Cancer-related approved paper proposals open for writing group nominations (6/16/2011)

Ms1310 - Occupational exposures throughout life course and late life lower-body bone health – Michael
Ms1332 - Postdiagnosis diet quality, the combination of diet quality and physical activity, and survival among postmenopausal women with breast cancer: Results from the Women’s Health Initiative – George
Ms1435 - Moderate alcohol consumption and total mortality in the Women’s Health Initiative: a comparison of sub-groups by age and breast cancer risk - Rahilly-Tierney
Ms1436 - Caregiving stress, stressful life events, endogenous sex steroid hormones, and breast cancer risk – Kroenke
Ms1443 - Urinary levels of melatonin, sleep duration and risk of breast cancer – Sturgeon
Ms1448 - Confirmation of promising breast cancer early detection biomarkers – Li
Ms1462 - Association between sleep and breast cancer incidence among women participating in the Women’s Health Initiative – Vogtmann
Ms1468 - A longitudinal study of the metabolic syndrome and risk of postmenopausal colorectal cancer – Kabat
Ms1469 - Genotype imputation in Hispanic-Americans in WHI SHARE – Divers
Ms1475 - Weight cycling and risk of breast cancer by subtype in post menopausal women: the Women’s Health Initiative – Mason
Ms1477 - Sleep pattern and incidence of colorectal cancer in post-menopausal women – Jiao
Recently published cancer-related WHI papers:


PURPOSE The Study of Tamoxifen and Raloxifene (STAR) demonstrated that raloxifene was as effective as tamoxifen in reducing the risk of invasive breast cancer (IBC) in postmenopausal women and had lower risks of thromboembolic events, endometrial cancer, and cataracts but had a nonstatistically significant higher risk of noninvasive breast cancer. There is a need to summarize the risks and benefits of these agents.

PATIENTS AND METHODS Baseline incidence rates of IBC and other health outcomes, absent raloxifene and tamoxifen, were estimated from breast cancer chemoprevention trials; the Surveillance, Epidemiology and End Results Program; and the Women’s Health Initiative. Effects of raloxifene and tamoxifen were estimated from STAR and the Breast Cancer Prevention Trial. We assigned weights to health outcomes to calculate the net benefit from raloxifene compared with placebo and tamoxifen compared with placebo.

Results: Risks and benefits of treatment with raloxifene or tamoxifen depend on age, race, breast cancer risk, and history of hysterectomy. Over a 5-year period, postmenopausal women with an intact uterus had a better benefit/risk index for raloxifene than for tamoxifen. For postmenopausal women without a uterus, the benefit/risk ratio was similar. The benefits and risks of raloxifene and tamoxifen are described in tables that can help identify groups of women for whom the benefits outweigh the risks.

CONCLUSION We developed a benefit/risk index to quantify benefits from chemoprevention with tamoxifen or raloxifene. This index can complement clinical evaluation in deciding whether to initiate chemoprevention and in comparing the benefits and risks of raloxifene versus tamoxifen.
The incidences of esophageal adenocarcinoma and squamous cell carcinoma (SCC) are higher in males than in females. We investigated whether female-related hormonal factors are associated with risks of these two types of esophageal cancer. We examined the association between use of hormone therapy (HT) and the risks of esophageal adenocarcinoma and SCC in postmenopausal women enrolled in the Women’s Health Initiative (WHI) clinical trials and observational studies. Twenty-three esophageal adenocarcinoma and 34 esophageal SCC cases were confirmed among the 161,080 participants, after a median of 11.82 years of follow-up.

Risk of esophageal SCC was lower among HT users (past users: HR = 0.25, 95% CI: 0.06-1.10 in 2 cases; current users: HR = 0.41, 95% CI: 0.18-0.94 in 9 cases). A decreased esophageal SCC risk was observed for current users of estrogen plus progestin (E+P) therapy (HR = 0.25, 95% CI: 0.07-0.86 in 3 cases) but not for current users of estrogen-only therapy (HR = 0.96, 95% CI: 0.28-3.29 in 6 cases). No association was observed between the use of HT and the risk of esophageal adenocarcinoma. No other reproductive or hormonal factors were significantly associated with the risk of either SCC or adenocarcinoma. Current use of E+P therapy was found to be associated with a decreased risk of esophageal SCC, but no association was observed with esophageal adenocarcinoma. To provide more definitive evidence, a pooled analysis of all available studies or a much larger study would be needed.
ABSTRACT: BACKGROUND: Observational studies and randomized trials have suggested that estrogens and/or progesterone may lower the risk for colorectal cancer. Inherited variation in the sex-hormone genes may be one mechanism by which sex hormones affect colorectal cancer, although data are limited.

METHOD: We conducted a comprehensive evaluation of single nucleotide polymorphisms (SNPs) in genes encoding 3 hormone receptors (ESR1, ESR2, PGR) and 5 hormone synthesizers (CYP19A1 and CYP17A1, HSD17B1, HSD17B2, HSD17B4) among 427 women with incident colorectal cancer and 871 matched controls who were Caucasians of European ancestry from 93676 postmenopausal women enrolled in the Women’s Health Initiative Observational cohort. A total of 242 haplotype-tagging and functional SNPs in the 8 genes were included for analysis. Unconditional logistic regression with adjustment for age and hysterectomy status was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS: We observed a weak association between the CYP17A1 rs17724534 SNP and colorectal cancer risk (OR per risk allele (A) =1.39, 95% CI=1.09-1.78, corrected p-value=0.07). In addition, a suggestive interaction between rs17724534 and rs10883782 in 2 discrete LD blocks of CYP17A1 was observed in relation to colorectal cancer (empirical p value=0.04). Moreover, one haplotype block of CYP19A1 was associated with colorectal cancer (corrected global p value=0.02), which likely reflected the association with the tagging SNP, rs1902584, in the block.

CONCLUSION: Our findings offer some support for a suggestive association of CYP17A1 and CYP19A1 variants with colorectal cancer risk.
BACKGROUND: Colorectal cancer (CRC) incidence and mortality rates are higher in African Americans as compared to other racial/ethnic groups. The Women's Health Initiative (WHI) study sample was used to determine whether differences in CRC risk factors explain racial/ethnic differences in incidence and mortality.

METHODS: The WHI is a longitudinal study of postmenopausal women recruited from 40 centers. Baseline questionnaires were used to collect socio-demographic and health status information. All CRC diagnoses were centrally adjudicated. Cox regression models were used to compute hazard ratios (HRs) and 95% confidence intervals (CIs) for invasive CRC by race/ethnicity.

RESULTS: The study sample included 131,481 (83.7%) White, 14,323 (9.1%) African American, 6,362 (4.1%) Hispanic, 694 (0.4%) Native American and 4,148 (2.6%) Asian/Pacific Islanders. After a mean follow-up of 10.8 years (SD 2.9), CRC incidence was highest in African Americans (annualized rate = 0.14%), followed by Whites and Native Americans (0.12% each), Asian/Pacific Islanders (0.10%) and Hispanics (0.08%). After adjustment for age and trial assignment, Hispanics had a lower risk compared to Whites, HR 0.73 (95% CI: 0.54-0.97) (p=0.03), and African Americans had a marginally greater risk, HR 1.16 (95% CI: 0.99-1.34), p=0.06. Multivariable adjustment attenuated the difference in incidence between African Americans and Whites (HR 0.99, 95% CI: 0.82-1.20), while strengthening the lower HR for Hispanics (HR 0.68, 95% CI: 0.48-0.97).

CONCLUSIONS: African American/White differences in CRC risk are likely due to sociodemographic/cultural factors other than race. Impact: A number of modifiable exposures could be a focus for reducing CRC risk in African Americans.

BACKGROUND: Glycemic effects of the Women's Health Initiative (WHI) low-fat dietary intervention are unknown. OBJECTIVE: Our objective was to analyze the effects of the WHI low-fat dietary intervention on serum glucose and insulin and insulin resistance up to 6 y after random assignment. DESIGN: Postmenopausal WHI Dietary Modification trial intervention (DM-I) and comparison (DM-C) participants with blood measures at least at baseline and year 1 (n = 2263) were included. Anthropometric measures, dietary assessments, serum glucose and insulin concentrations, homeostasis model assessment of insulin resistance (HOMA-IR) measures, and quantitative insulin sensitivity check index (QUICKI) values were obtained at baseline, year 1, year 3, and year 6. Changes in measures were compared between groups at years 1, 3, and 6 overall and within stratified analyses. RESULTS: Mean (±SD) differences in changes at year 1 between the DM-I and DM-C groups were as follows: glucose, -1.7 ± 17.9 mg/dL; insulin, -0.7 ± 5.1 μIU/mL; HOMA-IR, -0.2 ± 1.9; and QUICKI, 0.004 ± 0.019 (all P < 0.05). Similar findings resulted from repeated-measures analyses comparing the intervention and comparison groups over the 6 y. Whereas normoglycemic women at baseline had a decrease in glucose at year 1 that was 1.9 ± 17.2 mg/dL greater in the DM-I than in the DM-C group, diabetic women had an increase in glucose that was 7.9 ± 20.3 mg/dL greater in the DM-I than in the DM-C group (P for interaction <0.001). CONCLUSIONS: A low-fat diet was not significantly associated with adverse glycemic effects up to 6 y after random assignment in postmenopausal women. However, diabetic women experienced adverse glycemic effects of the low-fat diet. This trial is registered at clinicaltrials.gov as NCT00000611.
BACKGROUND: Elective bilateral salpingo-oophorectomy (BSO) is routinely performed with hysterectomy for benign conditions despite conflicting data on long-term outcomes.

METHODS: This is a prospective cohort of 25 448 postmenopausal women aged 50 to 79 years enrolled in the Women's Health Initiative Observational Study who had a history of hysterectomy and BSO (n = 14 254 [56.0%]) or hysterectomy with ovarian conservation (n = 11 194 [44.0%]) and no family history of ovarian cancer. Multivariable Cox proportional hazards regression models were used to examine the effect of BSO on incident cardiovascular disease, hip fracture, cancer, and death.

RESULTS: Current or past use of estrogen and/or progestin was common irrespective of BSO status (78.6% of cohort). In multivariable analyses, BSO was not associated with an increased risk of fatal and nonfatal coronary heart disease (hazard ratio, 1.00 [95% confidence interval, 0.85-1.18]), coronary artery bypass graft/percutaneous transluminal coronary angioplasty (0.95 [0.82-1.10]), stroke (1.04 [0.87-1.24]), total cardiovascular disease (0.99 [0.91-1.09]), hip fracture (0.83 [0.63-1.10]), or death (0.98 [0.87-1.10]). Bilateral salpingo-oophorectomy decreased incident ovarian cancer (0.02% in the BSO group; 0.33% in the ovarian conservation group; number needed to treat, 323) during a mean (SD) follow-up of 7.6 (1.6) years, but there were no significant associations for breast, colorectal, or lung cancer.

CONCLUSIONS: In this large prospective cohort study, BSO decreased the risk of ovarian cancer compared with hysterectomy and ovarian conservation, but incident ovarian cancer was rare in both groups. Our findings suggest that BSO may not have an adverse effect on cardiovascular health, hip fracture, cancer, or total mortality compared with hysterectomy and ovarian conservation.

Although studies have shown that physically active breast cancer survivors have lower all-cause mortality, the association between change in physical activity from before to after diagnosis and mortality is not clear. We examined associations among pre- and postdiagnosis physical activity, change in pre- to postdiagnosis physical activity, and all-cause and breast cancer-specific mortality in postmenopausal women. A longitudinal study of 4,643 women diagnosed with invasive breast cancer after entry into the Women's Health Initiative study of postmenopausal women. Physical activity from recreation and walking was determined at baseline (prediagnosis) and after diagnosis (assessed at the 3 or 6 years post-baseline visit). Women participating in 9 MET-h/wk or more (~3 h/wk of fast walking) of physical activity before diagnosis had a lower all-cause mortality (HR = 0.61; 95% CI, 0.44-0.87; P = 0.01) compared with inactive women in multivariable adjusted analyses. Women participating in ≥ 9 or more MET-h/wk of physical activity after diagnosis had lower breast cancer mortality (HR = 0.61; 95% CI, 0.35-0.99; P = 0.049) and lower all-cause mortality (HR = 0.54; 95% CI, 0.38-0.79; P < 0.01). Women who increased or maintained physical activity of 9 or more MET-h/wk after diagnosis had lower all-cause mortality (HR = 0.67; 95% CI, 0.46-0.96) even if they were inactive before diagnosis. High levels of physical activity may improve survival in postmenopausal women with breast cancer, even among those reporting low physical activity prior to diagnosis. Women diagnosed with breast cancer should be encouraged to initiate and maintain a program of physical activity.