

# 2022 NCI Cohort Consortium ANNUAL MEETING

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VIRTUAL MEETING

## ABSTRACT SUBMISSIONS

**Project Title:** Accelerometer-measured physical activity and risks of hospitalization for 25 common conditions

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**Abstract:**

Higher levels of physical activity are associated with lower risks of cancer, cardiovascular disease, and diabetes, but associations with many common, less severe health conditions are not known. These conditions impose large healthcare burdens and reduce quality of life. We aimed to investigate the relationships between accelerometer-measured physical activity and subsequent risk of hospitalization for 25 common reasons for hospitalization and estimate the proportion of these hospitalizations that might have been prevented if participants had higher levels of activity.

We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for average accelerometer-measured physical activity (per 1 standard deviation (SD)) and risk of hospitalization for 25 conditions. Population attributable risks were used to estimate the proportion of hospitalizations for each condition that might be prevented if participants increased moderate-to-vigorous physical activity (MVPA) by 20-min/day. Participants consisted of 82,000 respondents from the UK Biobank.

Higher levels of accelerometer-measured physical activity were associated with lower risks of hospitalization for nine conditions: gallbladder disease (HR per 1 SD increment = 0.74, 95% CI 0.69-0.79), diabetes (0.79, 0.74-0.84), urinary tract infections (0.76, 0.69-0.84), venous thromboembolism (0.82, 0.75-0.90), pneumonia (0.83, 0.77-0.89), ischemic stroke (0.85, 0.76-0.95), iron deficiency anemia (0.91, 0.84-0.98), diverticular disease (0.94, 0.90-0.99), and colon polyps (0.96, 0.94-0.99). We observed positive associations between physical activity and carpal tunnel (1.28, 1.18-1.40), osteoarthritis (1.15, 1.10-1.19), and inguinal hernia (1.13, 1.07-1.19), relating to light physical activity. Increasing MVPA by 20-min/day was associated with 3.8% (1.8-5.7%, for colon polyps) to 23.0% (17.1-28.9%, for diabetes) reductions in hospitalizations for these conditions.

Physical activity may play an important role in reducing risks of hospitalization across a broad range of health conditions. Aiming to increase MVPA by 20-min/day may be a useful non-pharmaceutical intervention to lower healthcare burdens and improve quality of life.

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**Project Title:** Levels of urinary 7,8-dihydro-8-oxo-2'-deoxyguanosine, associated characteristics and survival among colorectal cancer patients: Results from the ColoCare Study

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**Abstract:**

Introduction: Insufficient physical activity, smoking, and regular alcohol consumption can favor the development of colorectal cancer (CRC). Many of these factors contribute to increased oxidative stress which can result in DNA damage. A central biomarker of oxidative stress is 7,8-dihydro-8-oxo-2'-deoxyguanosine (8-oxo-dG). This study aims to assess associations between 8-oxo-dG and clinical and lifestyle factors, and survival among CRC patients.

Materials and Methods: This work is nested within the ColoCare Study, an international prospective cohort study among women and men newly diagnosed with a primary invasive CRC at all stages. Pre-surgery urinary levels of 8-oxo-dG in 190 CRC patients from the Heidelberg (Germany) study site were measured using an enzyme-linked immunosorbent assay and normalized to urinary creatinine. Multivariate models adjusted for potential confounders were applied to investigate associations of age, sex, tumor site, tumor stage, neoadjuvant treatment, body mass index, alcohol consumption, smoking status, and recreational physical activity with urinary 8-oxo-dG levels. Cox proportional hazard regression models were conducted to assess associations with overall survival and stratified by tumor site.

Results: CRC patients with advanced stage (IV) (n=47) showed significantly higher urinary 8-oxo-dG levels than patients with an earlier stage (I-III) (n=143); p=0.02. Ever-active smokers (n=120) showed significantly higher 8-oxo-dG levels compared to never smokers (n=61); p=0.027. CRC patients with high 8-oxo-dG levels had a statistically significant increased risk of overall death (Hazard ratio (HR)=1.86, 95% confidence interval (CI): 1.001-3.44; p=0.049). Exploratory analysis by tumor site revealed that high 8-oxo-dG levels were associated with a 2.93-fold increase in risk of overall death for colon cancer (HR=2.93, 95% CI: 1.20-7.14; p=0.018) compared with no association for rectal cancer (HR=1.14, 95% CI: 0.49-2.67; p=0.76).

Conclusion: Our findings suggest that urinary levels of 8-oxo-dG are associated with advanced tumor stage and smoking in CRC and poor overall survival in metastasized colon cancer patients.

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**Project Title:** Global metabolomics profiling, dietary factors, and colorectal cancer risk in the NIH-Consortium of Metabolomics Studies (COMETS)

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**Abstract:****BACKGROUND**

An improved understanding of the etiology of colorectal cancer (CRC) is needed to allow more accurate disease prevention. This is the first large-scale multi-cohort study that considers diet-related exposures and whether metabolites mediate the diet-CRC relationship. This project recently received NIH-funding (R03CA270473) and is in its early phase. This abstract is focusing on describing the study methods.

**METHODS**

We will perform individual-level and meta-analyses using existing data from 8 prospective cohort studies from the Consortium of Metabolomics Studies. All samples were analyzed using state-of-the art, highly reproducible global platforms: Metabolon, Inc., Broad Institute, UPLC-QTOFMS, and the International Agency for Research on Cancer. This study includes 3,278 matched case-control pairs (2,093 for discovery and 1,185 for validation). We expect n~130 overlapping metabolites, some of these were previously related to CRC risk. Multivariable conditional logistic regression models will be performed to identify metabolites associated with CRC risk. Heterogeneity between studies will be assessed using Q-value and I2 statistics. Metabolites at the 0.05 false discovery rate adjusted significance levels will be carried forward to the validation set. A nutritional metabolomics approach will be used to evaluate diet-related exposures (e.g., red meat) and whether metabolites mediate the diet-CRC relationship.

## RESULTS

Demographic and lifestyle data (e.g., age at blood draw, age at diagnosis, sex, race, body mass index, smoking, and dietary intake (e.g., processed meat)) are available. Data on tumor site is >95% complete. Tumor stage is available for >85% of patients. Development of data dictionaries, harmonization protocols, and statistical code are currently underway.

## CONCLUSIONS

This is the largest study investigating associations of metabolomics with CRC risk. The proposed analyses have the potential to identify biomarkers that may enhance population-wide screening. Biomarkers that reflect lifestyle factors (e.g., diet) may highlight exposures that warrant exploration for their cancer prevention or promoting effects.

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**Project Title:** Perfluoroalkyl Substances (PFASs) and Liver Cancer Risk in the United States

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**Abstract:**

Liver cancer is one of the most rapidly increasing cancers over the past decades in the United States. The causes for this long-term increase are unclear but could stem from exposures to possibly carcinogenic environmental contaminants. One likely source is per- and polyfluoroalkyl substances (PFAS), a group of synthetic chemicals that are highly persistent and accumulate in human liver tissue. Emerging, converging evidence from laboratory animals and occupational mortality studies strongly support the role of PFAS in liver carcinogenesis. However, these studies are limited by small sample sizes, restriction to occupational exposure, and studying single types of PFAS. Hence, we propose the first comprehensive prospective pooled cohort study in non-occupational settings to examine real-world human exposure to PFAS (of multiple types and mixtures) in relation to liver cancer incidence. This pooling project includes a racially/ethnically diverse population from the Liver Cancer Pooling Project followed for up to 32 years, along with pre-diagnosis plasma samples and validated covariate data. Our specific aims are to characterize the associations between plasma levels of PFAS and risk of developing liver cancer in this pooled nested case-control study with measured HBV/HCV status data; and assess the extent to which certain PFAS mixture patterns act synergistically to increase liver cancer risk. We will quantify the aforementioned associations by major liver cancer subtypes, and further estimate the associations between plasma PFAS levels and survival among patients with liver cancer. The contribution is significant because this research will generate new insights into the etiology of liver cancer enable design of new prevention/intervention strategies and actions that reduce liver cancer morbidity and mortality and related disparities. These findings will also provide new information on health effects of PFAS for practitioners and regulatory agencies to make solid decisions, regulations, and action plans to improve public health.

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**Project Title:** Preventative health behaviors and health system engagement among male cancer survivors and older men during the COVID-19 pandemic

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**Abstract:**

Background: The COVID-19 pandemic impacted health behaviors, particularly among individuals at an increased risk of severe SARS-CoV-2 infections. This study examined COVID-19 preventative behaviors and health system engagement during the pandemic in a cohort of older males and cancer survivors.

**Methods:** We administered three web-based supplemental questionnaires among participants of the Health Professionals Follow-up Study with known email addresses (in October 2020, January 2021, and April 2021). We analyzed the prevalence of COVID-19-related preventive behaviors and healthcare utilization descriptively by cancer history and among cancer survivors, by treatment status.

**Results:** Of 4,416 participants (54% of those invited) who were aged 74-101 (median 79) years, 1,104 (25%) were cancer survivors, and of those, 160 (15%) were actively undergoing treatment. By April 2021, COVID-19 vaccination uptake was high among respondents (96%), and the majority wore masks outside the home at least most of the time (82%). In April 2021, 39% of survivors undergoing active treatment were tested for COVID-19 in the last 90 days compared to 28% among survivors not on active treatment. Approximately 32% of survivors on active treatment wore N95 masks when outside the home compared to 23% among those not on active treatment. Telehealth utilization was common (40% in October 2020, 56% in January 2021), with many individuals initiating virtual services only after the pandemic began (29% in October 2020). Telehealth use was greater among cancer survivors (44% in October 2020) than individuals with no cancer history (38% in October 2020). At all timepoints, <10% of the men reported cancer screening disruptions, and we observed no differences based on treatment status.

**Conclusion:** Our results suggest that older men with active internet usage engaged in COVID-19 preventative health behaviors during the pandemic, including masking and vaccination. Telehealth was an important healthcare modality during the pandemic, particularly among cancer survivors.

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**Project Title:** Socioeconomic status and lung cancer incidence: An analysis of prospective cohorts in Europe, Asia, Australia, and North America

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**Abstract:**

**Background:** Lung cancer is the leading cause of cancer death worldwide. Lower socioeconomic status (SES) has been proposed as a possible lung cancer risk factor, independent of smoking. We aimed to assess whether and how the relationship between SES and lung cancer varies in different world regions.

**Methods:** Our study analyzed the harmonized database of the Lung Cancer Cohort Consortium (LC3). We estimated the association between education and incident lung cancer using Cox proportional hazards models. Education was modeled as an ordinal variable in 4 categories and models were adjusted for participant age, sex, smoking intensity, quit years, and smoking duration. We estimated associations stratified by smoking status, cohort, and world region.

**Results:** This study included 2,615,586 participants and 62,645 lung cancer cases from 15 countries. Among ever smokers, increased education level was associated with decreased lung cancer incidence in most countries after adjustment for age, sex, smoking intensity, quit years, and smoking duration, with HRs ranging from 0.77 per 1-unit increase in educational level (95%CI: 0.42-1.41) in the Iranian Golestan cohort to 1.02 (95%CI: 0.95-1.09) in the Australian MCCS cohort. When grouping by world region, the association between education and lung cancer incidence was similar for USA (HRpooled=0.88, 95%CI: 0.87-0.89), Europe (HRpooled=0.89, 95%CI: 0.88-0.91), and Asia (HRpooled=0.91, 95%CI: 0.86-0.96), but attenuated in the Australian MCCS cohort (HR=1.02, 95%CI: 0.95-1.09). Among never smokers, there was no association between education and lung cancer incidence with the exception of the American SCCS cohort with HR of 0.75 (95%CI: 0.62-0.90) after adjustment for age and sex.

**Conclusion:** Higher educational level was independently associated with decreased risk of incident lung cancer in most countries among ever smokers, but not in most never smokers. Our results emphasize the importance of including disadvantaged groups in tobacco prevention and low-dose CT screening programs.

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**Project Title:** Consolidation of Mexican Teachers Cohort for the study of breast cancer in women of Mexican heritage

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**Abstract:**

Background

Our understanding of breast cancer (BC) etiology is critically lacking in women of Mexican origin. We aimed at consolidating the Mexican Teachers' Cohort (MTC) as a unique resource to advance BC research.

Methods

We followed 115,307 women from baseline (2006-2008) to 2019. We identified incident BC cases through self-reports (in 2011 and 2014), administrative databases (medical appointments and hospital discharge by oncological procedures, medical leave, and electronic medical records), and cancer and mortality registries. Cases were defined as probable or confirmed based on histopathology reports, telephone interviews, or BC treatment in medical records. We defined women as indigenous based on speaking or having a parent who spoke an indigenous language. We estimated age-standardized incidence and mortality rates and their 95% confidence intervals (95%CI) using Segi's world standard population.

Results

After a median follow-up of 11.0 years (1,298,288 person-years), we identified 404 pre- and 879 postmenopausal incident BC cases. We confirmed 77% of cases, with 301 remaining for confirmation. Age-standardized BC incidence rate was 92.2 (95%CI 84.7, 99.6) per 100,000 person-years. For premenopausal cancer, the incidence rate was 55.4 (95%CI 50.0, 60.8). Corresponding estimates for postmenopausal cancer were 112.9 (95%CI 101.0, 124.8). Among 9,280 indigenous women, we identified 62 cases (incidence rate: 51.4; 95%CI 37.2, 65.6). The age-standardized mortality rate was 12.9 (95%CI 9.9, 15.8) per 100,000 person-years. The mortality rate for premenopausal BC was 7.7 (95%CI 5.7, 9.7) and 12.3 (95%CI 8.6, 16.0) for postmenopausal. Corresponding estimates for indigenous women were 6.7 (95%CI 0.9, 12.6).

Conclusion

BC incidence in the MTC was higher than previous estimates for Mexico, while mortality was comparable to prior reports. Indigenous women may be at a lower risk for BC incidence and mortality. We demonstrated our capacity to identify incident BC cases and have consolidated the MTC as a ready resource for BC research.