NURSES' HEALTH STUDY NEWSLETTER

Volume 2, June 1995

We are pleased to present the second volume of the Nurses' Health Study Newsletter. As you know, the two studies (the Nurses' Health Study and the Nurses' Health Study II) are conducted using biennial questionnaires to collect information on reproductive factors, lifestyle practices, and diet in relation to the occurrence of breast cancer and other major illnesses in women. Every year we learn more about the causes of these conditions and come closer to finding the means for their prevention. Even if you are no longer active in the nursing profession, we need you! The scientific integrity of these studies is largely dependent on your continued participation.

In the past year, we published fourteen original manuscripts pertaining directly to women's health. This exciting research draws on the responses you and your colleagues have given. Here are summaries of a few of them.

Weight, weight change, and coronary heart disease in women.
The 1990 US weight guidelines for women support a substantial weight gain at approximately age 35 and recommend a range of body mass index (defined as weight in kilograms divided by the square of the height in meters) from 21 to 27 kg/m^2. We assessed the validity of these guidelines in terms of coronary heart disease risk in women. On the basis of 14 years of follow-up in the Nurses' Health Study, we found that higher levels of body weight, even within the "normal" range, as well as weight gains after age 18 appear to increase the risk of coronary heart disease in middle-aged women. These data indicate that current US weight guidelines may be falsely reassuring to the large proportion of women older than 35 years whose weight is within the current guidelines. (Willett et al. J Am Med Assoc 1995; 273:461-465.)

A prospective study of smoking cessation and weight change in women.
We examined the relation between smoking cessation and weight gain in the Nurses' Health Study. During a two-year period, women who stopped smoking gained on average only 2.4 kg (5.3 lbs) more than women who continued smoking. The overall health benefits of smoking cessation far outweigh any risks associated with this weight gain. We are presently studying factors, such as exercise, that minimize post-cessation weight gain. (Kawachi et al. J Smoking-Related Dis 1994; 5(S1):91-100.)

Reproducibility and validity of a self-administered physical activity questionnaire.
In a representative sample of the Nurses' Health Study II, we assessed whether our questionnaire accurately measures physical activity and inactivity. Using past-week activity recalls and 7-day activity diaries, we determined that the short, simple items included in our questionnaire are reasonably valid measures for epidemiological research. (Wolf et al. Int J Epidemiol 1994; 23:991-999.)

A prospective study of symptomatic gallstones in women: relation to oral contraceptives and other risk factors.
Among 96,211 Nurses' Health Study II participants younger than 45, we examined the relation between the risk of symptomatic gallstones and oral contraceptives, body mass index, weight change, alcohol consumption, and smoking. We found no substantial increase in risk among women who had ever used oral contraceptives, although current and long-term users had somewhat elevated risks. The risk of symptomatic gallstones increased with increasing body mass index. (Grodstein et al. Obstet Gynecol 1994; 84:207-214.)

A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in US women.
This study had two purposes: 1) to assess the association between smoking and risk of colorectal adenoma and colorectal cancer in women; and 2) to estimate the minimum time period between the start of smoking and increased risk of cancer. We found that cigarette smoking was unrelated to colorectal cancer until 35 years after smoking began and then became more strongly related with time. These findings suggest that cigarette smoking may be a previously unrecognized, preventable cause of colorectal cancer among women.
(Giovannucci et al. J Natl Cancer Inst 1994; 86:192-199.)

Oral contraceptive use and mortality during 12 years of follow-up.
We compared the risk of all-cause mortality among Nurses' Health Study participants who had ever used oral contraceptives and those who had never used them. We found no evidence that oral contraceptive use adversely affects long-term risk for mortality, even after lengthy durations of use. (Colditz et al. Ann Intern Med 1994; 120:821-826.)

A prospective study of permanent hair dye use and hematopoietic cancer.
In the Nurses' Health Study population, we investigated the relation between the use of permanent hair dyes and the risk of lymphoma, leukemia, and multiple myeloma. Our findings indicated that there is no association between permanent hair dye use and any of these hematopoietic cancers. (Grodstein et al. J Natl Cancer Inst 1994; 86:1466-1470.)

QUESTION & ANSWER

Here are some commonly asked questions from participants and our answers to them.

Q: If I'm healthy and have no diseases to report, do you still want me in the Nurses' Health Study?

A: We definitely want you to remain an active participant in the study! While our research papers might make it seem that we study only women who have had some illness, the members of the study who do not have diseases are just as important. In most analyses, we compare various characteristics of women who have a particular disease with those of women who do not have that illness. For example, to look at the effect of smoking on heart disease, we compared smoking patterns among women who developed heart disease with patterns among those who did not. We found that smokers are much more likely to develop heart disease than non-smokers. Without the responses of the "healthy" participants, this analysis would not have been possible.

Q: You seem to ask many of the same questions on every questionnaire. Why do we have to give this same information over and over?

A: The primary goal of each biennial questionnaire is to learn about changes in your health status and lifestyle in the previous two years. To do this we have to ask a lot of the same questions to learn what changes have occurred. For example, we continue to ask whether

your natural menstrual periods have ceased. Although some women's last period was 25 years ago, many women are premenopausal and others have gone through menopause in the preceding two years. For those whose periods have ceased, we apologize for repeating this question each time. However, we must continue to inquire so that we can identify those participants who are still premenopausal.

Similarly, the questions regarding the use of replacement hormones allow us to maintain up-to-date information about which study members are using hormones, how long they have been taking them during the last two years, and at what doses. So remember, we're not asking the same questions because we forgot what you said the last time; we just want to find out if anything has changed since we last heard from you!

Q: Nurses are exposed to a wide variety of potential toxic agents in the work environment. Why don't you investigate them in the Nurses' Health Study?

A: These issues **are** worthy of examination in the proper context. However, it is nearly impossible in a mail-based study to collect useful and accurate information on exposure to known or suspected environmental toxins. In addition, on-the-job exposures to environmental agents vary widely, even among nurses performing similar tasks. These areas are better studied by research with a more interventional or clinical focus. Our study is designed to evaluate the impact of lifestyle factors like diet, exercise, and hormone use on disease risk.

Q: How many of the original members are still active participants in the studies?

A: The Nurses' Health Study began in 1976 with 121,701 participants; the Nurses' Health Study II enrolled 116,680 women in 1989. In the two questionnaire cycles since 1990, we have obtained complete follow-up information on over 90% of each group. In addition, 6,675 members of the Nurses' Health Study and 144 participants in the Nurses' Health Study II have died.

The Nurses' Health Studies are the largest investigations of women's health in the world that collect and maintain repeated follow-up information. This research depends on your continued willingness to complete our often-lengthy surveys. The updating of each respondent's history every two years provides a strong base of data from which new insights into women's health can emerge.

WE'D LIKE TO UPDATE YOUR ADDRESS

If you have a new street address as a result of the addition of "911" service in your area, or if you have moved, we would like to know! Please note the change on the enclosed coverletter and mail it to the address shown, fax it to us at (617) 432-0335, or call us at (617) 432-2279. We look forward to staying in touch!

FOR YOUR INFORMATION

In the March/April 1995 issue of the Journal of the American Medical Women's Association, Dr. Graham Colditz presents a comprehensive look at the history of the Nurses' Health Study. In the article, Dr. Colditz summarizes our follow-up and confirmation methods, discusses the use of biologic specimens and outlines major findings (JAMWA 1995; 50:40-44).

FOCUS

Over its nearly 20-year history, the Nurses' Health Study has provided a rich environment for doctoral students training in epidemiology at the Harvard School of Public Health. Walter Willett, Principal Investigator of the Nurses' Health Study II, and co-investigators Graham Colditz, Susan Hankinson, David Hunter, JoAnn Manson, and Meir Stampfer were once doctoral students honing their research skills on the Nurses' Health Study. Now we'd like you to meet another up-and-coming investigator, whose work focuses on ethnic differences in diet and obesity.

Michelle Holmes is currently an Instructor in Medicine at Harvard Medical School and a primary care internist at Cambridge Hospital. She is also studying for a doctorate in epidemiology at the Harvard School of Public Health. Dr. Holmes' undergraduate degree and her medical and public health master's degrees are from Harvard University. Her internal medicine residency (1982-1985) was at Montefiore Hospital in the Bronx, NY, with a clinical practice in an economically depressed neighborhood in the South Bronx.

During her fellowship in General Internal Medicine at Beth Israel Hospital in Boston from 1985 to 1988, Dr. Holmes performed research on sexually transmitted infections in female prison inmates. In addition, she was one of five subcommittee chairs for the admissions committee at Harvard Medical School from 1989 through 1991; she was responsible for examining all applications of under-represented minorities to Harvard Medical School.

In our substudies, we try to employ a random, or representative, sample of participants to ensure that our results will apply to the general population of women. While minority groups make up only 6% of the Nurses' Health Study II cohort, these 6,500 nurses constitute the largest population of minority women currently being studied. We inevitably "oversample" these groups in substudies, but this underscores the vital importance of high response rates to our research efforts.

Dr. Holmes has been conducting several analyses in the Nurses' Health Study cohorts. The first is an analysis of the causes of ethnic differences in obesity among Nurses' Health Study II participants. The second analysis updates an earlier study on the relationship between fat and fiber intake and the risk of breast cancer, utilizing four additional years of follow-up, and looking at various components of fat and fiber. Dr. Holmes hopes to eventually use her research skills to examine health trends among women of color and among economically disadvantaged groups. She has ongoing practical experience with these groups as her patient practice is in a neighborhood health center situated within a low-income housing development.



Photograph by Ricardo Guthrie

FUTURE DIRECTIONS

FUNDING RENEWAL

As you may know, the Nurses' Health Study projects are supported financially by federally funded grants. Every five years, we must submit an application to secure funds for the next five years of research. There are no guarantees that funding will continue beyond any given five-year period.

Last summer, we were awarded five more years of funding for the Nurses' Health Study II from the National Institutes of Health/National Cancer Institute in Bethesda, Maryland. In a summary statement from NIH/NCI that recommended this funding, reviewers remarked that "the hypotheses of primary interest are of considerable public health importance, the study is well-designed and could contribute new and meaningful information. Particular strengths include the prospective collection of data, the use of a knowledgeable and motivated study population, the large sample size involved, and the strong team of collaborating investigators." Overall, "the panel expressed a high level of enthusiasm for continued support of this study."

In March of this year, the Nurses' Health Study was also awarded funds for another five years. Reviewers noted: "The design and conduct of this investigation have been exemplary." It is a "unique investigation [with] an extremely high rate of follow-up."; the "population represents a resource of national importance [that] should be continued." We congratulate you and thank you all for your part in making these efforts so successful.

BLOOD COLLECTION

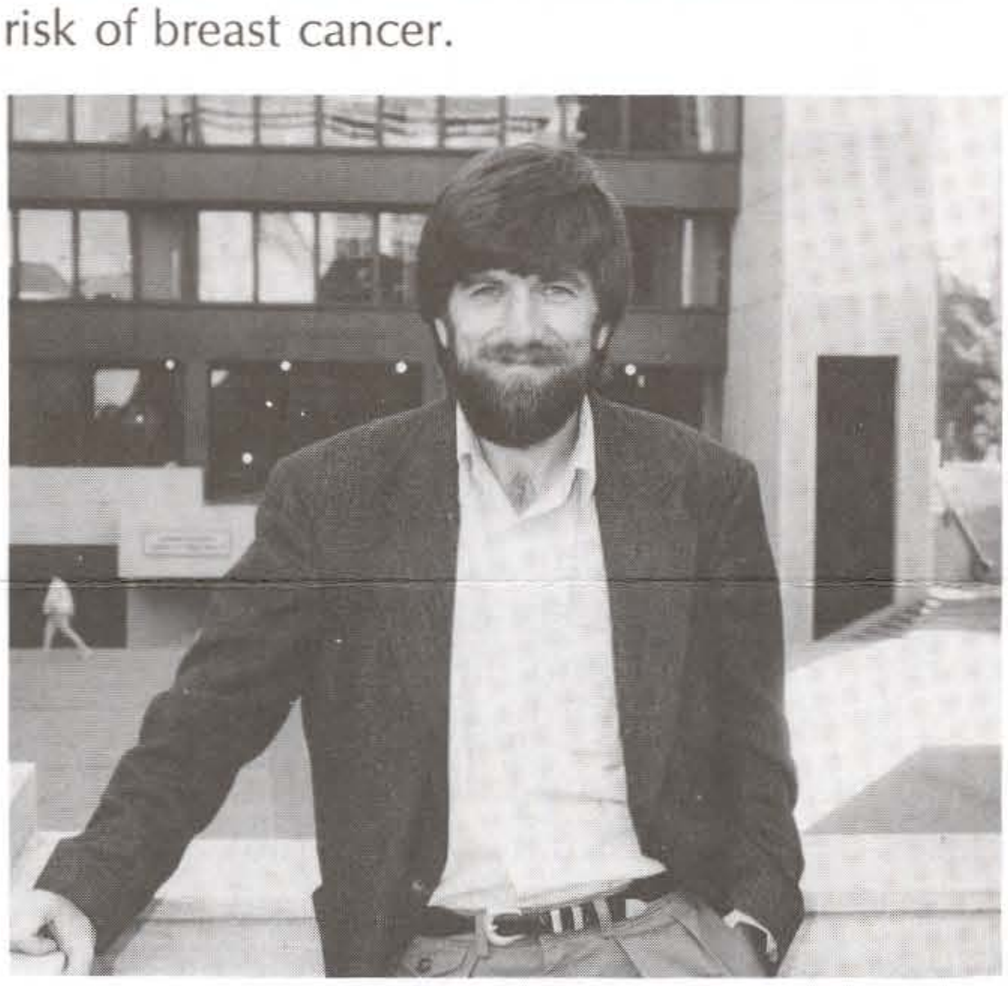
The Nurses' Health Study II is an ideal context in which to investigate how hormonal and other biochemical markers in premenopausal women influence their subsequent breast cancer risk. As you may recall, in 1989 we collected blood samples from over 33,000 Nurses' Health Study participants. Now we are seeking funding to collect blood and urine samples from approximately 40,000 women in the Nurses' Health Study II. Once all the samples have been collected, we will examine various hypotheses relating risk of breast cancer with sex hormone levels in plasma, antioxidant levels in plasma, and estrogen metabolism in premenopausal women. The blood and urine samples will provide an invaluable resource that can be used over the next several decades to study the relation of biological markers to subsequent risk of breast cancer and other diseases.

Using the same mail-based collection method we used for sample collection in the Nurses' Health Study, we hope to obtain samples from Nurses' Health Study II participants who fit the following criteria: (1) are premenopausal, (2) have no previous diagnosis of cancer (except nonmelanoma skin cancer), (3) have not used oral contraceptives or hormonal treatments for infertility in the past six months, and (4) have not been pregnant and have not breast-fed in the past six months. Plasma from blood drawn during both the follicular and luteal phases of the menstrual cycle, white and red blood cells, and urine will be stored in liquid nitrogen freezers and analyzed at a later date. If we receive funding, we will contact all potentially eligible participants in 1997.

BREAST CANCER RESEARCH

Breast cancer is the leading cause of death among US women 30 to 50 years of age, and this predominance continues through older ages except among smokers (where death from lung cancer prevails). The continued increase in breast cancer rates cannot be fully explained by more widespread mammography. Some relatively rare genetic causes of breast cancer have been established, but other genetic causes with lower degrees of risk remain to be found. Few studies have assessed whether the effect of known breast cancer risk factors (e.g., reproductive determinants) and suspected risk factors (e.g., alcohol consumption) varies according to familial, or inherited, predisposition.

In the Nurses' Health Study, we are using the blood samples collected in 1989 and 1990 to assess whether levels of hormones and antioxidant vitamins are associated with the risk of breast cancer.



Photograph by Richard Chase

Dr. David Hunter is currently investigating whether levels of pesticide metabolites in blood are associated with breast cancer risk and whether these metabolites interact with genetic markers of carcinogen metabolism.

We are also seeking funding to answer two key questions:

- *What genetic alterations are involved in the origin and progression of breast cancer and other cancers?*

- *What roles do lifestyle variables play in modulating genetic risk factors for breast cancer?*

The discovery of interactions of environmental exposures with inherited susceptibility would certainly cast light on mechanisms of breast carcinogenesis and might suggest lifestyle changes for women with inherited risk.

READY TO MOVE

In our last newsletter, we told you that a new facility was under construction and that we would relocate in June 1996. The builders are on schedule, and we have already begun our preparations for the move. We will be leaving what has been home to the Nurses' Health Study for nearly 20 years.

The Nurses' Health Studies will occupy one floor in the new building, seen here in the foreground; the columned structure in the upper-right corner is our current facility.



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