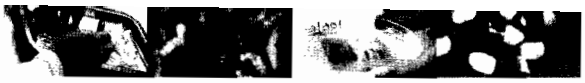

Keynote Lecture IX

Findings from the Nurses' Health Study; informing Cancer Etiology and Prevention

Graham A Colditz

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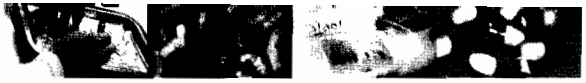
After graduating in Medicine at the University of Queensland in 1979, Graham Colditz completed his internship at the Royal Brisbane Hospital. Dr Colditz then completed his MPH and DrPH at the Harvard School of Public Health. In 1986 he joined the faculty at Harvard Medical School and has been Professor of Medicine at Harvard Medical School since 1997 and Associate Director of the Channing Laboratory within the Department of Medicine since 2005.

His main research contributions have drawn on the Nurses' Health Study, which he has served as Project Director since 1986 and Principal Investigator since 2000. His research has focused on modifiable risk factors for cancer including postmenopausal hormone therapy and risk of cancer, physical activity, obesity, diet and other lifestyle factors.

In 2003 he was the recipient of the American Cancer Society-Cissy Hornung Clinical Research Professorship and awarded the 2003 AACR-DeWitt Goodman Memorial Lectureship and most recently, the ASPO Distinguished Achievement Award.

The Nurses' Health Study was founded by Frank E Speizer, MD with funding from the National Cancer Institute in 1976. One hundred and twenty one thousand, seven hundred women (121,700), ages 30-55 responded to the baseline questionnaire and have been followed every two years with questionnaires to update their information on lifestyle and health outcomes. The original Nurses' Health Study questionnaire inquired about reproductive risk factors for breast cancer, history of benign breast disease, and family history of breast cancer. Questions about use of oral contraceptives, the primary hypothesis of the study, were asked. With follow-up through ten years, current users of oral contraceptives were at significantly increased risk of breast cancer compared to never users. Past users had not elevation in risk. In 1980, dietary data were added to the study. Follow-up of the cohort showed that alcohol was independently related to increased risk of breast cancer and that dietary fat in adult life was not related to risk. In 1989, blood samples were provided by over 32,000 participants. Analyses drawing on these samples have shown a direct relation between circulating estrogen and testosterone and subsequent risk of breast cancer.

Based on results from modeling, the age-incidence curve for breast cancer, which shows the steepest increase in risk from menarche to menopause, we have increased our focus on earlier life exposures. In a detailed evaluation of benign breast disease biopsies and subsequent risk of breast cancer, we have shown that proliferative disease without atypia, atypical hyperplasia, and microscopic radial scars all increase subsequent risk of breast cancer. Drawing on proliferative benign breast changes identified through biopsies, we have evaluated adolescent diet as a risk factor for this intermediate marker of breast cancer risk. Higher intakes of fiber and polyunsaturated fat are associated with substantial reductions in risk. We have also evaluated childhood adiposity in relation to this endpoint and observed that the most obese children at ages 5 and 10 are at substantial reduction in the risk of proliferative changes on benign biopsy. Extending this finding to breast cancer, we



have evaluated adiposity of ages 5 and 10 and have observed a similar reduction in risk of breast cancer that is independent of adult weight and weight gain.

Evaluating postmenopausal hormone therapy we have shown that the combined use of estrogen + progesterone significantly increases risk above estrogen alone and both increase risk above that for women who do not use postmenopausal hormones. Emerging data from the cohort shows that the use of testosterone is associated with an increased risk of breast cancer and that women who lose weight after menopause are at lower risk compared to women who maintain a study weight after menopause.

In addition to these breast cancer findings, numerous evaluations of diet and other cancers have highlighted the role of multi-vitamins containing folate and have allowed us to evaluate the trade-offs of increased cancer risk with high alcohol intake against a reduction in risk of cardiovascular disease. Drawing on the unique strength of the cohort, the evaluation of total mortality allows us to weigh the overall impact of lifestyle on health. Results for obesity and physical activity will also be discussed.