A Prospective Evaluation of Insulin and Insulin-like Growth Factor-I as Risk Factors for Endometrial Cancer

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This is critical, given the mutual association of hyper-

age-adjusted hazard ratio estimates for the association of free IGF-I and endometrial cancer between batches and confirmed that the results did not significantly differ (P = 0.35).

Statistical Analysis. The baseline characteristics of cases and the subcohort were compared using the Wilcoxon rank sum test (for continuous data) or Pearson•s χ^2 (for categorical data). Serologic assay results were expressed as quartiles or tertiles based on the distribution of values in the subcohort. For those assays conducted in two separate batches, we determined the quartiles separately for each batch. This was done to minimize the possibility that even unrecognized variations in laboratory results across batches might affect our findings. Correlations between these serologic data, age, and body mass index (BMI) were assessed in the subcohort using Spearman•s correlation coefficient. To assess the effects of hormone therapy on each of the measured serologic factors, we determined their mean values by hormone therapy stratum categorized as (a) users of combined estrogen and progesterone or (b) nonusers of estrogen and progesterone and compared these values using the Wilcoxon rank sum test. Hazard ratios measuring the associations of our serologic data, as well as other risk factors, with risk for endometrial cancer were estimated using multivariable Cox proportional hazard regression models that used the Self-Prentice method for robust standard error estimates (to account for the case-cohort design), with time to event as the underlying time scale. Our main models were adjusted for (a) age, categorized as 50-54 (reference), 55-59, 60-64, 65-69, 70-74, or 75-79 years of age; (b) BMI, categorized as <18.5, 18.5 to <25 (reference), 25.0 to <30, 30 to <34, or $\geq$34 kg/m ^{2}; and (c) hormone therapy use or endogenous estradiol levels. Estradiol data were assessed in non… hormone therapy users only because hormone therapy complicates estradiol measurement. This created four nonoverlapp0(4)19.82indings.hormco7

users) to be modeled. Reported epidemiologic risk factors for endometrial cancer (that is, parity, age at first live birth, age at menopause, oral contraceptive use, physical activity, smoking, and alcohol consumption) were tested as potential confounding variables by stepwise inclusion in these multivariable models, and variables that altered the hazard ratio by 10% or more were retained in the final model. Analyses stratified by hormone therapy use (user/nonuser) and BMI (<25.0 or

adenocarcinoma, we detected no significant heterogeneity in the results stratified by hormone therapy use. There was no association between any of the serologic factors and non-endometrioid adenocarcinomas (data not shown).

Stratification by BMI.

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