

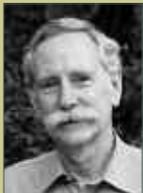


NHS News



Dear Colleagues,

The past year has been a time of transition at the Nurses' Health Studies. I (Susan Hankinson) am very pleased to be assuming the role of Principal Investigator of the Nurses' Health Study, following in the footsteps of Dr. Frank Speizer and Dr. Graham Colditz, both of whom remain very involved in the study. Together with Dr. Walter Willett, the Principal Investigator of the Nurses' Health Study II, I look forward to many more years of working with you.



In the next year, we'll be applying to the National Institutes of Health for an additional five years of funding for NHSII. We are optimistic that, even with substantial decreases in federal research funding, our application will be reviewed favorably because of our tremendous progress over the past 18 years in Nurses' Health Study II.

This newsletter highlights some of that progress. For example, our lead article describes what we've learned about preventing memory loss. We also provide an update on the health effects of trans fats, an area where the vital information you have provided is now helping to transform national food policy. For more of our recent findings, please visit www.NursesHealthStudy.org.

As always, thank you for your ongoing commitment to the Nurses' Health Studies.

Sincerely,

Susan E. Hankinson, Sc.D, R.N.
Principal Investigator, Nurses' Health Study

Walter C. Willett, MD, DrPH
Principal Investigator, Nurses' Health Study II

Preventing or Delaying Memory Loss

Memory loss is often thought of as an inevitable part of getting older, but it might not be. In the Nurses' Health Study, we've been learning how to prevent, or at least delay, memory loss, and while we don't have all the answers yet, we are making headway.

Our studies in this area focus on 20,000 women who started completing telephone interviews when they were ages 70 and older. Every two years they are called again to update their test results. Each interview involves several items that evaluate different elements of cognitive function, such as verbal memory, working memory, and attention. For example, one test involves listening to a list of words and then recalling it later in the interview. Other tests involve naming as many animals as possible in 1 minute and repeating back long series of numbers in reverse order. Together, these tests give a fairly complete picture of several aspects of a woman's memory and how these aspects have changed over time.

Small changes in memory often have little immediate consequence, but in some instances, they might predict the development of dementia many years later. By understanding how diet and lifestyle affect these small changes, we can help women ensure that they maintain their memories for as long as possible.

Physical Activity

Being physically active obviously keeps the body strong, but what about the mind? Our study suggests that walking, the most common form of exercise in older adults, can help prevent memory loss. We found that the more women walked during their late 50s and 60s, the better their memory was at age 70 and older. Those who walked at least 90 minutes

Continued on page 3

ALSO IN THIS ISSUE

| | |
|--|---|
| Inside the NHS | 2 |
| Recent Findings | 4 |
| Study Updates..... | 5 |
| Trans Fats: Banned and for Good Reason | 6 |
| Focus on Our Research Team..... | 7 |
| Questions & Answers | 8 |

INSIDE THE NHS

Our External Scientific Advisory Committee

Like most large-scale studies, the Nurses' Health Studies are guided not only by our own research team but also by an external advisory committee that meets annually. The committee provides feedback about overall study progress and new areas of investigation in women's health. In addition, they offer advice about data sharing, confidentiality, and collaboration with outside researchers. Members of the committee rotate every few years, and all are highly accomplished and nationally recognized in their respective fields. Our current members are as follows.

LESLIE BERNSTEIN, PhD (Committee Chair)
Professor and AFLAC, Inc., Chair in Cancer Research
Department of Preventive Medicine
University of Southern California

REBECCA M. PATTON, MSN, RN, CNOR
President, American Nurses Association

JOHN A. BARON, MD
Professor of Medicine
Dartmouth Medical School

VIRGINIA HARTMULLER, PhD, RD
Program Director, Diet and Nutrition Epidemiology Research,
Division of Cancer Control and Population Sciences
National Cancer Institute

COLIN BEGG, Ph.D
Chair, Department of Epidemiology and Biostatistics
Memorial Sloan-Kettering Cancer Center

LEWIS A. CHODOSH, MD, PhD
Vice Chair, Department of Cancer Biology
University of Pennsylvania School of Medicine

HANS-OLAV ADAMI, MD, PhD
Professor and Chair, Department of Epidemiology
Harvard School of Public Health

DAVID HOUSEMAN, PhD
Ludwig Professor of Biology
Massachusetts Institute of Technology

LILLI HORNIG, PhD
Executive Director (emeritus)
Higher Education Resource Services (H.E.R.S.)
Wellesley College

Our Approach to Data Sharing

All recipients of NIH funding have been asked by the U.S. Congress to do a better job of sharing our data with other scientists. However, the best approach for doing this — while also maintaining the privacy of study participants — has not yet been determined. Our approach has always been to collaborate with scientists who have high standards and who are pursuing issues that we agree are important. Together we analyze any shared data and prepare joint reports for publication. Notably, we never allow these scientists to access personally identifiable information: confidentiality is of the utmost importance to us, and we only work with scientists who value your privacy as much as we do. Over the past five years, we've participated in more than 50 collaborative projects and are proud that NHS data have helped to advance science in so many ways. As NIH continues to develop its data-sharing recommendations, we'll keep you abreast of any changes in how we approach our collaborative efforts.

Your Privacy

As an NHS participant, you provide us with very personal information through your questionnaires and biological specimens. We're grateful for the trust you've shown in us and want to assure you that we hold ourselves to the highest standards in the safekeeping and use of your data. For example, only authorized study personnel are granted access to your personal information, and all genetic results are coded so that they are never stored with individual identifying information.* We also have a certificate of confidentiality from the Department of Health and Human Services, which means that under current laws we cannot be forced to disclose information that could identify you in any legal proceedings. Your trust is essential to the success of the study, and we would never do anything to risk losing your faith in us. Thank you for your continued commitment.

* To learn more about how Brigham and Women's Hospital and its affiliates use protected health information, visit www.partners.org and click on Patient Privacy.



Preventing or Delaying Memory Loss

Continued from cover

a week had cognitive function similar to that of women 1.5 years younger than them. Small clinical trials have shown similar findings, although the underlying biology is not yet completely understood. One possible explanation is that exercise helps maintain a steady flow of blood to the brain.

Insulin Levels When the body is unable to effectively use the insulin it produces, the amount of insulin in the blood can start to rise, having negative effects on the heart and possibly the brain. To determine whether high insulin levels affect memory loss, we first compared cognitive-function scores in women with and without type 2 diabetes (a condition initially characterized by high insulin levels). We found that women with diabetes had worse cognitive function, but that adequate control of the diabetes seemed to help. Next, we evaluated blood insulin levels and cognitive function in women without diabetes. Those with the highest insulin levels had cognitive-function scores similar to those of women 6 years older than them. Fortunately, most women can avoid rises in insulin by maintaining a healthy weight, staying active, and eating a healthy diet.

Fruit and Vegetable Consumption Fruits and vegetables are the cornerstone of a healthy diet, but do they have a role in maintaining memory? Our data suggest that fruits are not beneficial in this regard, but that vegetables are. Women who ate cruciferous vegetables or green leafy vegetables regularly had cognitive function similar to that of women 1 to 2 years younger than them. The more vegetables women ate in their 50s and 60s, the less likely they were to experience memory loss in their 70s and beyond.

Vitamin Supplements Although vitamin supplements can't take the place of a healthy diet, some do offer important health benefits. In terms of memory loss, we've examined the role of two common antioxidant vitamins, E and C. We found no cognitive benefit of vitamin C, but taking vitamin E supplements did seem to be associated with better cognitive-function scores, particularly among women who consumed very little vitamin E from food. However, it took at least 10 years of taking vitamin E to see any benefits, and the benefits were still fairly modest.

Sleep Patterns

Many women, especially those who are postmenopausal, have trouble sleeping or getting enough sleep. Unfortunately, poor sleep patterns are not only exhausting but might also contribute to cognitive impairment and

memory problems. In our study, women who typically slept less than 6 hours a night had cognitive-function scores similar to those of women 5 years older than them. In addition, women who had difficulty falling or staying asleep had more memory problems than those who slept well. Snoring did not appear to have any effect on memory.

Alcohol Consumption Several studies, as well as the Nurses' Health Study, have suggested that moderate alcohol intake might be related to better memory in older women. We found that women who drank up to one alcoholic beverage a day had slightly better memory than those who never drank alcohol. These women were also less likely to experience any declines in memory over a 2-year period. Although these results are promising, they must be considered in relation to alcohol's other risks and benefits. Moderate alcohol consumption has been shown to lower the risk of heart disease but raise the risk of breast cancer.

Nonsteroidal Anti-Inflammatory Drugs Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin, are commonly used by older people and may offer some protection against memory loss. In the Nurses' Health Study, women who took ibuprofen or aspirin regularly for at least 8 years performed slightly better on several tests of cognitive function than did women who never took the drugs. Although both drugs offered some benefit, the effect was stronger for ibuprofen. Other studies support these findings, but women should still be cautious about using NSAIDs for this purpose: like any medication, they do have side effects, such as bleeding ulcers.

Other Factors Memory loss is one of our most active areas of research. In addition to identifying factors that probably do influence memory, we've also identified a host of factors that probably do not. Use of vitamin C supplements, blood levels of folate and vitamin B12, use of postmenopausal hormones, and history of cataracts all appear *not* to influence cognitive function.

Conclusion

Although we still have much to learn about preventing memory loss, our initial findings are definitely encouraging. Many of the same healthy behaviors that keep women's bodies strong will also keep their minds strong. The most important steps are to stay physically active, eat vegetables regularly, maintain a healthy weight, and get a good night's sleep.

RECENT FINDINGS

During the past year, the Nurses' Health Studies have produced more than 100 publications on women's health. Below are some of our most important findings. To view a complete list of NHS publications, visit www.NursesHealthStudy.org and click on [Publications](#).

Red Meat and Breast Cancer Risk

Several years ago, we reported that a high intake of animal fat might raise a woman's risk of developing premenopausal breast cancer. Now, we've updated our analyses to include another 4 years' worth of information and to look specifically at red meat (including beef, pork, and lamb). We found that eating red meat on most days of the week moderately increased the risk of premenopausal breast cancer, but only the type that is sensitive to estrogen. These findings suggest that the hormones in red meat may be playing a role. (Cho E et al. *Arch Intern Med* 2006; 166:2253)

Postmenopausal Testosterone Use and Breast Cancer Risk

During the past 20 years, estrogen plus testosterone has become an increasingly popular form of postmenopausal hormone therapy. However, little is known about its effects on breast cancer risk. In the Nurses' Health Study, we found that women who used estrogen plus testosterone were about twice as likely to develop breast cancer as women who had never used postmenopausal hormones. This increase in risk was comparable to — or even slightly greater than — that seen with estrogen plus progesterone. Although postmenopausal hormones have beneficial effects on mood, libido, and bone health, the increased risk of breast cancer likely outweighs these benefits. (Tamimi R et al. *Arch Intern Med* 2006; 166:1483)

Work Schedules and the Risk of Miscarriage

Many nurses work rotating shifts, night hours, and extended hours (more than 40 hours per week) and are concerned about the effects on their health. To determine whether work schedules influence the risk of miscarriage, we analyzed data from nearly 8500 women who reported being pregnant while working as nurses. We found that two specific patterns of work during the first trimester of pregnancy — consistent night work and extended hours of work — were associated with an increased risk of miscarriage. The reasons for these findings are not yet known but may be related to hormonal changes, sleep disturbances, or stress. (Whelan E. *Epidemiology* 2007; in press)

Potato Consumption and Diabetes Risk

Potatoes are a staple in the American diet, but do they contribute to diabetes risk? Potatoes have what is called a high glycemic index, which means that they can raise blood glucose levels rapidly and, in turn, force the body to produce insulin in large amounts. In the Nurses' Health Study, we found that eating potatoes and French fries was associated with a modestly increased risk of type 2 diabetes. When women substituted one serving of potatoes per day for one serving of whole-grain foods (like whole-wheat bread, brown rice, or whole-grain pasta), their risk of diabetes went up about 30%. (Halton T et al. *Am J Clin Nutr* 2006; 83:284)

Breastfeeding and the Risk of Diabetes

In addition to being beneficial for infants, breastfeeding can help protect a mother's health. Studies have shown that it can reduce the risk of breast cancer, and now our data suggest that it might also lower the risk of type 2 diabetes. We looked at the total amount of time that women spent breastfeeding by adding up the time spent nursing each child. We found that for each additional year that women spent breastfeeding, their risk of diabetes went down by about 15%. Although breastfeeding does facilitate postpartum weight loss, and obesity is associated with diabetes risk, this did not completely explain our findings. (Stuebe A et al. *JAMA* 2005; 294:2601)

Endogenous Hormones and Premenopausal Breast Cancer Risk

High levels of endogenous hormones (such as estrogens, androgens, progesterone, and other hormones that are naturally produced by women's bodies) are known to influence the risk of postmenopausal breast cancer, but what about premenopausal disease? We found that premenopausal women with high blood levels of estradiol, particularly in the follicular phase of the menstrual cycle, and high blood levels of androgens were at 2-3 times the risk of breast cancer compared with women with lower levels. When we looked at specific cancer types, we found a strong link between endogenous hormones and those tumors that had hormone receptors on their surfaces. (Eliassen A et al. *J Natl Cancer Inst* 2006; 98:1406)

Nurses' Health Study III

Times change, and so do the lifestyle and environmental exposures of women. To determine the impact of this on women's health, we are launching the Nurses' Health Study 3 to examine new hormone preparations, dietary patterns, and nursing occupational exposures. We will recruit female RNs and LPNs age 22-45 from across the country to join the new cohort, which will be entirely web-based. Prominent new features will include a closer look at fertility and pregnancy events and a greater focus on adolescent diet and breast cancer risk. A pilot study will be conducted in 2007, and we plan to roll out the full national study in 2008 with an invitational mailing to one million nurses. Please encourage your younger colleagues to join, and tell them about the long history of the Nurses' Health Studies contributing to knowledge about women's health.

NHS and the National Genetics Effort

The NHS is the lead study in a consortium of studies funded by the National Cancer Institute to use a new technology – whole genome association scanning – to search for genes that underlie the inherited component of breast cancer. Previous studies that we have reported to you have examined the relation of inherited variation in specific genes with risk of breast and other cancers. In a whole genome scan, over half a million gene variants can be assessed in a single DNA sample, and thus much of the genome can be interrogated in a single study. No personal identifiers are attached to the samples, so only grouped results for cases and non-cases are available. These summary results are available to all researchers on the web <http://cgems.cancer.gov/>. With so many gene variants being tested, many are probably associated with breast cancer just by chance, so replication of the results in other studies is a key step. We are working with colleagues from other breast cancer studies to do this, and have made the summary, grouped, and non-identifying results available on the web to facilitate the discovery of new breast cancer genes.

The Growing Up Today Studies

The original Growing Up Today Study (GUTS) is now 10 years old! We could not have reached this milestone without your support. In addition, we've had a great response to the GUTS II study we announced in the last NHS newsletter. Now, more than ever, we appreciate the encouragement you give your children to stay interested and involved in these studies.

In the past year we have published findings showing frequent tanning bed use is often associated with health risk behaviors¹ and infants who are breast-feeding are less likely to be overweight as adolescents². The study continues to receive funding for exciting new research aims, such as exploring behaviors associated with cancer prevention, the link between diet and asthma, and how the experience of violence impacts the health of young adults.

Looking towards the future it will be crucial to maintain a list of current email addresses as more GUTS participants complete the survey online (we've had a 66% increase just this year!) Boys may need more prodding than girls to complete the their surveys, but the information that has been provided by your children continues to make the GUTS studies some of the most important studies of adolescent health in the country today.

1. O'Riordan DL et al. *Cancer Causes Control* 2006 Jun;17(5):679-86
2. Gillman M et al. *Epidemiology* 2006 Jan; 17(1): 112-4

visit us online at
www.NursesHealthStudy.org

- Complete list of all NHS research publications
- Detailed history of the Nurses' Health Studies
- Past newsletters and questionnaires
- Medical record release forms
- Photo gallery

Trans Fats: Banned and for Good Reason

Trans fats have been banned from New York City restaurants, eliminated from many popular foods, and even referred to as “toxic.” Are they as bad as they seem? The simple answer is yes. There are many different types of fats, but trans fats are easily the worst, causing more potential harm than even saturated fats do.

Trans fats are vegetable fats that have been altered during a special heating process (called hydrogenation) and are solid at room temperature (think stick margarine and vegetable shortening). Most of the trans fat in the American diet comes from packaged baked goods, processed foods, and commercially fried foods, like French fries and onion rings. Because of their chemical structure, trans fats can raise the level of LDL or “bad” cholesterol in the blood and lower the level of HDL or “good” cholesterol. They can also cause inflammation and compromise the cells that line the inner surface of the blood vessels, arteries, and veins. Together, these effects lead to an increased risk of heart disease and type 2 diabetes. In the Nurses’ Health Study, women who consumed the most trans fats were 50% more likely to develop

heart disease — and 30% more likely to develop type 2 diabetes — than women who consumed the least trans fats. A high intake of trans fats has also been associated with an increased risk of non-Hodgkin’s lymphoma and ovulatory infertility.

Based on such evidence, the Institute of Medicine has concluded that no amount of trans fat in the diet is safe. The best way to eliminate these fats from your diet is to remain vigilant about what you’re eating:

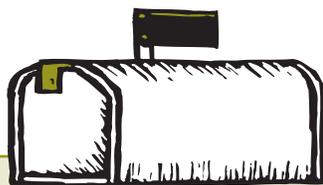
Check the nutrition labels of all food products. Trans fat are now required to be listed there, along with other bad fats (saturated fats) and good ones (unsaturated fats). If the label says anything other than zero grams of trans fat, pick another product.

Even if the label says zero grams of trans fat, check the ingredient list because the product may still contain up to a half-gram of trans fats, according to the FDA. The words “partially hydrogenated vegetable oil” and “vegetable shortening” in the ingredient list indicate the presence of trans fats.

When eating out, avoid deep-fried foods. Many restaurants (particularly fast-food ones) still use partially hydrogenated oils in their fryers.

For more information on trans fats, visit www.hsph.harvard.edu/nutritionsource

NHS MAILBOX



“ I hear information on the news quite often regarding the findings of a Harvard Research Study. It makes me proud to be a part of the Nurses' Health Study. Keep up the good work! ”

“ It feels good to be a participant in one of the biggest and best healthcare and research projects ever. We all hope for complete funding forever!! ”

“ I have enjoyed participating in this survey. I am a Hispanic female, from a poor family. I went to school to become a registered nurse and then to become a nurse practitioner. I am very proud of my parents, family, and my accomplishments. ”

“ This is an amazing study and I am proud to be part of it....Keep up the good work.... ”

FOCUS ON OUR RESEARCH TEAM



Like her predecessors, the new Principal Investigator of the Nurses Health Study has a wealth of research experience, an impressive array of academic degrees, and a deep seated commitment to women's health. What makes her unique, though, is what she has most in common with all of you: a background in nursing. **Dr. Sue Hankinson** is the first nurse — and the first woman — to lead the Nurses' Health Study since its inception in 1976.

After obtaining her Bachelor of Science degree in Nursing in 1979, Dr. Hankinson took to the surgical floors at Massachusetts General Hospital and the University of Minnesota Hospital. As rewarding as that experience was, she found that she enjoyed research, particularly in the area of disease prevention, and so turned to a career in public health. She completed two Master's degrees (in Environmental Health and Epidemiology) and worked at both the Minnesota and Massachusetts Departments of Public Health before pursuing her doctorate degree in Epidemiology at the Harvard School of Public Health in the late 1980s. While there, she began studying risk factors for cataracts in the Nurses' Health Study and has been an invaluable member of our team ever since.

During the past 20 years, Dr. Hankinson has focused her research on how hormones affect cancer risk. She served first as Project Director and then as Principal Investigator of the blood and urine collection studies in both NHS and NHSII. One aspect of her work that she finds particularly interesting is the opportunity to piece together so many different sources of data — the biennial questionnaires, blood and urine samples, tumor tissue, and mammograms — to determine what causes disease and how to prevent it.

In her new role as Principal Investigator of the Nurses' Health Study, Dr. Hankinson will not only continue her own research but also guide the direction of the study as a whole. That means identifying funding opportunities, approving new research projects, fostering collaboration among colleagues, and, her favorite task, mentoring junior investigators. In those rare moments when she actually gets to relax, Dr. Hankinson enjoys walking her dog, pilates, cooking, reading, and spending time with her husband and family.

Keeping Us Up-To-Date

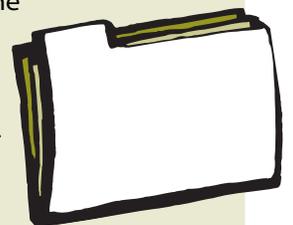


Authorization for Release of Medical Records

As members of the Nurses' Health Study get older, some will unfortunately develop conditions that make it difficult to respond to future mailings. Should you become disabled, it would greatly help our research if someone could notify us of your health status and subsequently allow your pertinent medical records to be released to us. To help facilitate this process, in 2004 we mailed a copy of our Authorization for Release of Medical Records to every NHS participant. (Copies of that form can also be downloaded at www.NursesHealthStudy.org.) While this Authorization form will generally not be accepted to release your medical records to us, by keeping it with your will or personal papers, your desire to have someone notify the study about changes in your health status will be known.

Medical Records Review

Participants who report a new diagnosis in their biennial questionnaires often receive a letter from our study, requesting permission to review their pertinent medical records. This review is important because it allows us to obtain specific information about treatment and diagnosis that only original records can provide. We want to extend a special thank-you to all of the nurses who have helped our work by allowing us to confidentially review their records. We would also like to encourage participants who receive these requests to complete and sign the release forms and then mail them back to us (not directly to the physician). This allows us to keep study information together in an organized and secure manner.



QUESTIONS & ANSWERS

The questionnaire always asks about illnesses that were diagnosed in the past two years, and yet there is also a column for diseases that are more than two years old. This is confusing. Do I need to report old illnesses?

For most study participants, we are looking to update the information they provided on the last questionnaire (two years earlier). Even though some members of the study occasionally miss a cycle of the questionnaire, we still need to learn about any major diagnoses that they have had since we last heard from them. Thus, we provide a space for “older” diagnoses.

How long will the Nurses’ Health Studies continue?

Since the inception of the Nurses’ Health Study in 1976 and the Nurses’ Health Study II in 1989, the studies have expanded and diversified to stay relevant to the lifestyles and interests of the participants. Any participant who chooses to do so may of course decline further participation, although it’s always sad to lose members of the study after all these years. As long as we are making significant contributions to women’s health, we hope to continue our work with you.

Funding the Nurses’ Health Studies

We are strongly committed to the Nurses’ Health Studies and are doing everything we can to assure their long-term stability. In addition to seeking grants from major foundations and government institutes, we also solicit support from private donors in our effort to sustain the continued operation of the Nurses’ Health Studies. As the largest ongoing studies of women’s health that include repeated measures of diet, physical activity, and other lifestyle factors related to a broad range of chronic conditions, we are confident we will meet our goal of diversifying the funding base for the NHS. If you or someone you know is interested contributing to the study, please contact Dr. Hankinson or Dr. Willett at 617-525-2258, or visit the web site www.nurseshealthstudy.org and click the "Donate" link.

When women are diagnosed with benign breast disease, the Nurses’ Health Studies request tissue samples that were removed during biopsy. What do you hope to learn from these samples?

There is consistent evidence that having a personal history of benign breast disease increases a woman’s risk of breast cancer. However, there are many different types of benign breast disease, and only a small proportion of women with these conditions actually go on to develop breast cancer. By studying the morphology and molecular characteristics of the tissue samples we collect, we hope to get a better sense of which types of disease are most likely to lead to breast cancer. This could help identify women who might benefit most from intensive screening and/or chemoprevention. It could also help alleviate anxiety for women found to be at low risk.

I sent in my latest questionnaire recently but just received another in the mail. Should I complete this one as well?

In nearly all cases, this will simply be a duplicate questionnaire sent out upon not receiving your original by a certain date. We do not want you to duplicate your effort, so we tell all participants that if you’ve sent your questionnaire in within the last month, disregard the second mailing.

THE NURSES’ HEALTH STUDY

**Channing Laboratory
181 Longwood Avenue
Boston, MA 02115
617-525-2279 (tel)
617-525-2008 (fax)**

Letters & feedback are welcome.

To report name or address changes, visit www.NursesHealthStudy.org & click [Contact Us](#).

Donations & bequests to the Friends of the Nurses’ Health Study Fund can be sent to the Channing Laboratory.