivors, clinicians/healthcare staff. Process mapping of the HNC healthcare system will be coordinated across each center.
Expected Results: This approach will allow for the following: 1) explore knowledge, attitudes, and beliefs in relation to the healthcare system; 2) identify barriers/facilitators across the pathway to early detection and diagnosis of HNCs; 3) evaluate compliance to National Comprehensive Cancer Network (NCCN) guidelines; 4) propose guideline amendments considering regional differences in treatment availability.
Impact: The comprehensive approach to understand late diagnosis beyond genomics ensures that we have complete analyses of the reasons underpinning late diagnoses of HNC cancer from the socio-demographic, cultural, societal, organizational and biological view.

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **40**

GEN10 - GEM 4.2.18 Genomic characterization of oral pre-neoplasia

Content

Introduction: Oral potentially malignant disorders (OPMDs) have an estimated global prevalence of 4.47% and can confer a 5–100 times increased risk for oral squamous cell carcinoma (OSCC) development. Tobacco, alcohol consumption and chewing betel quid, are well-established risk factors, although idiopathic cases which exhibit higher rates of malignant transformation have been reported. The current knowledge on the natural history of OPMDs is still limited. Therefore, this study was designed to understand the major genomic alterations leading to the development of OPMDs and their association with etiological risk factors to enable the identification of biological pathways and routes of carcinogenic processes and eventually indicate potential biomarkers of malignant transformation.
Design: Whole exome sequencing of a retrospective collection of OPMDs will be conducted to explore the association of mutational signatures and driver mutations with known risk factors and to describe the microbiota of OPMDs and evaluate the presence of transcriptionally active HPV. In parallel, we will establish a multicentric prospective collection of biological samples and clinical follow up from OPMDs to allow for future sequencing studies with a specific focus on complementary genomic analyses and evaluation of the potential use of noninvasive biomarkers for OPMDs early detection and prognosis.
Expected results: To unravel the natural history of OPMDs by elucidating the mutagenic processes attributed to different exposures or biological process that are driving the development of OPMDs.
Impact: Ultimately, our findings may identify biomarkers of malignant transformation useful for risk prediction and implementation of prevention strategies.

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Presenter: DE CARVALHO, Carol (IARC)

Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **41**

GEN11 - GEM 4.2.19 CLINITERT: Towards clinical implementation of urinary TERT promoter mutations as biomarkers for monitoring minimal residual disease or recurrence of urothelial cancer

Content

Introduction: There is a tremendous need for robust and cost-effective non-invasive bladder cancer (BC) biomarkers to complement or replace the gold-standard cystoscopy for the early detection and monitoring of this highly recurrent disease. We have shown that TERT promoter mutations, the most common mutations in BC, detected in urinary DNA (uTERTpm) have excellent sensitivity and specificity for the detection of all forms of the disease and were also detectable in urine of asymptomatic individuals years prior to clinical diagnosis. The potential of uTERTpm as markers of BC recurrence, however, requires further investigations.
Design: Using our validated droplet droplet assays, we will screen for uTERTpm in post-diagnostic urine samples of BC cases (n=54) currently under regular medical surveillance to investigate whether uTERTpm could indicate post-surgery minimal residual disease or whether mutation load evolution could be modelled to predict BC relapse.
Expected Results: In July 2019 uTERTpm detected in follow-up urine samples were predictive of BC recurrence in 17 of 18 cases (sensitivity of 94.4%). Out of 31 disease-free patients, 19 patients tested positive in post-diagnostic urine samples (15 at low-level mutation). Complete 5-year follow-up will enable to evaluate the true specificity of the markers.
Impact: uTERTpm biomarkers may profoundly change BC clinical management. It could improve BC monitoring by complementing or replacing urine cytology or existing urine-based markers, which lack sensitivity and specificity for clinical utility. It could also provide a substitute to cystoscopy avoiding the discomfort and the risk of complications while reducing high costs associated to BC clinical management.

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **42**

GEN12-GEM4.2.20 OPICO: Understanding the role of opioids in cancer onset

Content

Introduction: The recent crisis of opioid overuse has affected many countries. Emerging evidence on the tumor promoting and chromosomal damaging effects of some opioids, and the identification of opioid receptors in cancer tissues and their roles in tumor development, have raised substantial concerns on the long-term effects of using opioids.
Design: We are initiating the opioid cohort consortium (OPICO) to address the long-term health consequences of using opioids by organizing data on opioid use from large-scale prospective cohorts around the world. We will harmonize data from contributing cohorts and assess the risk of cancer incidence and mortality among opioid users. We will then link the harmonized data to the whole genome sequencing data and perform genome-wide association studies, and if applicable Mendelian Randomization studies to investigate the possible causal associations between regular opioid use and cancer onset.
Expected Results: This project will provide the most reliable evidence on the relationship between using different types, doses, and routes of opioids and risk of developing cancers. The results of the genetic epidemiology analysis will further allow triangulation of evidence to assess causal relationships between using opioids and cancer development.
Impact: OPICO will serve as a strong international resource for multidisciplinary studies on using opioids and their health consequences. By providing insights on the harms of regular opioid prescriptions, our results could aid in the development of evidence-based guidelines for using opioids in chronic pain management, as well as comprehensive prevention policies to reduce the long-term health-related and economic harms of opioid use.

Primary authors: SHEIKH, Mahdi (IARC); ROBBINS, Hilary (IARC); BRENNAN, Paul (IARC)

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Track Classification: GEN - GEN

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **43**

INF1 - Epidemiology of anal human papillomavirus infection and high-grade lesions in men, according to age, sexuality, and HIV status: an IARC-led collaborative pooled analysis

Content

Introduction: Prevalence of anal human papillomavirus (HPV) and high-grade squamous intraepithelial lesions (HSIL) in men by age are still unknown.
Design: We re-analysed individual-level data from 58 studies totalling 26,738 men across four risk groups: HIV-positive men who have sex with men (MSM), HIV-negative MSM, HIV-positive men who have sex with women (MSW) and HIV-negative MSW. Pooled estimates of high-risk (HR) HPV and HSIL or worse (HSIL+) were compared using adjusted prevalence ratios (aPR).
Results: Anal HPV prevalence was lowest among HIV-negative MSW (HPV16=1·7%; HR-HPV=6·6%), followed by HIV-positive MSW (8·1%; 26·2%) and HIV-negative MSM (13·5%; 40·9%), and highest in HIV-positive MSM (28·6%; 73·3%). Among HIV-positive MSM, HR-HPV prevalence increased from 15-18 (55·9%) to 23-24 years (74·5%) (ptrend<0·001), then declined from 25-34 (77·3%) to ≥55 years (65·1%) (ptrend<0·001). HR-HPV in HIV-negative MSM also increased from 15-18 (23.9%) to 23-24 years (43·6%) (ptrend=0·011), plateauing thereafter (ptrend=0·622). No significant differences were found by age for either HIV-positive or
HIV-negative MSW. HIV was a determinant of HSIL+ (aPR=1·54, 95%CI 1·37-1·74) and HPV16- positive HSIL+ (1·65, 1·34-2·02) among MSM, even when restricted to HPV16-positive MSM (1·20, 1·04-1·38), while age was not.
Discussion: Rapidly increasing anal HR-HPV prevalence among younger MSM highlights the benefits of gender-neutral HPV vaccination prior to sexual debut over catch-up vaccination.
HIV-positive MSM should be the priority for anal cancer screening programmes, targeting HPV16- positive HSIL+.
Conclusion: Robust age-specific anal HPV and HSIL+ prevalence estimates inform the impact of both primary and secondary prevention of anal cancer.

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Presenter: WEI, Feixue

Track Classification: INF - INF

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **44**

INF2 - Epstein-Barr virus-associated gastric cancer: a global meta-analysis

Content

Introduction: Over 1 million new cases of stomach cancer occur each year. Some evidence suggests that Epstein-Barr virus (EBV), a known carcinogenic agent, may be associated with a fraction of gastric adenocarcinoma. Our aim was to provide an estimate of the global proportion of EBV- associated gastric cancer.
Design: A systematic review and meta-analysis were conducted on eight databases until end September 2020. Representative studies with more than 20 patients, which assessed EBV prevalence in tumour tissue by in-situ hybridization for EBV-encoded small RNA were included. Risk ratio (RR) analyses were conducted for gender, the anatomical region of the stomach, and Lauren's classification.
Results: 214 studies including 66,344 cases of gastric adenocarcinoma were included. The pooled prevalence of EBV was estimated to be 7.0% (95% confidence interval (CI): 7.0–8.0). RR analysis showed an increase in the risk for tumours arising in men versus women (RR 2.30 [95%CI: 2.07– 2.54]), in the proximal region of the stomach compared to the distal region, (RR 1.97 [95%CI: 1.77– 2.18]), and in diffused type versus intestinal type (RR 1.38 [95%CI: 1.24–1.53]). There was no clear difference in RR by region, but certain regions such as sub-Saharan Africa and Oceania were under- represented.
Conclusion: EBV was more prevalent among men, in the proximal region of the stomach, or in diffused histological type. Worldwide, 7% prevalence of EBV in gastric adenocarcinoma suggests 70,000 adenocarcinoma cases per year may be associated with EBV.

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Presenter: HIRABAYASHI, Mayo (IARC)

Track Classification: INF - INF

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **45**

INF3 - Laboratory tools for epidemiological studies on virus-induced cancers

Content

Introduction: The development of sensitive and robust assays for the detection of nucleic acids of infectious agents is a key step to perform epidemiological studies.
Design: We have established a platform to detect approximately 250 infectious agents that include more than 190 viruses (e.g. alpha-Papillomaviruses, beta-Papillomaviruses, gamma-Papillomaviruses, Polyomaviruses and Herpesviruses) and bacteria that colonize, the oral cavity, the gut and genital tract. This assay combines two different steps: (i) multiplex PCRs using type-specific primers for the amplification of viral and bacterial DNA and (ii) typing assays using bead-based hybridization (LUMINEX® technology).
Results: Due to its high throughput, flexibility and robustness, the platform can be used to address various scientific questions both in biological and epidemiological studies. We have shown that these highly sensitive and reliable luminex-based assays are extremely valuable tools for epidemiological studies aimed at determining the prevalence of infectious agents, and evaluate their potential role in human disease. In addition, the high specificity and sensitivity of our luminex- based assays allowed the identification of viral biomarkers in body fluids, e.g. urine and blood, offering the possibility to use affordable and noninvasive procedures in epidemiological studies as well as in clinical routine setting.
Conclusion: The high sensitivity of the assay allowed the completion of epidemiological studies with limited amount of specimen available, archive material of bad quality, and specimens that are representative of the primary site of infection, and where viral DNA is present as contaminant (e.g. HPV in saliva or oral gargles, urine for monitoring HPV infection in the cervix).

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Presenter: GHEIT, Tarik (IARC)

Track Classification: INF - INF

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **46**

INF4 - Functional studies on oncogenic viruses

Content

Introduction: Infectious agents represent a major group of risk factors for cancer development and contribute to about 13% of human cancer worldwide. Different lines of evidence support the involvement of additional infectious agents in human carcinogenesis. In line with the mission of IARC to identify the causes of human cancers and reduce cancer burden, our aim is to discover new associations between infections and cancer.
Design: In the last decade, our group has developed several in vitro and in vivo experimental models to characterize the biological properties of specific infectious agents
Results: Our findings highlighted a new model of virus-mediated carcinogenesis, in which cutaneous β-HPV type 38 cooperates with ultraviolet (UV) radiation in the development of cutaneous squamous cell carcinoma (cSCC). HPV38 appear to be required only at an early stage of carcinogenesis, facilitating the accumulation of UV-induced DNA mutations. However, after full cSCC establishment, this virus is dispensable for the maintenance of the cancer phenotype. These biological properties of HPV38 are in part explained by its ability to deregulate p53 and integrin network.
In an independent study, we have characterized the biological properties of a novel putative human Polyomavirus, Lyon IARC polyomavirus (LIPyV) that has been recently isolated by our group. Our findings show that LIPyV early proteins display transforming activities in primary human epithelial cells.
Conclusion: Our studies support the hypotheses that additional human cancers are associated with viral infections.

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Track Classification: INF - INF

Status: SUBMITTED

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Abstract ID: **47**

LSB1 - The Biobank and Population Cohort Network (BCNet)

Content

In contrast to many high-income countries where support might be committed for the long-term development of research infrastructure facilities, such as biobanks, the latter are much less developed in LMICs. This constitutes a serious barrier to high-quality scientific research projects in LMICs. In line with IARC's and WHO's mission in contributing to worldwide cancer research, and in collaboration with the US National Cancer Institute - Centre for Global Health (NCI-CGH) and other international partners, a biobank network (BCNet) was set up as an opportunity for LMIC to work together in a coordinated and effective manner and jointly address the shortfalls in biobanking infrastructure and other shared challenges, including ethical, legal and social issues.

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Track Classification: LSB - LSB

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **48**

LSB2 - The IARC Laboratory Services

Content

The IARC LSB provides core laboratory and biobank support to the Agency's research activities, now and in the Nouveau Centre as well as technical and safety needs. The following core activities are provided:

- Optimal laboratory services such as the laboratory stores, glass washing facilities, mycoplasma testing, quarantine, and pipette checking. The LSB oversees the common laboratory platforms and ensures equipment is well maintained.
- Health and Safety, as aligned with international guidelines, applies to all IARC members of staff and the many visitors to the Agency. The security manual has been completely re-written to be- come a key document at IARC. Additionally LSB organizes IARC's authorizations for the restricted use of genetically modified organisms (GMO), of carcinogenic substances, as well as the authorization to house and use radionuclides.

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Track Classification: LSB - LSB

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **49**

LSB3 - The IARC Biobank: A Research Infrastructure supporting Global Operations

Content

Medical research in the era of precision medicine is based on the analysis of samples with clinical data – and, because the associations are often weak, both these samples and data are required in large quantities. The implication is clear: the more well-characterized, high-quality samples and associated data are available through biobanks, the faster research will advance and impact the delivery of healthcare today.
Therefore, there is a growing requirement on the IARC biobank to have increased operational capacity and sufficient informatics capabilities in order to ensure these demands are met. As a consequence, modern biobanking is shifting its focus from sample-driven to data-driven strategies. The Smart and Open Biobank for the IARC Nouveau Centre incorporates these aspects into its designs for the long-term support of the Agency activities.

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Track Classification: LSB - LSB

Status: SUBMITTED

Submitted on **Friday 11 December 2020**

Abstract ID: **61**

MCA1 - The role of asbestos exposure in ovarian carcinogenesis: an integrative molecular epidemiological study

Content

Epidemiological studies suggest a causal role of environmental and occupational exposure to asbestos in ovarian carcinogenesis, prompting IARC to classify asbestos fibers as ovarian carcinogen. Here we integrated epidemiology, exposure assessment and genome-scale analysis approaches to investigate the association between asbestos exposure and ovarian cancer histological subtypes, and to determine whether asbestos associates with specific genome-scale mutational signatures. Of the 254 patients with epithelial ovarian tumor included in the study, we estimated that 13.4% had been exposed to asbestos occupationally and 16.5% had possibly been exposed indirectly, at varying levels, via a close relative. The prevalence of direct exposure appeared higher than in the general population. We did not observe significant association between asbestos exposure and the high-grade serous epithelial tumor subtype.

Whole-genome sequencing of FFPE-preserved tumors and matched normal tissues of 25 cases with established mode, probability and levels of exposure identified mutational signatures SBS1 (age), indel-based ID1/ID2 (replication errors), ID16, APOBEC signatures SBS2/SBS13 and SBS26 (MMR deficiency) enriched in exposed patients. Signatures SBS3 (BRCA1/2 deficiency), SBS8 (un- known etiology) and ID10 associated with unexposed patients. These findings suggest exposure- associated mutagenic processes underlying cancer-cell natural selection. Next, genome-wide mutagenesis by chrysotile asbestos was studied in an in vitro clonal cell immortalization system, revealing exposure-specific induction of oxidative DNA damage (elevated signature SBS18) and in- creased mapping of a mechanistic template mutation matrix representing oxidative DNA damage. Our integrated molecular epidemiology study provides new mechanistic insights into the environmental and occupational exposure to asbestos as an important risk factor underlying ovarian carcinogenesis.

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Track Classification: MCA - MCA

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **62**

MCA2 - Mutational signatures of nicotine-derived nitrosamine ketone: implications for tobacco-associated cancers

Content

Somatic mutations contribute to tumorigenesis and cancer genome sequencing studies have substantially enhanced our knowledge of their origins and functional impact. Mutational signatures, specific mathematical readouts of global mutagenic effects, associate with cell-endogenous processes or extrinsic exposures. The signature of tobacco exposure is more complex than that of its well-studied major carcinogenic component benzo[a]pyrene (B[a]P), while little is known about mutation spectra of other tobacco compounds.

Using controlled exposure of a lung cell line A549, followed by single-cell subcloning and genome- scale sequencing, we identified a novel and reproducible mutational signature of nicotine-derived nitrosamine ketone (NNK), a rodent carcinogen and common ingredient of nicotine delivery systems. It is mainly characterized by T>A, T>C and T>G alterations, with transcriptional strand bias toward more mutated T than A on the untranscribed strands of genes, consistent with the presence of O2-POB-thymidine DNA adducts found in A549 cells treated with NNK. Interestingly, characteristic mutation spectra associated with NNK exposure were not detected in another lung cell line (BEAS-2B), despite a comparable formation of the O2-POB-thymidine adduct, an observation raising the possibility of DNA repair-dependent differences in the accumulation of the signature. We currently use targeted bioinformatics approaches and synthetic genome modeling to screen for the experimentally derived NNK signature in public genome-sequencing data from smoking- associated cancers. This work will enhance our mechanistic understanding of the contribution of components of nicotine delivery systems to the mutation profile of cancer, which is of critical importance for developing appropriate molecular markers for cancer prevention and regulatory strategies.

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Track Classification: MCA - MCA

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **63**

MCA3 - Genome topography remodelling during mutagen-driven primary cell immortalization: A multi-omics approach

Content

Chromatin-associated proteins play key roles in numerous cellular processes, determining the cell fates including cell immortalization, a hallmark of cancer. Key mechanisms emerged linking exogenous insults by carcinogens to complex genome topography changes and consequent deregulation of gene expression underlying cell transformation and tumorigenesis.
To understand these complex changes, we used primary mouse embryonic fibroblasts (MEF) with human TP53 gene knock-in, as a model recapitulating major (epi)genomic cancer driver events. The MEFs were exposed to different carcinogens, immortalized via senescence bypass and analyzed for genome-scale mutational signatures (WGS) and associated global functional impact at the level of chromatin structure (ATAC-seq), histone modification (ChIP-seq), DNA methylation (RRBS) and transcriptome remodeling (RNA-seq).
The transition toward cell transformation revealed deregulation of cell adhesion, cell cycle, cell proliferation, cell differentiation and DNA repair. A number of cancer signaling pathways (MAPK, TP53, ATM, ATR, BRCA1) were commonly deregulated. Transformation-specific changes in chromatin accessibility and epigenetic profiles were addressed by integrating ATAC-seq analysis and DNA methylation changes. The functional contribution of acquired mutations to changes in the gene regulatory landscape will be cross-compared to analogous data from human cancer genomics repositories. Ongoing work involves MEFs harbouring conditional knockout of the chromatin remodeller Smarca5, to address its specific role in the global changes in chromatin accessibility, local susceptibility to mutagenesis, histone modification, DNA methylome patterns and transcriptome remodelling.
Our integrative multi-omics analysis systematically explores the functional link between global mutagenesis by carcinogens, dynamic chromatin landscape and transcriptome changes with the phenotypic transitions between the primary and immortalized cell states.

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Track Classification: MCA - MCA

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **64**

MCA4 - Pan-cancer multi-omics analysis and orthogonal experimental assessment of epigenetic driver genes.

Content

Recent genome sequencing studies have shown that mutations in the genes encoding epigenetic regulators are highly frequent and common in cancer. This constitutes a “genetic smoking gun”, whereby epigenetic mechanisms lie at the very heart of cancer biology and that altered epigenetic states play a key role in its onset and progression. To identify epigenetic drivers (epidrivers) of cancer, we conducted a pan-cancer analysis integrating (epi)genome and transcriptome alterations in 426 epigenetic regulator genes (ERGs) across 33 cancer types. We found that, in addition to mutations, copy number alterations in ERGs, which were tightly linked to expression aberrations, were more frequent than previously anticipated further arguing that deregulation of ERGs is a widespread phenomenon in almost all malignancies. We then developed and applied novel multi- Omics and Pan-Cancer Driver prediction tools revealing ERGs with driver potential whithin and pan-cancer. We further established and tested a conceptual framework to identify and validate in cellular models functionally important epidrivers through a novel systematic approach integrating the strengths of state-of-the-art genome-editing screens (CRISPR/Cas9). This revealed ERGs with driver roles within and across malignancies which is consistent with the notion of a shared driver mechanism operating across multiple cancers. Our study represents the largest and most comprehensive analysis thus far of the cancer-associated disruption of ERGs complemented with experimental efforts identifying functionally important epidrivers of oncogenic processes. This will be further extended to investigate whether epidrivers are centrally involved in mediating the effect of environmental exposures onto (epi)genome disruption patterns and critical events of carcinogenesis.

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Track Classification: MCA - MCA

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **65**

MCA5 - DNA methylation signatures in whole blood as predictors of breast cancer risk

Content

Epigenetic changes in surrogate tissue have emerged as promising markers of cancer risk. How- ever, much of the current evidence is based on findings in retrospective studies, and may reflect epi- genetic patterns that have already been influenced by the onset of the disease. Here, we established genome-scale DNA methylation profiles of a prospective collection of blood samples from 696 participants in a nested case-control study by reduced representation bisulphite sequencing (RRBS). We applied machine learning classification algorithms in conjunction with backward feature selection to identify a panel of 440 DNA methylation events that could discriminate participants who developed breast cancer over the course of follow-up from matched controls. Moreover, we observed that methylation levels in 154 of these predictors were significantly correlated with length of time to diagnosis. RRBS analyses of breast tumour tissue obtained from a subset of the cases revealed that the blood-based methylation markers were largely distinct from tumour-specific methylation markers. Genomic region enrichment analyses on the blood-based and tissue-specific differentially methylated regions (DMRs), however, show that the epigenetic events in both tissues share enrichment for the binding sites of mitogen-activated protein kinase kinase (MEK) effectors c-myc, c-Fos or c-Jun. Taken together, our findings provide evidence that epigenetic profiles in blood associated with cancer risk can be detected years before clinical manifestation of cancer and reveals attractive markers for risk stratification, and, ultimately, the targeted prevention of cancer.

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Presenter: CHUNG, Felicia (IARC)

Abstract ID: **66**

MCA6 - Early-Life Factors and Epigenetic Precursors of Childhood Cancer

Content

Introduction: Exposure-health risks depend on vulnerability windows, a major one being fetal life due to the capacity for alterations in cell fate. Epigenetic mechanisms are crucial herein because of their heritable nature and driver role. We hypothesize that DNA methylation underlies pathways linking early-life factors to later disease onset, with focus on childhood cancer (CC) as the leading cause of disease-related mortality in children.
Design: We test our hypothesis through a three-way modelling in which we (1) screen for epigenetic markers of exposures in neonatal blood from large population based studies using DNA methylome-wide analyses, (2) investigate in a subset of cohorts enriched in nested cases, whether identified neonatal markers associate with CC risk, and (3) assess the proportions by which DNA methylation mediates such associations.
Results: We identified several genes differentially methylated between childhood leukemia cases (the most common type) and controls, with dependency on child sex and ethnicity. Among tested early-life factors, DNA methylation levels of a non-coding RNA mediated the effect between birth- weight (a collective proxy of in utero exposures) and childhood leukemia.
Discussion: This study is the first to interrogate at birth CC blood epigenome, reporting findings reproducible in several populations. It also represents a proof-of-concept for identifying early origins of cancer evident in blood samples since birth.
Conclusion: This work can afford new opportunities in identifying robust predictors of CC risk that serve for prevention, early-diagnosis and targeted therapy. Ongoing efforts aim to expand the scope to child brain tumors.

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Track Classification: MCA - MCA

Status: SUBMITTED

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Abstract ID: **67**

MCA7 - DNA methylome profiling of esophageal squamous cell carcinoma from high incidence regions of the world identifies potential markers for earlydetection

Content

Background: Esophageal squamous cell carcinoma (ESCC) is one of the most aggressive and lethal forms of cancer, and is often diagnosed at later stages, resulting in high mortality rates. Aberrant DNA methylation (DNAme) is an epigenetic mechanism involved in many cancers, including ESCC, however critical DNA methylation events driving ESCC development are poorly under- stood. Here, we aimed to investigate tumor-specific DNAme in ESCC cases from nine high incidence countries spanning the Asian ESCC belt, Africa ESCC corridor and South America.
Methods:
Infinium MethylationEPIC (HM850K) array was used on 108 tumors and 51 normal tissue adjacent to the tumor (NAT) for methylome analysis in the discovery phase. Replication of the selected targets was done on an independent set of 132 tumors and 36 NAT using targeted pyrosequencing. Results:
Methylome analysis comparing tumor and NAT identified 6,796 differentially methylated positions (DMPs) and 866 DMRs with 30% Δβ difference. The majority of the identified DMPs and the DMRs were hypermethylated in tumors, particularly in the promoters and gene-body regions. The top three prioritized genes for replication, namely PAX9, SIM2 and THSD4 had similar methylation differences in discovery (PAX9: Δβ=0.41, P<1.83x10-300; SIM2: Δβ=0.40, P<1.83x10-300; THSD4: Δβ=0.39, P=1.33x10-112) and replication sets (PAX9: Δβ=0.20, P=0.0008; SIM2: Δβ=0.30, P=3.38x10- 08; THSD4: Δβ=0.53, P=2.49x10-26).
Conclusion:
Our study identified novel, robust and early tumor-specific DNAme events in ESCC tumors across several high incidence populations of the world. These identified aberrant DNAme could be potentially developed into ESCC biomarkers for early detection in minimally invasive samples.

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Track Classification: MCA - MCA

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **68**

NME1 - An International Network of Microbiome Cohorts Nested within Colorectal Cancer Screening Programs – Concept, Feasibility and Future Directions

Content

Alterations in gut microbiome diversity may play a role in the development of chronic diseases, including cancers. However, robust evidence from prospective cohort studies is lacking because many have not prospectively collected faecal samples. This is inherently difficult/expensive, particularly if implemented within existing cohorts. A cost-effective approach is to nest new prospective population-based cohorts within colorectal cancer screening programs applying Faecal Immuno-chemical Tests (FIT), which can yield considerable microbiome information. Individual cohorts developed under comparable design protocols within different FIT-based screening programs may be pooled together for sufficient study power to assess major cancers, such as colorectal. Envisioned design elements are collection of detailed baseline and longitudinal epidemiologic, anthropometric, clinical and dietary/lifestyle data, FIT-samples and bio-specimens (e.g. blood/saliva), with follow-up linkage to disease registries for end-point assessments.

This concept, developed by IARC (Drs M. Gunter and M. Jenab) and US-NCI (Dr R. Sinha) scientists, was the focus of a meeting held in April 2019 at IARC. Representatives of European and American FIT-based colorectal cancer screening programs participated. Outcomes were general agreement on the concept and initiation of feasibility studies to assess recruitment, provision of informed consent, response rates (participation, questionnaire-based data collection) and logistics of FIT-sample collection. One feasibility study is underway in Italy and 3 others are planned (Ireland, Malta, Spain). Projects confirming microbiome stability, suitability, accuracy, and comparability in different stool-tests used in screening programs have been conducted. A large, multi-national prospective cohort with microbiome and detailed epidemiologic data will be a unique resource for cancer etiology research.

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Presenter: ZOUIOUICH, Semi (IARC)

Track Classification: NME - NME

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **69**

NME2 - Establishing an epidemiological study in Afghanistan: Kandahar Obesity Research

Content

Introduction: Due to rapid economic, social, and cultural changes the prevalence of obesity in Afghanistan is increasing, and dietary habits are shifting from the traditional pattern to a more westernized pattern, with concomitant increases in non-communicable diseases (NCDs).
Design: A population-based cross-sectional study was designed in Kandahar city and data were collected on socio-demographic characteristics, health history, anthropometry, physical activity and diet. We used stratified sampling to recruit an equal number of normal weight, overweight and obese participants. Body fat composition was analyzed using bioelectric impedance analysis (BIA) and blood, urine and stool samples were collected for biomarker analyses.
Results: The study included 712 participants (411 men and 301 women): 92% lived in urban areas, 73% were married, 42% were aged 20 to 30 years old, 51% were not formally educated, 79% were never smokers and 68% had central obesity. Regarding NCDs, 38% were hypertensive, 18% were diabetic, 30% had dyslipidemia, 36% had fatty liver disease and 50% were symptomatic for anxiety/depression.
Discussion: This is the first study which will assess dietary patterns, lifestyle factors and their as- sociation with obesity and metabolic health in Afghanistan. The data collected will constitute an invaluable resource for future studies on biomarkers or the microbiome and could be used to train future public health scientists in Afghanistan. The findings will also help in designing and implementing effective public health strategies to promote a healthy lifestyle and prevent the epidemic of overweight and obesity, and hence, reduce the burden of NCDs in the region.

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Track Classification: NME - NME

Status: SUBMITTED

Submitted on **Monday 14 December 2020**

Abstract ID: **70**

NME3 - Sex hormones and colorectal cancer: observational and Mendelian randomization analyses

Content

Introduction: Epidemiological studies evaluating associations between sex steroid hormones and colorectal cancer risk have yielded inconsistent results. We conducted complementary observational and Mendelian randomization (MR) analyses to elucidate the role of circulating levels of various sex hormones in colorectal cancer development.
Design: The relation of circulating sex hormone levels and colorectal cancer risk was studied in a nested case-control study of 1,120 postmenopausal women within the EPIC and NSHDS studies, and a whole cohort analysis of 333,530 participants enrolled in the UK Biobank. For the MR analyses, genetic variants robustly associated with sex hormone levels were identified and their association with colorectal cancer (42,866 cases/42,752 controls) was examined using two-sample methods.
Results: In the nested case-control study, a statistically non-significant positive association was found between circulating levels of estrone and colon cancer risk. No associations were found be- tween circulating levels of estradiol, free-estradiol, testosterone, and free-testosterone, androstenedione, DHEA, progesterone, and SHBG with colon cancer risk. In the UK Biobank, there was little evidence that circulating levels of testosterone were associated with colorectal cancer risk. We found a positive effect estimate for testosterone with colorectal cancer risk in the MR analyses, although alternative pathways may explain this result (i.e. pleiotropy). In the UK Biobank, higher SHBG levels were associated with greater colorectal cancer risk for women, but this result was unsupported by the MR analysis.
Discussion and Conclusion: These results from complementary observational and MR analyses provide little evidence of an association between endogenous sex hormones levels and colorectal cancer risk.

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Abstract ID: **71**

NME4 - Onco-Metabolomics – Application of Metabolomics methods for Exploration of Cancer Etiology and Biomarker Discovery

Content

Metabolomics assesses the totality of metabolic responses to environmental, lifestyle or dietary exposures and can be used to better understand their cancer risk associations and delineate underlying mechanisms. The newly formed Onco-Metabolomics Team at IARC aims to apply metabolomics methods to elucidate the role of nutritional exposures, the exposome and metabolic perturbations and their mechanisms in cancer development. It employs liquid-chromatography coupled with high-resolution mass-spectrometry to assess thousands of molecular features in biospecimens in high-throughput analyses compatible with large-scale epidemiologic studies, such as those from the European Prospective Investigation into Cancer (EPIC). Extensive effort has been placed into custom development of analytical methods, bioinformatics, and data management tools to enable robust metabolomic analyses, metabolite identification, and biological interpretation of findings. A major example is our recent publication on hepatocellular carcinoma in EPIC showing major differences in cases vs controls for 92 distinct metabolites from various metabolic pathways and dietary exposures, up to 10 years prior to diagnosis. The Team also specializes in identifying novel biomarkers of dietary exposures. A recent effort utilized a controlled dietary intervention study and a cross-sectional study to identify syringol and pepper alkaloid metabolites as markers of smoked meat and sausage consumption, respectively. The Team also develops unique methods targeted at specific metabolic pathways, such as the tryptophan and serotonin metabolism pathway to study its role in colorectal cancer development. It brings together expertise in cancer- nutrition-metabolic epidemiology, laboratory analyses, and bioinformatics to establish itself as a world-leading group in the application of metabolomics to cancer epidemiology.

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Track Classification: NME - NME

Status: SUBMITTED

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Abstract ID: **72**

NME5 - Application of targeted metabolomics for identification of circulating markers of mammographic density in premenopausal women from the Mexican Teachers' Cohort

Content

Introduction: While mammographic density (MD) is one of the strongest risk factors for breast cancer, little is known about its modifiable determinants, especially in young women. Our aim was to apply targeted metabolomics to identify circulating metabolites specifically associated with MD in premenopausal women, to be used as markers of high density in a population where mammograms are often not available. In addition, we aimed at identifying potential modifiable determinants of these biomarkers, to support preventive actions.
Design: A total of 132 metabolites (acylcarnitines, amino acids, biogenic amines, glycerophospholipids, sphingolipids, hexose) were measured in plasma samples from 573 premenopausal participants in the Mexican Teachers' Cohort by tandem liquid chromatography/mass spectrometry. Associations between metabolites and percent MD (PMD) were assessed using linear regression models, adjusting for breast cancer risk factors and accounting for multiple tests. Mean concentrations of metabolites associated with PMD were estimated across levels of several lifestyle and metabolic factors.
Results: Sphingomyelin (SM) C16:1 and phosphatidylcholine (PC) ae C30:2 showed inverse associations with PMD after correction for multiple tests. Linear trends with PMD were observed for SM C16:1 only in women with body mass index below the median (27.4 kg/m²). SM C16:1 and PC ae C30:2 concentrations were positively associated with cholesterol (total and HDL), and decreased with increasing number of metabolic syndrome components.
Discussion: These findings, if replicated, will help better identify premenopausal women with a high MD, and will provide new perspectives regarding investigation of modifiable determinants of MD that will help support preventive actions.

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Track Classification: NME - NME

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Abstract ID: **73**

NME6 - The impact of pre-existing cardiometabolic comorbidities on all-cause and cancer-specific mortality among cancer survivors in the EPIC study

Content

Background: Chronic diseases are frequent among cancer survivors and these comorbidities might affect cancer survival. We investigated associations between pre-existing cardiometabolic comorbidities and all-cause and cancer-specific mortality among cancer survivors.
Design: 26,987 participants with a primary cancer diagnosed in the European Prospective Investigation into Cancer and Nutrition (EPIC) were included in the study. Cardiometabolic comorbidities were defined as either type-2 diabetes (T2D), cardiovascular disease (CVD: stroke or myocardial infarction) or both, diagnosed prior to cancer. Overall and cancer mortality hazard ratios (HR) and 95% confidence intervals (CI) were estimated in multivariable Cox-regression in relation to cardiometabolic conditions. We also performed analyses after stratification by cancer survivability (5-year net-survival 40%, 40-80, ≥80) and duration of comorbidities.
Results: During a mean follow-up of 7.2 years, 12,782 deaths were recorded. Pre-existing comorbidities were positively associated with all-cause mortality with HRs equal to 1.25 (95% CI: 1.17- 1.34), 1.30 (1.21-1.39), and 1.60 (1.42-1.80) for participants with T2D, CVD, or both, respectively, compared to absence of pre-existing comorbidity. Similar positive associations were observed for cancer-specific mortality. Associations were slightly stronger among participants diagnosed with more survivable cancers (≥80%), but no interaction with duration of comorbidities was observed. Discussion: We corroborate and go beyond existing evidence by investigating the combined impact of T2D and CVDs, and their duration, on all-cause and cancer-specific mortality among cancer survivors.
Conclusions: CVD and T2D occurring before cancer have a strong impact on cancer prognosis, thus calling for specific attention to cancer survivors with cardiometabolic comorbidities.

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Presenter: DAVILA BATISTA, Veronica (IARC)

Track Classification: NME - NME

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Abstract ID: **74**

NME7 - Alcohol and Cancer: New insights into an established relationship

Content

Introduction: Alcohol intake causes colorectal, liver, upper aero-digestive tract (UADT) and female breast cancers, but evidence with other cancer sites is inconsistent. Within the NCI Cohort Consortium we evaluated the associations between alcohol intake with UADT squamous cell carcinoma (SCC) and with thyroid cancer, overall and by smoking status.
Design: After pooling 36 cohorts from North America, Europe and Asia, UADT and thyroid cancer hazard ratios (HR) in relation to alcohol were obtained in two-stage analyses summarizing cohort- specific Cox regression HRs into a meta-analytical summary estimate.
Results: The UADT HR for a 12g/day increase in alcohol intake was 1.14 (95%CI: 1.10,1.18) in men and 1.24 (1.16,1.32) in women. In never-smokers, the HR for a 12g/day increase in alcohol intake was 1.15 (95%CI: 1.09,1.21) in men and HR 1.18 (1.07,1.30) in women. Similar patterns were observed for oral cavity, pharynx and larynx, and esophagus in both sexes. For thyroid cancer, a 12g/day increase in intake was 0.94 (0.90, 0.98) in men and 0.91 (0.87, 0.95) in women. Similar associations were found in papillary carcinomas, with a HR of 0.95 (0.90, 0.99) in men and 0.90 (0.85,0.95) in women.
Discussion: After accounting for the confounding role of smoking, alcohol was independently associated with UADT cancer in never-smokers, while an inverse association was observed with thyroid cancer, overall and by sub-site.
Conclusion: This is the largest pooled analysis on alcohol and cancer to date which allowed the relationship between alcohol and relatively rare cancers to be examined by subtype and smoking status.

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ETR - Learning and Capacity Building Branch

Content

Master presentation and video only - No abstract

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Track Classification: ETR - ETR

Status: SUBMITTED

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