Pre- and Post-Diagnostic Non-Steroidal Anti-Inflammatory Drug Use and Colorectal Cancer Survival in Seattle Colon Cancer Family Registry

Hua X, Adams SV, Phipps AI, Cohen SA, Burnett-Hartman A, Hardikar S, Newcomb PA

Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the general population, and regular NSAID use is associated with improved survival among colorectal cancer (CRC) patients. We examined the association of NSAID use prior to, and after, diagnosis in relation to CRC-specific and overall survival. Methods: Study subjects were incident, invasive CRC cases from the population-based Seattle Colon Cancer Family Registry. Eligible cases were 20–74 years of age, diagnosed from 1997 to 2008, and identified from the Puget Sound Surveillance, Epidemiology and End Results (SEER) Registry. NSAID use two years prior to the interview date ("pre-diagnosis period") was collected by telephone interview at study enrollment an average of eight months after diagnosis. A follow-up questionnaire was administered approximately five years after the cases' CRC diagnosis ("post-diagnosis period"). Regular NSAID use was defined as having taken aspirin or ibuprofen at least twice per week for more than a month. Follow-up for survival and cause of death was completed through linkage to the National Death Index. Cox proportional hazard regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for associations of pre- and post-diagnostic NSAID use, and initiation, continuation and discontinuation of NSAIDs between pre- and post-diagnostic periods with survival after CRC diagnosis. Results: Compared to never users, regular NSAID use after diagnosis was associated with better overall survival (HR = 0.69, 95% CI, 0.54–0.89) and CRC-specific survival (HR = 0.48, 95% CI, 0.29–0.80). Among people who survived five years after diagnosis, both overall and CRC-specific survival were better for patients who initiated NSAID use post-diagnosis compared to never users, with HRs (95% CI) of 0.70 (0.51–0.95) and 0.43 (0.23–0.82), respectively. HR estimates were stronger for CRC-specific survival among those with non-advanced (local and regional) CRC (HR = 0.38, 95% CI, 0.18–0.77). Conclusion: Our results suggest that among long-term CRC survivors, regular use of NSAID after CRC diagnosis, including when initiated after diagnosis, is significantly associated with longer CRC-specific survival. This association is more pronounced for patients with non-advanced CRC.

Published online March 4, 2016
doi: 10.1158/1055-9965.EPI-16-0083

Pancreatic Cancer: Associations of Inflammatory Potential of Diet, Cigarette Smoking, and Long-Standing Diabetes

Antwi SO, Oberg AL, Shivappa N, Bamlet WR, Chaffee KG, Steck SE, Hebert JR, Petersen GM

Background: Pancreatic cancer (PanC) is a rapidly lethal malignancy with poorly understood etiology. Epidemiologic studies show strong associations between PanC and inflammatory conditions or stimuli such as cigarette smoking and diabetes, suggesting that inflammation may play a key role in PanC. Studies of dietary patterns and cancer outcomes also suggest that diet might influence an individual's risk of PanC through modulation of inflammation. We, therefore, examined independent and joint associations between inflammatory potential of diet, cigarette smoking and long-standing type II diabetes (greater than 5 years) in relation to risk of PanC. Methods: Data were from a clinic-based, case-control study of rapidly ascertained patients with incident adenocarcinoma of the exocrine pancreas ($n = 819$) evaluated at Mayo Clinic and non-cancer control patients ($n = 1,769$) recruited from Mayo Clinic primary care facilities. Controls were frequency-matched to cases on age, race, and sex. Inflammatory potential of diet was measured using the dietary inflammatory index (DII), calculated from dietary intake assessed via a 144-item food frequency questionnaire and adjusted for energy intake. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age, sex, race, body mass index, diabetes, smoking, and education. Results: Higher DII scores, reflecting a more pro-inflammatory diet, were associated with increased odds of PanC (OR Quintile5vs1 = 2.80, 95% CI, 2.06–3.79, Ptrend < 0.0001). Increased odds of PanC also were observed among current (OR = 2.55, 95% CI, 1.75–3.72) and former (OR = 1.26, 95% CI, 1.05–1.51) smokers as compared to non- smokers, and among participants with long-standing type II diabetes (OR = 2.96, 95% CI, 1.95–4.51) compared to non-diabetics. Joint associations were observed for the combined effect of having greater than the control median DII score and a) being a current smoker (OR = 4.20, 95% CI, 2.67–6.61),or b) having long-standing type II diabetes (OR = 6.13, 95% CI, 3.47–10.80) as compared to having less than or equal to the control median DII score and being a non-smoker or non-diabetic, respectively. Conclusion: These findings suggest that a pro-inflammatory diet may act synergistically with cigarette smoking and diabetes to increase the risk of PanC beyond the risk of any of these factors alone.

Published online March 4, 2016
doi: 10.1158/1055-9965.EPI-16-0084

HPV Infection among Sexual Minority Women: Does it Matter How Sexual Orientation Is Measured?

Reiter PL, McRee AL

Background: Sexual minority women are at risk for infection with human papillomavirus (HPV), yet little is known about the prevalence of HPV infection among this population. Further, it is not known how the prevalence of HPV infection might vary based on how sexual orientation is measured and operationalized. Methods: We analyzed data from the 2003–2012 National Health and Nutrition Examination Survey (NHANES) among women ages 20–59 ($n = 7,132$). We examined two dimensions of sexual orientation for each woman (sexual identity and sexual behavior), as well as multiple

operational definitions for each dimension (aggregating sexual minority women into one group and disaggregating sexual minority women into subgroups). Weighted logistic regression models determined how HPV infection outcomes (any HPV type, high-risk HPV type, and vaccine-preventable HPV type) varied by dimension. Results: Similar patterns emerged for sexual identity and sexual behavior. In bivariate analyses, HPV infection outcomes were more common among non-heterosexual women compared to heterosexual women (any type: 49.7% vs. 41.1%; high-risk type: 37.0% vs. 27.9%), as well as among women who reported any same-sex partners compared to women who reported only opposite-sex partners (any type: 55.9% vs. 41.0%; high-risk type: 37.7% vs. 28.2%; vaccine-preventable type: 19.1% vs. 14.0%) ($P < 0.05$). When we disaggregated dimensions of sexual orientation into subgroups, bisexual women and women who reported partners of both sexes had greater odds of HPV infection outcomes ($P < 0.05$ in bivariate analyses). Multivariate models attenuated several of these differences, though lesbian women and women who reported only same-sex partners had lower odds of most HPV infection outcomes in multivariate analyses ($P < 0.05$). Conclusions: HPV infection is common among sexual minority women. However, prevalence estimates vary slightly between sexual orientation dimensions and greatly depending on how a dimension is operationally defined. These findings highlight the importance of measuring sexual orientation in various ways and can help inform targeted HPV and cervical cancer prevention efforts for sexual minority women.

Published online March 4, 2016
doi: 10.1158/1055-9965.EPI-16-0085

Perspectives from Healthcare Providers and Women about Completing Human Papillomavirus (HPV) Self-Testing at Home

Zimmermann BJ, Katz ML, Moore D, Paskett ED, Reiter PL

Purpose: Cervical cancer (CC) incidence and mortality rates are increased and CC screening rates are low among women living in Ohio Appalachia. Mailing human papillomavirus (HPV) self-tests to women to complete at home is a potential new strategy in the United States to engage women in the CC screening process. Our study sought to understand both providers' and women's perspectives on an HPV self-test that could be mailed to women and how those viewpoints may differ and/or concur. Methods: Focus groups were conducted (2014–2015) among: 1) healthcare providers practicing in four Federally Qualified Health Centers (FQHCs) located in three Ohio Appalachia counties; and 2) women living in Ohio Appalachia. Results: Providers ($n = 28$) and women ($n = 15$) were accepting of HPV self-testing, however, the reason for acceptance differed between groups. Providers thought HPV self-testing would increase the possibility that under-screened women would return to the healthcare system, while women thought completing HPV self-tests at home would eliminate logistical/psychological CC screening barriers. Facilitators of completing an HPV self-test at home reported by women included decreased embarrassment, and the time and money saved by avoiding a doctor's appointment. Barriers to completing an HPV self-test at home reported by providers and women included women not being aware of the test, concerns about incorrectly completing the test and potential contamination of the obtained specimen, potential discomfort associated with completing the test, safety of the sample when returning it through the mail, issues associated with communicating test results (timing, channel, findings), and needed follow-up care. Both providers and women stressed the importance of including educational information about HPV and cervical cancer and detailed HPV self-test instructions with the mailed device. Conclusions: Findings provide insights into the facilitators and barriers of completing an HPV self-test at home, returning it, reporting results, and providing needed follow-up care. This information will be useful in developing CC screening programs that include mailed HPV self-tests.

Published online March 4, 2016
doi: 10.1158/1055-9965.EPI-16-0086

Association Between Post-Cancer Diagnosis Dietary Inflammatory Potential and Survival in WHI Observational Study and Dietary Modification Trial

Zheng JL, Tabung FK, Zhang JJ, Shivappa N, Ockene JK, Caan B, Kroenke C, Hebert JR, Steck SE

Background: Inflammation regulates key biologic processes in chronic disease and can be modulated by diet. Our objective was to use the dietary inflammatory index (DII), a novel tool to characterize the inflammatory potential of diet, to examine how post-cancer diagnosis dietary quality is associated with overall survival in the Women's Health Initiative (WHI) Observational Study (OS) and Dietary Modification Trial (DM). Methods: After excluding baseline cancers and energy outliers, the analytical cohort had 4,241 postmenopausal women (19% of total cancer cases), aged 50 to 79 years at baseline, in the WHI OS ($n = 1,852$) and DM ($n = 2,389$), who developed invasive cancer during follow-up and completed a food frequency questionnaire after diagnosis. These women were followed from dietary assessment until death from any cause. Energy-adjusted DII scores from food only and from food plus supplement (any reported dietary supplement related to DII parameters) after cancer diagnosis for each subject were calculated by multiplying the inflammatory effect scores determined based on extensive literature review and intake values for each food parameter, and then summing across all the food parameters. Death was ascertained by clinical center follow-up or by searching the National Death Index with central or local adjudication. Cox proportional hazards models were fit to estimate multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for all-cause mortality comparing women in higher DII quartiles with those in the first quartile. Results: After a median 11.2 years of follow-up, 1,470 deaths occurred. After adjustment for key covariates, women who consumed a more pro-inflammatory diet (in higher quartiles of DII score from food only) after a cancer diagnosis had a significantly