NURSES' HEALTH STUDY NEWSLETTER

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The year 1996 marked the twentieth anniversary of the Nurses' Health Study. We celebrated this important milestone by hosting the *Update on Women's Health* symposium in February 1997. Nearly 800 Nurses' Health Study and Nurses' Health Study II participants traveled to Boston to take part in this three-day conference. Many topics were presented in plenary and break-out sessions, and there was much spirited interaction between participants and investigators. Below, we summarize key findings from the Nurses' Health Studies that were presented at this successful event.



Photo by Justin Knight

☞ **Smoking** is the dominant cause of lung cancer and heart disease in women, and has also been linked with cataracts, stroke, pancreatic cancer, and possibly colon cancer. However, 10 to 14 years after stopping smoking, ex-smokers' risk of death approaches that of women who never smoked.



☞ **Use of oral contraceptives** for five or more years at any time in a woman's life decreases her risk of ovarian cancer by about 35%, and having a tubal ligation may also reduce this risk. Nonetheless, current use of birth control pills in women in their 40s slightly increases the risk of breast cancer and heart disease (especially when combined with smoking), although there is no association between past use of oral contraceptives and these diseases.

☞ **Hormone replacement therapy (HRT)** reduces risk of heart disease and osteoporosis. However, women who take estrogen therapy for five or more years incur a modest increase in breast cancer risk. In deciding whether to embark on HRT, women should consider other risk factors they may have for breast cancer or heart disease, such as family history.

☞ **Moderate alcohol intake** (even one or two drinks per day) increases the risk of breast cancer but cuts the risk of heart disease in half.



☞ **Hair dye** does not cause cancer as was once suspected.

☞ **Eating red meat** is associated with colon cancer.



☞ **Trans-fatty acids** in most margarines and vegetable shortening (commonly found in store-bought baked goods) drive up the risk of heart disease. To reduce your trans-fatty acid intake, avoid "partially hydrogenated" fat, and do not eat deep fried fast foods.

☞ Although **fat intake** was once thought related to breast cancer risk, no association has been found — though monounsaturated fat (as found in olive oil) appears to decrease risk slightly.



Photo by Norman Stein

Project Coordinator Gary Chase discusses questionnaire processing at a break-out session.

☞ **A diet high in fruits and vegetables** protects against heart disease and stroke and may reduce breast cancer risk.



☞ **Some vitamins** protect against disease. Vitamin E supplements taken for 2 years or more lower heart disease risk by about 40%. Vitamin B_6 along with folic acid (another B-complex vitamin) also may lower that risk. Vitamin C, however, does not. Folic acid may also reduce the risk of colon cancer. The amounts of folic acid and vitamin B_6 in standard multiple vitamins are sufficient to achieve these benefits.

☞ **Calcium supplements** slightly increase risk of kidney stones, while foods naturally high in calcium appear to decrease risk. The benefits of high calcium intake in reducing fractures remain unclear.

☞ **Excessive sun exposure** is related to cataracts and malignant melanoma.

☞ **Drinking coffee** does not appear to increase the risk of heart attack. Drinking coffee in moderation — about two cups per day — was associated with less risk of suicide, a finding that suggests coffee may have a beneficial effect on mood.



☞ Even **moderate weight gains** of 15 to 20 pounds by mid-life increase the chance of premature death, and women 30% or more above their recommended weight are four times more likely to die from heart disease and face twice the risk of death from cancer. Obesity is the leading risk factor for adult onset diabetes, hypertension, and heart disease, and is also associated with gallstones.

☞ **Regular physical activity** protects against diabetes, heart disease, osteoporosis, and colon cancer and, in helping to keep weight down, also protects against many other diseases.



Photo by Justin Knight

Growing Up Today Study



In October 1996, 25,000 children of Nurses' Health Study II participants were invited to participate in the Growing Up Today Study. This new project is funded by the National Institutes of Health and focuses on physical activity, diet, weight concerns, growth and development, and general health and well-being. The questionnaire we mailed to the 9- to 14-year old population was similar to past Nurses' Health Study questionnaires but was adapted for these young people.

Obesity among adolescents in the U.S. is increasing; through this study we hope to examine relations among diet, physical activity, and growth. Many behaviors and lifestyle patterns, such as physical activity and diet, are established early in life, and may have health consequences in both childhood and adulthood. Thus, it is essential that we understand clearly how they are established. By following children over time and into adulthood, we hope to gain much-needed information on how these patterns are established, maintained, and interrelated.

Thanks to both the young people who filled out and returned their completed Growing Up Today Study questionnaires, and the Nurses' Health Study II mothers who gave encouragement and general support to their children, we received over 16,500 responses and have begun preliminary data analyses. The children will receive a follow-up questionnaire every September so that we can update their information. We hope to follow them for many years, since this is one of the very few prospective studies of youth in the world; its potential to contribute to our understanding of health is immeasurable.

A note to mothers of Growing Up Today Study participants:

If you move, please let us know explicitly that your child(ren) also moved. You may reach us by:

- **telephone** 617-525-2279
- **fax** 617-525-2008
- **U.S. mail** Channing Laboratory
  181 Longwood Avenue
  Boston, MA 02115-5804

Blood Collection in the NHSII

In 1996, we began the collection of blood and urine samples from premenopausal women in the Nurses' Health Study II. This study is funded by the National Cancer Institute to evaluate the relationship between plasma and urinary hormone levels and subsequent risk of breast cancer. Although it is clear that hormones play an important role in breast cancer, little is known about what specific hormones are most important and at what hormone levels risk is affected. The samples will be stored at Harvard University (identified by ID number only) and, over the next five to ten years, will be selectively analyzed for a range of potentially useful biochemical and genetic markers of disease risk in women, such as the relation of vitamin D and antioxidant levels to breast and colon cancer.

No previous study has been able to collect a large number of blood and urine samples (collected at specific times during the menstrual cycle). However, this is possible in the Nurses' Health Study II because of your strong commitment to research and your medical knowledge. Over the next decade the information provided by these samples will uniquely contribute to improving women's health.

To date over 10,000 women have been invited to participate in the study; samples have been received from about 5,000 women. We will continue to collect samples over the next two years. If you have already returned a sample — *THANK YOU!* If you have not yet been contacted or have not yet returned your sample, we look forward to your participation.

Recent Findings from the Nurses' Health Studies

Prospective study of oral contraceptives and non-insulin dependent diabetes mellitus (NIDDM) among U.S. women.

We found no appreciable increase in the 4-year risk of NIDDM among current users of oral contraceptives in the Nurses' Health Study II population. Nor was there any increase in risk among past users. (Chasan-Taber et al. Diabetes Care 1997; 20:330-335.)

Dietary fiber, glycemic load, and risk of NIDDM in women.

We identified 915 cases of diabetes during six years of follow-up in the Nurses' Health Study, and we examined information on total and specific sources of dietary fiber and foods that increase blood glucose. Our results indicated that diets with a high glycemic load and a low cereal fiber content increase risk of diabetes in women. The diets associated with low risk of diabetes were characterized by whole grains, high fiber foods, and low intake of highly refined grains and potatoes. (Salmerón et al. JAMA 1997; 277:472-477.)

Physical activity, obesity, and risk of colorectal adenoma in women.

Among 13,057 Nurses' Health Study participants age 40-65 in 1986, we found an inverse association between physical activity and occurrence of adenomas in the distal colon. Obesity was associated with an elevated risk of large polyps. (Giovannucci et al. Cancer Causes and Controls 1996; 7:253-263.)

Prospective study of cigarette smoking and the risk of pancreatic cancer.

We obtained data on cigarette smoking and other risk factors for pancreatic cancer from 118,339 Nurses' Health Study participants age 30-55 years who were free from cancer. While cigarette smoking was associated with an increased risk of pancreatic cancer, the rapid reduction in risk associated with quitting suggests that smoking cessation could eliminate 25% of the 27,000 deaths from this type of cancer occurring annually in the U.S. (Fuchs et al. Arch Intern Med 1996; 156:2255-2260.)

Postmenopausal estrogen and progestin use and the risk of cardiovascular disease.

To determine the effect of combined estrogen and progestin therapy on cardiovascular disease risk, we followed 59,337 Nurses' Health Study participants age 30-55 years in 1976. We found that the addition of progestin does not appear to diminish the cardioprotective effects of postmenopausal estrogen therapy. (Grodstein et al. New Engl J Med 1996; 335:453-461.)

Protein consumption and bone fractures in women.

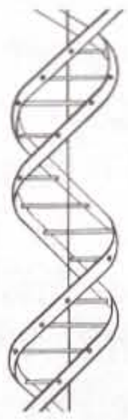
During twelve years of follow-up, we found that higher protein consumption was associated with an increased risk of osteoporotic forearm fractures among 89,500 Nurses' Health Study participants. No increase in risk was observed for hip fractures, although we were limited by the smaller numbers of such fractures in the study. (Feskanich et al. Am J Epidemiol 1996; 143:472-479.)

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 found no substantial increase in risk of gallstones among women who had ever used oral contraceptives, although current and long-term users had somewhat elevated risks. The risk for gallstones increased with increasing body mass index. (Grodstein et al. Obstet Gynecol 1994; 84:207-214.)



Inherited Susceptibility to Disease



The Nurses' Health Study has contributed important information on inherited genetic factors and risk of various diseases. Until recently, this information was based on reports of family history of those diseases. The results showed that inherited genetic factors account for only a small proportion of common diseases such as breast cancer, colorectal cancer, diabetes, and myocardial infarction. Recently, the genes which may contribute to some of this inherited susceptibility have been found, and with the rapid progress of the Human Genome Project, it is predicted that many more genes will be identified in the next few years.

The blood samples provided by 30,000 Nurses' Health Study participants in 1989-90, and the samples that are currently being collected from Nurses' Health Study II participants, are an extraordinarily valuable resource with which to determine the specific importance of inherited genetic changes. We use DNA in the blood samples to establish whether an inherited alteration does or does not exist. Thus, we can make a significant contribution to understanding the balance of inherited genetic changes and lifestyle and environmental changes in the causation of common diseases. The National Institutes of Health and the American Cancer Society have recognized this potential and have given us several research grants to pursue some of these questions.

Our longstanding concern is to perform this research in a way that protects confidentiality. To ensure that confidentiality is maintained in the Nurses' Health Studies, we have obtained Certificates of Confidentiality from the Department of Health and Human Services to make both questionnaire and laboratory data immune from any third-party requests. In addition, for any gene that could convey a sufficient risk of disease to result in discrimination such as the "breast cancer" genes BRCA1 and BRCA2, we completely anonymize the samples by removing the ID number and other identifying information. These procedures further protect this data.

Much of the news about inherited genetic predisposition concerns rare genes associated with very high risks. The identification of many other genes is making it possible to look at genetic variations that may be associated with very modest increases or decreases in risk. Evaluating these lower risk variations may have significant public health implications as they often occur much more commonly in the population. The predictive value and clinical significance of these genes, however, are still very unclear. In addition, some of these genes may carry no risk, unless they are associated with lifestyle or environmental exposures, such as smoking or alcohol consumption. Ultimately, we hope to identify diet and lifestyle changes that can reduce any increases in risk due to inherited predisposition.

As members of the Nurses' Health Study continue to age, we can unfortunately expect that some will eventually develop debilitating diseases such as Alzheimer's, A.L.S., or Parkinson's, which may make it difficult to respond to future questionnaires. It is our hope that the Nurses' Health Studies can begin to examine these and other life-draining illnesses with an eye towards learning more about their causes. Thus, we would like to encourage you to discuss your participation in the Nurses' Health Study with your family and your doctor. Should you become disabled in the future, it would greatly help our research if someone would notify us of your health status and subsequently assist us by allowing your pertinent medical records to be released to us. By combining the long medical and dietary histories, which we have compiled over many years, with details of later illness, we can evaluate many different possible causes as well as ways in which these serious diseases may one day be prevented.

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) 525-2008 or call us at (617) 525-2279. We look forward to staying in touch.

Question and Answer

Here is a commonly asked question from participants:

Q: What do you do with the vitamin, cereal, and margarine brand names that I write on the questionnaire?

A: For each of these items we have exhaustive lists with hundreds (or thousands in the case of multivitamins) of brands and types from all over the country. Our database contains the dietary composition of each brand and type; thus, we can assign to you the proper nutrients, calories, fats, etc., from each of these products. Because we try to record these so precisely, it is essential that we have accurate and complete names of the products you use. Simply writing "Walmart" for the multivitamin isn't specific enough, since Walmart sells several different multivitamin preparations. For cereals, we sometimes get answers (like "Crunchy Oats") which are not the actual product names, thus making it difficult to accurately assign them a dietary code.

Friends of the Nurses' Health Study

At the suggestion of several nurses who attended the Update on Women's Health Symposium in February, we have established a fund to support additional projects in the Nurses' Health Study. Thanks to several research institutes, academic centers, and commercial and private contributors, we have already received over $20,000. We hope this fund, the Friends of Nurses' Health Study Fund, Channing Laboratory, Harvard Medical School, will grow over the years and allow us to finance educational and research opportunities. Two projects we have in mind are (1) purchasing freezers to start a pathology database for specimens obtained from nurses (like the blood specimen archive) and (2) creating opportunities for women to learn more about the Nurses' Health Study through a variety of educational initiatives.



Photo by Norman Stein

Nurses' Health Study Principal Investigator Dr. Frank Speizer talks with colleagues at the symposium.