# ECSA Scientific Week 2021

# Report of Contributions

Contribution ID: **11** Type: **Oral presentation**

# Shifting incidence and survival of epithelial ovarian cancer in seven countries (1995-2014)

*Monday, 22 March 2021 15:30 (12 minutes)*

In 2020, approximately 314,000 women were diagnosed with ovarian cancer and 207,000 deaths. The aim of the study is to provide a comprehensive assessment of the incidence of epithelial ovarian cancer (EOC) by histological subtypes and compare EOC survival across seven high income countries involved in the ICBP-SurvMark-2 project, (Australia, Canada, Denmark, Ireland, New Zealand, Norway, and the United Kingdom).

Incidence and survival analyses were limited to women diagnosed with ovarian cancer aged 15 years and older. Age standardized incidence rates (ASR) by subtype were calculated for all ages (15-99 years) and for two age groups (15-64 and 65+ years) by calendar year from 1995 to 2014. Net survival (NS) was estimated by subtypes, age groups, and 5-year study period (1995-2014) for all seven countries using the Pohar-Perme estimator.

Our findings showed serous carcinoma was the most common subtype across all age groups with ASR ranging between 8.3 per 100,000 women in Australia and 15.3 per 100,000 women in Norway for the 2010-2014 period. Substantial increase in serous carcinoma was observed between 2000-2014, particularly among women aged 65-99 years with statistically significant estimated annual percent change (EAPC) in Norway (EAPC=2.5%, 95% CI=0.8, 4.3), Australia (EAPC=2.6%, 95% CI=0.5, 4.7), and the United Kingdom (EAPC=5.8%, 95% CI=3.6, 8.0). In contrast, marked decrease in non-specific adenocarcinoma, NOS rate was observed in women aged 65-99 years with highest decrease observed in Australia (EAPC=-3.9%, 95% CI=-7.5, -0.2). Increase in cancer survival were also observed in the past 20 years for almost all EOC, except for adenocarcinoma, NOS where survival decreased. The highest survival increase was observed among women aged 65-99 years diagnosed with endometrioid carcinoma with median percentage point difference of 19.3% for 5-year NS across the seven countries.

In conclusion, this study highlights the rising incidence of serous carcinoma accompanied with a marked decrease in incidence of adenocarcinoma, NOS. Additionally, increase in survival was observed for almost all EOC subtypes across all seven countries. Progress in ovarian cancer staging, clinical management, and treatment over the past decades potentially plays a key role in the observed improvements in EOC survival.

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**Presenter:** CABASAG, Citadel (IARC)

**Session Classification:** Oral presentation

Contribution ID: **12** Type: **Lay audience presentation**

# Biomarkers for lung cancer screening

*Wednesday, 24 March 2021 16:30 (6 minutes)*

Lung cancer is the deadliest cancer in the world and its survival decreases with the stage at which it is diagnosed. It has been proven that screening people for lung cancer with low dose computed tomography (an X-ray machine that uses a small amount of radiation to make detailed images of the lungs) can reduce mortality by allowing to detect the cancer at an earlier stage when treatment are more effective.
However, currently this type of screening still has some limitations including missing half of future lung cancer cases, having a high detection of false positives (persons for whom the test suggest they have lung cancer when no cancer is present) which can lead to follow-up tests and surgeries that are not needed and may have more risks, and finding cases of cancer that may never have caused a problem for the patient (called overdiagnosis) which can lead to treatment that is not needed.
In this talk, I will explain how we used proteins measured in blood of healthy people to define their individual risk of getting a lung cancer and inform who should be screened.

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**Presenter:** GUIDA, Florence (IARC)

**Session Classification:** Lay audience session

Contribution ID: **14** Type: **Poster presentation**

# Exploring the “dark side”of the exposome

*Tuesday, 23 March 2021 17:00 (6 minutes)*

Only half of the global deaths in 2010 could be associated with known risk factors, namely smoking, alcohol, diet, environmental factors. It remains critical to build understanding around the remaining half of deaths occurring worldwide, and to identify other risk factors currently unknown or underestimated.
As a rule, extensive questionnaires are utilized to outline lifestyle and environmental exposures. Biomarkers also constitute a powerful and more objective way to assess such exposures. The advancement in mass spectrometry (MS) technologies has considerably expanded the coverage of the exposome. However, progress has been slowed down by limitations in our capacity to annotate unknown MS features and by the limited sensitivity to detect compounds present at low concentrations.
In this work, we applied a suspect screening approach to two epidemiological studies nested in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort (n=258 and n=466). Samples were analyzed on a UHPLC-QTOF-MS system with reversed-phase chromatography in both polarities.
In total, 101 metabolites derived from drugs, diet and food additives, contaminants, and gut microbial metabolism could be identified with high confidence (level 1 according to MSI standard). A large number of other MS features could also be annotated at level of confidence 2 or 3. Frequency of detection in the two sample sets will be presented. This new data will be used in future exposome-wide association studies in various cohorts.

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**Session Classification:** Poster session

Contribution ID: **15** Type: **Poster presentation**

# External validation of North American and European lung cancer risk prediction models in an Iranian population

*Monday, 22 March 2021 16:36 (6 minutes)*

Introduction: Some lung cancer screening guidelines recommend using individualized risk models to refer ever-smokers for screening. However, different models select different screening populations. The leading risk models were developed and validated in Western populations, and almost exclusively in non-Hispanic whites. Hence, there is an almost complete lack of evidence to support the deployment of existing risk models in settings beyond individuals of white race in North America and Europe. Our objective was to assess the performance of North American and European lung cancer risk models in an Iranian population. Models included the Prostate Lung Colorectal Ovarian model 2012 (PLCOm2012), Liverpool Lung Project model (LLP), Bach model, Lung Cancer Risk Assessment Tool (LCRAT), and Lung Cancer Death Risk Assessment Tool (LCDRAT). We also evaluated the additive information from novel risk factors (such as hookah and opium use) to the models.

Methods: We analysed current and former smokers from the Golestan Cohort Study (N=8662).
Calibration and discrimination were quantified respectively by the ratio of expected to observed cases (E/O) and the area under the ROC curve. Hazard ratios were estimated to quantify the association between risk factors and lung cancer in the Iranian population. A Cox regression model more appropriate for the Iranian population model was developed and internally validated with 5-fold cross validation.

Results: All models were overcalibrated (E/O>1). The best calibrated model was the Bach model (E/O=1.7 95%CI [1.3;2.2]).
Some effects of smoking were attenuated in the Iranian population compared with the Western models (e.g. smoking status comparing current with former smokers had a smaller effect in the Golestan version of the model with estimate of 0.08 vs 0.26 in the original model). A new model including age, body mass index, smoking intensity, smoking duration, history of chronic obstructive pulmonary diseases and opium use was developed. It performed well in the dataset with a cross-validated E/O of 1.27 95% CI [0.97; 1.64].

Conclusion: This study showed the limits in transportability of risk prediction models and the need to tailor them to each demographic. Incorporating novel risk factors relating to opium into the risk equation yielded a satisfactory predictive ability and calibration, ensuring accuracy of estimated risk scores.

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**Session Classification:** Poster session

Contribution ID: **16** Type: **Poster presentation**

# Papillary thyroid carcinoma genetic susceptibility factors in children exposed to radioiodine from Chernobyl fallout

*Monday, 22 March 2021 16:42 (6 minutes)*

Background: Statistically significant associations between papillary thyroid cancer (PTC) and specific common single nucleotide polymorphisms (SNP) in MGMT (rs2296675), promotor region of FOXE1 (rs1867277) and ATM (rs1801516) genes were reported in Belarusian children exposed to Iodine-131 (131I) after the Chernobyl nuclear power plant accident. We further pursued genetic determinants associated with individual susceptibility to radiation-related thyroid carcinoma (TC) within the framework of the EPITHYR consortium.
Methods: We investigated the associations between PTC risk and SNPs in candidate DNA repair genes, transcription factors (FOXE1, NKX2-1), growth factor (TGFBI), BRCA1 interacting protein (ZNF350), TSH receptor (TSHR) and RET signalling pathway genes (RET, GFRA1, EPAC) in 343 individuals who were <15 years old at the time of the Chernobyl accident, including 66 histologically verified PTC cases diagnosed between 1992 and 1998, and 277 population-based controls, genotyped using the OncoArray (Illumina). We used an arithmetic mean of 1,000 individual stochastic thyroid doses due to I-131 intake calculated using Monte-Carlo simulation method as radiation dose exposure. We evaluated the associations between 3,510 SNPs and PTC using logistic regression models assuming a log-additive allelic inheritance models and taking into account population stratification, and effects of age, sex and thyroid dose. We accounted for multiple testing by applying the Benjamini & Hochberg correction.
Results: We found some suggestive associations ($P < 0.001$) between PTC risk and polymorphism in the following genes: *POLN* (rs6830513, rs10018786, rs6855461) encoding DNA polymerase type-A family member involved in DNA repair and homologous recombination, and *RECQL* (rs3213212) involved in DNA repair. However, after adjustment for multiple testing, none of these SNPs remained statistically significant. Analyses on other possible pathways, as well as on potential gene-radiation interaction are ongoing.

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**Presenter:** ZUPUNSKI, L (International Agency for Research on Cancer, Lyon, France)

**Session Classification:** Poster session

Contribution ID: **17** Type: **Oral presentation**

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

*Tuesday, 23 March 2021 16:24 (12 minutes)*

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 SURVMARK 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 (oesophagus, 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.

Conclusion

The international benchmarking studies conducted show that cancer survival continues to increase globally; however, international disparities persist, particularly in LMICs. Future studies are needed to assess the impact of these factors to further our understanding of international disparities in cancer survival.

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**Presenter:** MORGAN, Eileen (IARC)

**Session Classification:** Oral presentation

Contribution ID: **18** Type: **Oral presentation**

# Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study

*Monday, 22 March 2021 15:42 (12 minutes)*

**Background:** Alcohol use is causally linked to multiple cancer sites. We present global, regional and national estimates of alcohol-attributable cancer burden in 2020 to inform alcohol policy and cancer control across different settings globally.

**Methods:** In this population-based study, we calculated population attributable fractions (PAFs) using relative risk estimates and alcohol use prevalence by age, sex, and country. Assuming a 10-year latency period between alcohol consumption and cancer occurrence, we used alcohol consumption prevalence from 2010 and GLOBOCAN 2020 data to estimate new cancer cases attributable to alcohol consumption. We also calculated the contribution of moderate (<20 g alcohol per day), risky (20 to 60 g per day), and heavy (>60 g per day) drinking to the total alcohol-attributable cancer burden.

**Results:** Globally, an estimated 725 000, or 4.0%, of all new cases of cancer in 2020 were attributable to alcohol consumption. Males represented 76% of the total alcohol-attributable cancer cases. The cancer sites which contributed the most alcohol-attributable cases were cancers of the oesophagus (190 000 cases), liver (155 000 cases), and breast (98 300 cases). PAFs were lowest in Northern Africa and Western Asia (less than 1%) in both sexes, and highest in Eastern Asia (8.5%) and Central and Eastern Europe (7.3%) in men, and in Central and Eastern Europe (3.4%), Western Europe (3.2%), and Australia and New Zealand (3.2%) in women. Risky and heavy drinking contributed most to the burden of alcohol-attributable cancers (39.5% and 46.5%, respectively), and moderate drinking contributed 14.0%.

**Conclusion:** Our findings highlight the need for effective policy and interventions to increase awareness of cancer risks associated with alcohol use and decrease overall alcohol consumption to avoid future rises in alcohol-attributable cancer burden in several regions of the world.

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**Session Classification:** Oral presentation

Contribution ID: **19** Type: **Oral presentation**

# Lifestyle, dietary, and anthropometric correlates of eight circulating metabolites prospectively associated with breast cancer risk in EPIC

*Tuesday, 23 March 2021 16:36 (12 minutes)*

Metabolomics is a promising molecular tool to identify novel etiologic pathways leading to cancer. Using a targeted approach in a prospective setting, we previously identified associations between 8 circulating metabolites (acetylcarnitine (positive association), arginine, asparagine, phosphatidylcholines (PCs) aa C36:3, ae C34:2, ae C36:2, ae C36:3 and ae C38:2 (negative associations)) and risk of breast cancer among women not using hormones at blood collection.

To identify possible novel preventive strategies, we conducted a cross-sectional analysis nested in the EPIC cohort to identify major correlates of circulating concentrations of these metabolites among lifestyle, anthropometric, and dietary factors. This work included 2358 women not using hormones at blood collection, defined as controls in previous case-control studies nested within EPIC, for whom concentrations of the 8 metabolites had been previously measured (AbsoluteIDQ p180 platform, Biocrates Life Sciences, Innsbruck, Austria). Associations of each metabolite concentration with 42 potential correlates were assessed using linear regression models adjusted for potential confounders in a discovery set of 1572 participants. Significant associations after correction of P-values for multiple testing were evaluated using the same models in a validation set of 786 women.

Concentrations of PCs ae C34:2, ae C36:2, ae C36:3 and ae C38:2 showed negative associations with adiposity, and positive associations with total and saturated fat intakes. PC ae C36:2 also showed a negative association with alcohol consumption, and positive associations with the WCRF/AICR lifestyle and the healthy living index scores. Asparagine concentrations were negatively associated with adiposity, and arginine concentrations were not associated to any of the factors examined. Acetylcarnitine concentrations were positively associated with age but with none of the other factors.

These associations bring new insights on possible mechanisms underlying associations between lifestyle and anthropometric factors and risk of breast cancer. Further work is needed to identify potential non-lifestyle correlates of arginine and acetylcarnitine, which could point to novel potential preventive strategies.

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**Presenter:** HIS, Mathilde (IARC)

**Session Classification:** Oral presentation

Contribution ID: **20** Type: **Oral presentation**

# Hot beverages and esophageal cancer risk in Malawi and Tanzania: Findings from the ESCCAPE case–control studies

*Monday, 22 March 2021 16:18 (12 minutes)*

Esophageal squamous cell carcinoma (ESCC) has distinctly high incidence rates in Malawi and Tanzania and much of East Africa, with an adverse prognosis and ill known etiology. Consumption of hot food/beverage, a probable carcinogen to humans, is associated with increased ESCC risk in other settings. We conducted a case–control study in Blantyre, southern Malawi and the Kilimanjaro region, northern Tanzania between June 2017 and May 2020, and between November 2015 and December 2019 respectively. Cases were patients with endoscopically confirmed esophageal cancer whose histology did not exclude ESCC. Some cases were also included on the basis of imaging or clinical criteria. Age and sex-matched controls were hospital visitors and in and outpatients, excluding those with digestive diseases. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated for self-reported tea, coffee and porridge consumption temperature, minutes from cooked to consumption and consumption speed using logistic regression models adjusted for potential confounders. The study included 849 cases and 906 controls. To capture the maximal "hotness", data from tea, coffee and porridge were combined. Because the final results were consistent between Malawi and Tanzania, we also combined them. "Very hot"compared to "hot"consumers had a 1.92 (95% CI: 1.50, 2.46) ESCC risk. Those who waited less than two minutes compared to those who waited two to five minutes before consumption had a 1.71 (95% CI: 1.34, 2.20) ESCC risk. Those who consumed at a "fast"versus a "slow"speed had a 2.27 (95% CI: 1.45, 3.56) ESCC risk. These trends were consistent in males and females. These findings give more evidence for the role of thermal injury from consuming very hot beverage/food, a potentially modifiable risk factor, in ESCC etiology.

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**Session Classification:** Oral presentation

Contribution ID: **21** Type: **Oral presentation**

# Performance of short-term repeat HPV testing, HPV viral load and HPV16/18 genotyping for triage of HPV positive women in Latin America

*Monday, 22 March 2021 15:54 (12 minutes)*

**Background.** A single HPV test is highly sensitive for precancerous cervical lesions but has limited specificity leading to unnecessary referral. We aimed to evaluate the performance of short-term repeat HPV testing, semi-quantitative HPV viral load, and HPV16/18 genotyping for triage of HPV positive women in the ESTAMPA study. **Methods.** ESTAMPA is a multicentric study across Latin America in which women aged 30-64 years are screened with HPV testing (HC2 or Cobas) and Pap, and referred to colposcopy if positive for either test. We evaluated the performance of short-term repeat HPV test done at colposcopy ~2 months after enrolment, viral load reflected by HC2 relative light units (RLU), and HPV16/18 genotyping by Cobas for the detection of cervical intraepithelial neoplasia grade 3 or more severe (CIN3+) in screened HPV positive women. Results were adjusted by age, study centre, and time to repeat HPV testing using random intercepts from linear mixed models. **Results.** 3,122 and 1,434 participants testing positive for HC2 and Cobas, respectively, were included in the analyses, of which 283 and 201 had CIN3+. The adjusted risk of CIN3+ in HPV positives was 8.8% (95%CI 6.7-10.8) for HC2 and 11.5% (95%CI 5.2-17.9) for Cobas. Positive predictive values (PPVs) of repeat HPV testing were 13.6% (95%CI 11.0-16.1) for HC2 and 16.4% (95%CI 11.1-21.8) for Cobas, with sensitivities greater than 80% (83.4% [95%CI 76.1-90.8] and 90.2% [95%CI 82.6-97.7], respectively), and referral rates around 60% (56.7% [95%CI 52.6-60.7] and 67.6% [95%CI 62.3-72.8], respectively). The performance of HC2 RLU≥10 (moderate/high viral load) was similar to repeat HC2 (PPV: 13.1% [95%CI 10.4-15.8], sensitivity: 83.3% [95%CI 76.2-90.4], and referral rate: 57.6% [95%CI 54.2-60.9]); while HC2 RLU≥100 (high viral load) had a higher PPV (20.0% [95%CI 17.3-22.7]) and lower referral rate (28.8% [95%CI 24.5-33]) but sensitivity was limited (59.3% [95%CI 52.5-66.1]). The sensitivity of combined approaches with repeat HPV testing in women with RLU<10 (93.3% [95%CI 90.4-96.2]) or RLU<100 (87.7% [95%CI 83.7-91.6]) was higher than strategies separately, although at the expense of a greater referral rate (72.1% [95%CI 69.7-74.4], and 62.5% [95%CI 59.7-65.3], respectively). The performance of HPV16/18 genotyping was similar to having a high viral load (PPV: 24.1% [95%CI 13.2-34.9], sensitivity: 59.4% [95%CI 41.8-77], and referral rate: 28.1% [95%CI 20.8-35.4]). The sensitivity of HPV16/18 genotyping with repeat HPV test for non-16/18 positives was similar to repeat HPV testing alone (91.7% [95%CI 85.2-98.2]) but the referral rate was higher (73.9% [95%CI 69.5-78.4]). **Conclusions.** Short-term repeat HPV testing alone or in combination with HPV testing intrinsic characteristics seems to be useful for triage of HPV positive women. This triage approach may have the potential to better guide clinical management of HPV positives in the short-term with the advantage of not requiring additional tests such as cytology or visual techniques which is appealing, even more in the context of self-sampling.

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**Session Classification:** Oral presentation

Contribution ID: **22** Type: **Oral presentation**

# Performance of Pap among HPV positive women according to laboratory characteristics in Latino America: an analysis within the ESTAMPA study

*Monday, 22 March 2021 16:06 (12 minutes)*

Introduction
Cervical cancer is the fourth most frequently occurring cancer in women around the world, most of cases occurring in low- and middle-income countries. High risk human papilloma virus (HR-HPV) DNA test is highly sensitive to detect cervical intraepithelial neoplasia grade 2 or worse (CIN2+). However, the specificity is limited as HPV infections are very common and the majority clear spontaneously. A good performance of cervical cancer screening program based on HPV requires a secondary triage technique which, within the group of HPV-positive women, will identify those women with risk of developing pre-invasive or invasive cervical lesions. Pap test represents the immediate test of triage because of the available installed capacity in many countries, particularly in Latin America. The aim of this work is to evaluate the performance of Pap read without knowledge of HPV status to detect CIN3+ among HPV positives women according to laboratory characteristics across Latin America countries participating in the ESTAMPA study (Multicentric study of cervical cancer screening triage with HPV testing, NCT01881659).

Methods
In nine Latin American countries, 45,000 women are being screened with Pap and HPV; those with ASCUS+ or being HPV+ have colposcopy, biopsy and treatment as needed. Women without disease are those with negative screening, negative colposcopy, or negative/CIN1 histology. Pap laboratories were classified by :1) type of laboratory (public vs private), and, 2) cytology interpretation protocol (pathologists read 100% of smears vs they only read ASCUS+ based on cyto-technicians interpretation), and in one public laboratory only Paps of HPV+ were processed and read. The sensitivity and specificity of Pap for CIN3+ detection among HPV+ were estimated overall and by laboratory characteristics.
Results
Among 4,661 HPV positive women included in the analysis, 223 (4.8%) CIN2, 422 (9.1%) CIN3 and 44 (0.9%) cancers were detected. Overall, the sensitivity and specificity for CIN3+ detection were 53.9% (95%CI 49.3-58.3) and 86.0% (95%CI 84.9-87.0), respectively. No differences in sensitivity between public and private laboratories were observed (49.5% [95%CI 42.6-56.4] vs. 48.1% [95%CI 40.4%-55.9]); and or when Paps were interpreted first by cytotechnicians and only smears ASCUS+ by pathologist and when pathologists interpreted 100% smears (42.9% [95%CI 35.3-50.8] vs. 53.5% [95%CI 46.6-60.2]). However, the laboratory where only Paps of HPV+ were processed and read had sensitivity and specificity of 70.0% (95%CI 60.9-77.8) and 85.9% (95%CI 83.7-87.8), respectively.
Conclusions
Pap sensitivity for CIN3+ detection among HPV+ was limited. However, the highest sensitivity was observed where only HPV+ smears were read. This suggests that Pap performance may be improved when HPV status is known, supporting its use as triage until better/accessible biomarkers are available. In this context, in the ESTAMPA study Paps are being re-read knowing HPV positivity in 12 laboratories to confirm this hypothesis.

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**Presenter:** Dr RAMÍREZ PINEDS, Arianis Tatiana (IARC)

**Session Classification:** Oral presentation

Contribution ID: **23** Type: **Oral presentation**

# Variation in global and enhancer-specific DNA methylation profile is an important feature of malignant pleural mesothelioma

*Tuesday, 23 March 2021 16:00 (12 minutes)*

Objectives
Malignant Pleural Mesothelioma (MPM) is a rare cancer of the pleura, primarily attributed to occupational asbestos exposure. Despite the world-wide reduction in asbestos exposure through legislation prohibiting its use, the incidence of asbestos-related cancers such as MPM continues to rise in many countries, in part due to the long latency period between exposure and tumour development. Furthermore, MPM is an extremely aggressive disease with an estimated five-year overall survival rate of 10-12%. In the MESOMICS Project, part of the Rare Cancers Genomics imitative at IARC, we aim to identify molecular characteristics of MPM with a view to better understanding tumour aetiology, and improving clinical classification and management of MPM.

Methods
We generated whole-genome sequencing, RNA sequencing and DNA methylation array data for 124 MPM, covering all three major histological types (epithelioid, sarcomatoid, and biphasic). Using these data we performed an integrative analysis with MOFA (multi-omics factor analysis) to generate a molecular map of MPM, then examined the clinical and molecular characteristics of tumour samples in association with their location on the map.

Results
Integrating gene expression, DNA methylation, copy number, and somatic variant datasets with MOFA resulted in a molecular map of MPM that displayed a continuous profile across the three histological types, rather than distinct clusters. DNA methylation level was found to be the biggest contribution to the first axis of the map, particularly at enhancer elements. DNA methylation data were further analysed by examining the global methylation level, and that of three distinct genomic regions: promoter, enhancer, and gene body. Global methylation level was associated with the more aggressive sarcomatoid histology, an increase in cell proliferation rate, and copy number burden. Methylation level of enhancer regions displayed the most variation across the spectrum of MPM, and was also associated with sarcomatoid histology. Pathway analysis of genes proximal to variable enhancer elements showed enrichment in epithelial-to-mesenchymal transition (EMT), and response to inflammation pathways, and expression of mesenchymal-associated genes was significantly correlated with enhancer methylation level. Lastly, motif enrichment analysis identified differential enhancer methylation in the binding sites of key transcription factors in EMT and inflammatory response pathways.

Conclusion
Through the MESOMICS project we have uncovered a continuous profile of molecular characteristics across the spectrum of MPM. Notably, we have found evidence of global and enhancer-specific DNA methylation profile in driving the development of the most aggressive tumours through promotion of genome instability, and mediating epithelial-to-mesenchymal transition.

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**Session Classification:** Oral presentation

Contribution ID: **25** Type: **Oral presentation**

# Pre-existing cardiometabolic comorbidities associated with all-cause and cancer-specific mortality among individuals with cancer in the EPIC cohort

*Tuesday, 23 March 2021 16:48 (12 minutes)*

Introduction: Chronic diseases frequently pre-exist among individuals with cancer and these comorbidities have been hypothesized to affect survival following cancer diagnosis. We investigated associations between pre-existing cardiometabolic comorbidities and all-cause and cancer-specific mortality among individuals with cancer.
Material and method: 26,987 men and women enrolled in the European Prospective Investigation into Cancer and Nutrition (EPIC) with a primary cancer were included in this analysis. Cardiometabolic comorbidities were defined as either type-2 diabetes (T2D), cardiovascular disease (CVD: stroke or myocardial infarction) or both, diagnosed prior to cancer. Associations of cardiometabolic conditions with overall and cancer-specific mortality were estimated using multivariable Cox proportional hazard regression adjusted for sex, educational level, alcohol intake, total energy intake, Mediterranean diet, physical activity, body mass index, hypertension status, menopausal status, and hormone therapy use and stratified for age at recruitment, country, smoking status, stage at diagnosis, and 5-year net-survival of cancer. We also stratified the analysis by the 5-year net-survival of cancer (≤40%, 40-80, ≥80).
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 hazard ratios (HRs) of 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, and both, respectively, compared to absence of these comorbidities. Similar positive associations were observed for cancer-specific mortality. Associations were slightly stronger among participants with cancers that have a 5-year net-survival ≥80%.
Discussion: We corroborate and go beyond existing evidence by investigating the combined impact of T2D and CVDs on all-cause and cancer-specific mortality among individuals living with cancer.
Conclusions: A CVD or T2D, and in particular the combination of CVD and TD2, before cancer is associated with increased mortality, thus calling for specific attention to individuals living with cancer with pre-existing cardiometabolic comorbidities.

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**Session Classification:** Oral presentation

Contribution ID: **26** Type: **Poster presentation**

# Using computer vision and artificial intelligence to improve lung neuroendocrine tumours (LNET) classification.

*Tuesday, 23 March 2021 17:18 (6 minutes)*

**Background:** Pulmonary carcinoids are rare and understudied diseases that account for 1-2% of all invasive lung malignancies. Recently, we performed the first multi-omics characterization of atypical carcinoids, unveiling the existence of the supra-carcinoids and providing the missing pieces for a complete characterization of lung neuroendocrine neoplasms. **Aims:** We are now aiming at using computer vision and artificial intelligence algorithm on whole-slide tissue images to identify the most clinically relevant morphological features. In particular, we will detect histopathological features associated with the increased aggressiveness of supra-carcinoids and other molecular sub-types we have previously identified. **Methods:** A unique series of >300 whole-slides images, enriched for atypical carcinoids, will be analysed through computer vision techniques. The convolutional neural networks will have to overcome different challenges; namely, a limited sample size with complex features hardly detectable even by expert pathologists. Data augmentation, image generation and few-shots learnings techniques will be explored to overcome these challenges. **Expected results:** The deep learnings models will help unveiling the histopathological features of pulmonary carcinoids associated with the increased aggressiveness of these tumors observed in a subset of patients. Integrating the molecular and morphological data will also shed light on the etiology of these diseases, and inform/improve their diagnosis, classification, and clinical management.

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**Presenter:** MATHIAN, Emilie

**Session Classification:** Poster session

Contribution ID: **27** Type: **Poster presentation**

# Identification and characterization of key epigenetic regulators (“epidrivers”) of breast cancer onset, progression and phenotypes

*Tuesday, 23 March 2021 17:24 (6 minutes)*

Epigenetic regulator genes (ERGs) are a group of over 400 genes which regulate gene expression by DNA methylation, histone modification and chromatin remodeling. ERGs play a crucial role in the establishment and maintenance of cell identity and genome integrity in health and disease. Indeed, ERGs are found to be commonly altered in cancer. This was further confirmed and extended by our pan-cancer genome, transcriptome and methylome analyses of ERGs’deregulations showing high rates of deregulations in specific ERGs within and across cancer types, including breast cancer (BC).
BC is the most frequent cancer type in women and represents most of the cancer-related deaths in this group. BC is a heterogeneous disease, categorized into four molecular subtypes according to the expression of estrogen, progesterone and HER2 receptors. The subtypes vary greatly in gene expression patterns, prognostic, phenotypes and response to treatments. Epigenetic deregulations play major roles in BC, with differential methylation patterns and histone modifications figuring as some of the known alterations contributing to this disease. Thus, we hypothesize that ERGs could act as drivers (epidrivers) of BC onset and progression, contributing to its molecular subtypes and their associated phenotypes.
To identify epidrivers of BC, we performed an in silico curation of ERGs’alterations in the BC subtypes using TCGA datasets and in vitro pooled loss-of-function genome editing screens targeting all ERGs. Our studies identified putative epidriver candidates that are currently under validation, and their role in cancer cell plasticity and different phenotypes is being assessed by an in depth functional and molecular characterization using non-tumorigenic breast and BC cell lines and patient-derived organoids.
Our study will advance the knowledge of mechanisms of BC and unravel novel epigenetics-based “Achilles heels”of BC which may be exploited to the development of targeted therapeutic approaches.

Keywords: epigenetics, breast cancer, CRISPR editing

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**Session Classification:** Poster session

Contribution ID: **28** Type: **Lay audience presentation**

# Classification of rare lung cancers

*Wednesday, 24 March 2021 16:48 (6 minutes)*

Traditionally cancer diagnoses have been made using histopathology techniques, whereby a pathologist examines pieces of tumour tissue under a microscope, observing physical features of the cells, or their 'histology'. However we now know that tumours which appear physically similar under a microscope can in fact behave very differently, for instance one tumour may grow faster than another. Often these behavioural changes are caused by differences in the activity of genes within the tumour, features that cannot be seen with a microscope. In the Rare Cancers Genomics team at IARC we are working to identify the invisible differences between physically similar tumours, with a particular focus on rare lung cancers, to improve the classification of such tumours.

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**Presenter:** SEXTON-OATES, Alexandra (IARC)

**Session Classification:** Lay audience session

Contribution ID: **29** Type: **Lay audience presentation**

# Insights on population-based cancer staging from the International Cancer Benchmarking Partnership SurvMark-2 project

*Wednesday, 24 March 2021 16:42 (6 minutes)*

Cancer stage at diagnosis is an important prognostic factor to assess the effectiveness of cancer clinical management and treatment. The two most used staging system by population-based cancer registries (PBCR) are TNM staging classification and the SEER summary (SS) staging or local variation of the SS. The lack of international standardization for recording stage information, the frequent changes in staging classification systems, and differences in completeness of stage information between PBCRs are some of the biggest challenges to international comparisons of stage-specific cancer survival estimates. The availability and comparability of staging information for colorectal, lung, female breast and ovarian cancer were previously assessed by the International Cancer Benchmarking Partnership (ICBP) Phase I. In this study, we aim to evaluate the completeness of stage information for esophageal, stomach, and pancreatic cancers by PBCRs from 1995-2014, and present stage conversion algorithms for these three cancer sites. Although these stage conversion approaches could be used to assess stage-specific survival between PBCRs, additional actions are needed to resolve the challenges we face in stage-specific survival comparisons globally. Consequently, we also aim to discuss recommendations for cancer registries to help improve international cancer survival comparison by stage: 1) Improve collection and completeness of staging data; 2) Promote a comparable definition for stage at diagnosis; 3) Promote the use of a common stage classification system; 4) Record versions of staging classifications; and 5) Use multiple data sources for valid staging.

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**Session Classification:** Lay audience session

Contribution ID: **30** Type: **Poster presentation**

# Circulating plasma phospholipid fatty acid levels and breast cancer risk in the CPS-II Nutrition Cohort

*Tuesday, 23 March 2021 17:06 (6 minutes)*

Background
The association between dietary fat intake and breast cancer risk has been a source of controversy with conflicting results reported in past decades. Additional prospective studies that objectively measure circulating levels of fatty acids are now needed to better understand the associations between dietary fat and breast cancer development.

Methods
We assessed the relation between breast cancer risk and plasma levels of 60 phospholipid fatty acids in a nested case-control study of 2,718 postmenopausal women (905 breast cancer cases and 1,813 matched controls) enrolled in the Cancer Prevention Study II (CPS-II) Nutrition Cohort. Blood samples were collected at baseline (1997-1998). Multivariable-adjusted conditional logistic regression models that included established breast cancer risk factors (alcohol use, postmenopausal hormone use, smoking status, waist circumference, body mass index, and weight change from age 18 years to blood draw) were used to compute odds ratios (OR) and 95% confidence intervals (CI). The false discovery rate (FDR; q-value) was computed to control for multiple comparisons.

Results
After adjustment for multiple comparisons and in continuous log-transformed multivariable models, plasma levels of myristic acid (a saturated fatty acid) were positively associated with breast cancer risk (OR per log-value, 1.17, 95% CI: 1.07-1.28; q-value = 0.03), with similar magnitude associations found for estrogen receptor (ER) positive and ER negative breast cancer (p-interaction = 0.39). Positive associations were also found for plasma levels of monounsaturated fatty acid (OR per log-value, 1.09, 95% CI: 1.00-1.18; q-value = 0.24), palmitoleic acid (OR per log-value, 1.14, 95% CI: 1.04-1.24; q-value = 0.09), palmitic acid (OR per log-value, 1.12, 95% CI: 1.01-1.24; q-value = 0.17), dihomo-ɣ-linolenic acid (OR per log-value, 1.14, 95% CI: 1.04-1.25; q-value = 0.09), and adrenic acid (OR per log-value, 1.13, 95% CI: 1.03-1.24; q-value = 0.11) with breast cancer risk; however, after adjustment for multiple comparisons these associations did not reach the threshold of statistical significance. Similarly, inverse associations between plasma levels of trans α-linolenic acid (OR per log-value, 0.85, 95% CI: 0.76-0.96; q-value = 0.09), heptadecanoic acid (OR per log-value, 0.90, 95% CI: 0.82-0.99; q-value = 0.17), and vaccenic acid (OR per log-value, 0.88, 95% CI: 0.80-0.97; q-value = 0.11) with breast cancer risk were not statistically significant after adjustment for multiple comparisons.

Conclusion
These findings suggest that higher circulating levels of myristic acid, that can be sourced from dietary intake of dairy foods or via de novo synthesis, may increase breast cancer risk. Additional studies are needed to replicate this finding and provide mechanistic insights.

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**Session Classification:** Poster session

Contribution ID: **31** Type: **Poster presentation**

# Exposure to pesticides and risk of Hodgkin lymphoma in an international consortium of agricultural cohorts (AGRICOH)

*Monday, 22 March 2021 16:48 (6 minutes)*

**Background:** There is strong evidence that the use of pesticides increases the risk of hematological malignancies, but associations with Hodgkin lymphoma remain poorly understood. Here, we report associations between Hodgkin lymphoma incidence and the use of 22 pesticide active ingredients and 13 chemical groups (organophosphate, carbamate, organochlorine, and pyrethroid insecticides; (phenyl) urea, chloroacetanilide, dinitroaniline, phenoxy, thiocarbamate, triazine, and triazinone herbicides; and dithiocarbamate and pthalamide fungicides) in three large agricultural cohorts from France, Norway and the USA participating in an international consortium of agricultural cohorts (AGRICOH).

**Methods:** Use of specific active ingredients was self-reported (USA) or derived from crop-exposure matrices applied to self-reported histories of crop production activity (France and Norway). Multivariable Cox regression models were used to estimate cohort-specific hazard ratios (HRs) and 95% confidence intervals (CIs ), which were then combined using random effects meta-analysis for each active ingredient and chemical group, by ever or duration of use (< or ≥16 years).

**Results:** Among a total of 316,270 farmers (75% male), 91 incident Hodgkin lymphoma cases were diagnosed during follow-up from 1993 to 2011 (3,574,815 person-years). Risks appeared elevated in association with use of dicamba (meta-HR=1.63, 95% CI: 0.83-3.22), DDT (meta-HR=1.79, 95% CI: 0.73-4.37), deltamethrin (meta-HR=1.86, 95% CI: 0.76-4.52) and esfenvalerate (meta-HR=1.86, 95% CI: 0.78-4.43), although precision of risk estimates was generally low.

**Conclusions:** We did not observe any statistically significant associations between use of pesticide chemical groups or specific active ingredients and HL risk among agricultural workers. Future studies analyses should aim to study examine larger number of cases, possibly stratified by histological subtype, EBV-status and age, and strive to further refine exposure assessment methods.

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**Presenter:** KIM, Joanne (Environment and Lifestyle Branch, IARC)

**Session Classification:** Poster session

Contribution ID: **32** Type: **Poster presentation**

# Epidemiology of anal human papillomavirus infection and high-grade lesions in 29 238 men, according to HIV status, sexuality, and age: a collaborative pooled analysis of 62 studies

*Tuesday, 23 March 2021 17:12 (6 minutes)*

Background Robust age-specific estimates of anal human papillomavirus (HPV) and high-grade squamous intraepithelial lesions (HSIL) in HIV-positive and HIV-negative men can inform anal cancer prevention efforts.
Methods We reanalysed individual-level data from 62 studies totalling 29,238 men across four 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 anal high-risk (HR) HPV, and HSIL or worse (HSIL+), were compared using adjusted prevalence ratios (aPR).
Findings Anal HPV prevalence was lowest among HIV-negative MSW (HPV16=1·8%;HR-HPV=6·9%), followed by HIV-positive MSW (8·7%;26·9%) and HIV-negative MSM (13·6%;41·0%), and highest in HIV-positive MSM (28·4%;74·5%). In HIV-positive MSM, HPV16 prevalence increased from 15–18 (5·7%) to 23–24 years (29·0%) (ptrend=0·011), then declined from 25–34 (31·6%) to ≥55 years (22·7%) (ptrend<0·001). HPV16 in HIV-negative MSM also increased from 15–18 (6·8%) to 23–24 years (13·9%) (ptrend=0·009), plateauing thereafter (ptrend=0·688). Similar age-specific patterns were observed for HR-HPV. 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 1·36–1·73) and HPV16-positive HSIL+ (1·66, 1·36–2·03) among MSM, even when restricted to HPV16-positive MSM (1·19, 1·04–1·37). Among HPV16-positive MSM, HSIL+ prevalence increased with age.
Interpretation High anal HPV prevalence among young HIV-positive and HIV-negative MSM highlights benefits of gender-neutral HPV vaccination prior to sexual debut over catch-up vaccination. HIV-positive MSM are a priority for anal cancer screening programmes targeting HPV16-positive HSIL+.

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**Presenter:** WEI, Feixue

**Session Classification:** Poster session

Contribution ID: **33** Type: **Poster presentation**

# Use of carbamate insecticides and risks of non-Hogdkin's lymphomas in the French agricultural cohort (AGRICAN)

*Monday, 22 March 2021 16:54 (6 minutes)*

*Background*
Agricultural use of carbamate insecticides and risks of non-Hodgkin's lymphomas (NHL) have been linked in some but not all occupational epidemiologic studies. Moreover, studies on associated risks of NHL by histological subtype of NHL and by type of carbamate insecticides used are scarce.

*Objectives*
We evaluated the effects of carbamate insecticides on the risks of NHL and three major histological subtypes of NHL - multiple myeloma (MM), chronic lymphocytic leukaemia / small lymphocytic lymphoma (CLL/SLL), diffuse large B-cell lymphoma (DLBCL) - in a sample of 65,630 French farmers from the prospective cohort AGRICAN.

*Methods*
AGRICAN participants completed a questionnaire on lifetime occupational history of agricultural practices including pesticides uses and other factors including body mass index, smoking, and alcohol consumption at study enrolment (2005-2007). Their answers were crossed with data from the French crop-exposure matrix, PESTIMAT, to assess their exposure to 19 specific carbamate insecticides by purpose of pesticide use (soil, animals, barns or seeds). Multivariate Cox proportional hazards models with age as time scale and gender as a covariate were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) for NHL risks (by subtype and overall) associated with exposure to carbamate insecticides. Non-users of pesticides were chosen as reference group.

*Results*
Between inclusion and end of follow-up in 2015, 533 cases of NHL were diagnosed in our analytical sample of farmers, including 125 cases of MM, 135 cases of CLL/SLL and 72 cases of DLBCL. The risk of MM was elevated in participants who had used any carbamate insecticides at least on barns (HR = 1.69, 95% CI: 1.00-2.87). The risk of MM was also increased for those who used any carbamate insecticides on animals (HR = 1.64, 95% CI: 0.96-2.81) and at least on soil (HR = 1.27, 95% CI: 0.75-2.15) although the 95% CIs included 1.00. Use of any carbamate insecticides was not associated with CLL/SLL (HR = 0.88, 95% CI: 0.57-1.36), DLBCL (HR = 0.69, 95% CI: 0.39-1.24) or NHL overall (HR = 1.01, 95% CI: 0.80-1.27).

*Discussion*
Our results may suggest a potential role of carbamate insecticides use on animals or barns in the etiology of MM. Further analyses on specific carbamate insecticides and respective duration of use are ongoing.

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**Session Classification:** Poster session

Contribution ID: **34** Type: **Lay audience presentation**

# Spotting the (metabolic) differences to better understand and prevent breast cancer

*Wednesday, 24 March 2021 16:36 (6 minutes)*

Several risk factors for breast cancer, the most common cancer in the world, have already been identified. These risk factors are of different types, often interrelated, such as lifestyle habits, or molecules in blood (hormones, inflammation markers). These molecules can be measured with some laboratory methods. Despite advances in our knowledge, however, most breast cancer cases are still not attributable to known risk factors.
I will explain how we used a new laboratory methodology, called metabolomics, to identify potential new risk factors for breast cancer in blood.
This technique enables to detect and measure simultaneously hundreds of small molecules in a given biological sample. We used it to analyze blood samples from thousands of participants from our epidemiological studies who also provided information on their health and lifestyle during 25 years.

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**Presenter:** HIS, Mathilde (IARC)

**Session Classification:** Lay audience session

Contribution ID: **35** Type: **Lay audience presentation**

# What have you been eating? Improving food intake measurements using biomarkers

*Wednesday, 24 March 2021 16:54 (6 minutes)*

Diet is an important modifiable risk factor for cancer and several foods have been associated with risk of cancer. In most studies, dietary intake is measured using dietary questionnaires which might be limited by a lack of detail or the memory of the participants. Biomarkers of food intake which can be measured in blood or urine have been proposed as a mean to improve intake assessment for foods that are poorly captured by dietary questionnaires. Such biomarkers for processed meat intake are still scarce.
We have conducted a dietary intervention study at IARC in which 12 volunteers consumed different processed and non-processed meat products. Urine and blood samples were collected and analysed using an untargeted metabolomics approach, covering a broad range of small molecule metabolites. We have identified metabolites originating from wood smoke that were specific for the intake of smoked meat and pepper constituents that were specific for the intake of sausages. We could then confirm their association with the diet of a free-living population using samples from the EPIC study.
These promising biomarkers might help to improve the measurement of intake for specific processed meat products and thereby identify meat products that are most strongly associated with colorectal cancer risk.

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**Presenter:** WEDEKIND, Roland (IARC)

**Session Classification:** Lay audience session

Contribution ID: **36** Type: **Poster presentation**

# Mapping social inequalities in cancer in Europe

*Monday, 22 March 2021 16:30 (6 minutes)*

Objective: To investigate the contribution of socioeconomic inequalities in the incidence and mortality of seventeen major cancer types and to compare the results across European countries.
Methods: The study will use the prospective multi-centric EPIC cohort data with an average follow up period of 14.1 years. Participants include 476,160 men and women free of major chronic diseases at enrolment across 29 centres in 10 European countries. Educational level of participants will be used as proxy for socioeconomic status. Cox proportional hazard regression model will be used to explore the association between educational attainments and cancer incidence and mortality by calculate hazard ratios (HRs) and 95% confidence intervals (95% CI). In addition, the Relative Index of Inequality (RII) across educational level will be also computed as a summary measure of inequality that can account for the size of the population of each of the socioeconomic groups. Analysis will be stratified by gender, age-groups and countries.
Results: We have carried out some preliminary analyses. Overall, men with the lowest education had a significantly higher risk of being diagnosed with cancer compared to their fellow citizens with the highest education, whereas the opposite was true for women (i.e., those with highest education had the highest risk). Despite these differences, mortality for cancer was always higher in the least educated individuals for both sexes. Corresponding preliminary results for specific cancer types showed a more variegated picture in the association of educational level with incidence and mortality. Results by geographical area/country will be assessed. We will also explore the potential role of modifiable risk factors (e.g., tobacco smoking or healthy lifestyle) in explaining and reducing these inequalities.
Conclusion: Our preliminary analyses showed that socioeconomic inequalities in cancer incidence and mortality depend on the specific cancer types considered. The comparison of the social gradient across cancer incidence and cancer mortality for specific cancer types is of public health relevance as it allows identifying areas for socioeconomic inequalities in cancer along the different stages of the cancer continuum.

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**Session Classification:** Poster session

Contribution ID: **37** Type: **Poster presentation**

# Determinants of circulating acylcarnitine concentrations in healthy participants of the European Prospective Investigation into Cancer and Nutrition study

*Monday, 22 March 2021 17:00 (6 minutes)*

Introduction: Acylcarnitines (ACs) play a key role in the transport of fatty acids in the cell and in energy metabolism. Their concentrations in blood have been associated with risk of diseases such as cancer and type 2 diabetes. Diet and lifestyle factors have been shown to influence AC concentrations but a more detailed knowledge of their determinants is needed.
Methods: Fifteen and forty-two circulating ACs were measured in blood by targeted and untargeted metabolomics in 7104 and 395 healthy participants of the European Prospective Investigation into Cancer and nutrition (EPIC) study, respectively. Associations with participants characteristics such as age and sex, fasting status, dietary patterns, intake of food and fatty acids, and with circulating fatty acids and amino acids were assessed.
Results: Fasting state, age, sex and diet explained a large fraction of AC variance. Circulating long chain fatty acids and foods containing particular fatty acids were associated with the corresponding AC species. Concentrations of C3 and C5 were highly associated with branched chain amino acids and decreased during fasting whereas other ACs increased. Intake of most foods and carnitine, physical activity and smoking showed little association with AC levels.
Conclusions: Our results suggest that most ACs are mainly influenced by participant characteristics and that determinants are specific for different AC species. These identified determinants of ACs will help interpret their associations with disease risk and can inform on potential confounders for which these studies should adjust.

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