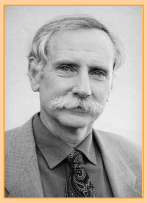
The Nurses' Health Study Annual Newsletter
Volume 13, 2006

NHS News

Celebrating 30 years of the Nurses' Health Study



Dear Colleagues,

We're excited to celebrate the 30th anniversary of the Nurses' Health Study. This represents a truly remarkable achievement of long-term participation by so many dedicated members of the study. Thanks to your continued commitment, the Nurses' Health Study remains the largest study of women's health with updated information on diet, activity, and other lifestyle factors. This information provides us with a unique opportunity to study how changes in lifestyle modify the risk of many chronic diseases among women. Over the past 30 years, the NHS staff has grown, and our productivity has steadily risen.

Just last year, nearly 100 papers were published based on information provided by NHS participants. Much of this research helps to create national weight, diet, and activity guidelines, which are then used to guide clinical and public health practices.

As always, you can learn more about our study findings at **www.NursesHealthStudy.org**. Thank you for your ongoing commitment to the Nurses' Health Studies.

Sincerely,

Graham A. Colditz, MD, DrPH
Principal Investigator, Nurses' Health Study

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

Preventing Colorectal Cancer

Colorectal cancer is the third most common cancer among women in the U.S., but it doesn't need to be. This disease is almost entirely preventable through the same healthy lifestyle that also reduces your risk of heart disease, stroke, and a variety of other cancers. That lifestyle includes regular screening tests, daily doses of physical activity, and a healthy diet.

Screening Tests

If you're 50 or older, getting regular screening tests is the most important thing you can do to lower your risk of colorectal cancer. These tests can detect cancer in its earliest stage, when it is more than 90% curable. Equally important is that the tests can find small growths called polyps that sometimes turn into cancer. If these polyps are found during a screening test, they can be removed immediately — before they ever have a chance to become cancerous.

There are currently three main screening tests for colorectal cancer: stool cards, flexible sigmoidoscopy, and colonoscopy. Stool cards, which test for hidden blood in the stool, are the least invasive means of testing, but they are not as sensitive as the other tests at picking up polyps and early-stage cancers. Flexible sigmoidoscopy involves having a healthcare provider examine the rectum and lower part of the colon with a thin, flexible, fiberoptic tube. Finally, colonoscopy is like sigmoidoscopy, except that the healthcare provider examines the entire colon and not just the lower part. Because it requires a more extensive exam, colonoscopy is considered more invasive and typically requires sedation. Stool cards, flexible sigmoidoscopy, and colonoscopy are all acceptable, recommended options for colorectal cancer screening.

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ALSO IN THIS ISSUE

Funding the Nurses' Health Studies

Throughout NHS history, we've enjoyed strong and continuous financial support from the National Institutes of Health (NIH) and, more specifically, the National Cancer Institute (NCI). As you may have heard, Congress has capped the NIH budget, and the NCI has implemented cost-saving approaches to their annual budget, resulting in reduced resources available to conduct our studies. Given this situation, we cannot be confident that we'll receive the same level of support in coming years that we have in the past.

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 (as we have in the past), we are also soliciting support from private donors. Given that the Nurses' Health Studies are the largest ongoing studies of women's health that include repeated measures of diet, physical activity, and other lifestyle factors, we are confident we will meet our goal of diversifying the funding base for the studies. If you or someone you know is interested contributing to the study, please contact Graham Colditz, the Principal Investigator of the Nurses' Health Study, at 617-525-2258 or visit www.NursesHealthStudy.org.

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.

Continued from cover

However, many experts believe that colonoscopy is the superior test. To decide which option is right for you, talk to your healthcare provider about the risks and benefits of each test.

You may have also heard about a new screening test called "virtual colonoscopy," which involves a CT scan of the colon and rectum. Although this test is promising, most authorities do not yet recommend it for widespread screening. In future NHS questionnaires, we'll be asking you if you've had such a test so we can better understand its potential for preventing cancer.

Weight and Physical Activity

Keeping your weight in check is a good idea for many reasons, with your health being at the top of the list. Our research shows that women who are overweight or obese have a higher risk of colorectal cancer than lean women. One of the best ways to maintain a healthy weight is to be physically active. In the Nurses' Health Study, women who are active tend to weigh less and have a reduced risk of many diseases. In fact, we've found that physical activity can halve the risk of both colorectal cancer and precancerous polyps. Now, we're trying to understand the complex biology behind these findings, and the key to that may be in the thousands of blood samples that NHS participants have provided over the years. For example, we're looking at insulin levels, which may be influenced by weight and activity and may, in turn, influence the likelihood that cells will become cancerous. We're also looking at questionnaire data from the past 25 years to see how weight and activity levels throughout life might be related to colorectal cancer.

Diet

Given that the colon and rectum are part of the digestive system, it's no surprise that diet is related to colorectal cancer. Still, it's been challenging to figure out exactly which aspects of diet have the most influence. So far, the evidence is probably strongest for meat, alcohol, and folate.

Meat. In the Nurses Health Study, we've found a moderately increased risk of colorectal cancer among women who routinely eat red meat (including beef, pork, and lamb) or processed meat (such as bologna and other lunch meats). Other sources of protein, such as fish or white-meat chicken, are probably healthier alternatives.

Alcohol. Women who consume alcohol may have an increased risk of colorectal cancer and many other diseases, but we also know that modest alcohol intake can lower the risk for heart attack. How should you balance these risks and benefits? If you drink, do so in moderation: heavy drinking is never recommended.

Folate. Found in fruits, vegetables, and multivitamins, folate has been shown to lower the risk of colorectal cancer, even in women with a family history of the disease.

Calcium. Most evidence, including that from the Nurses' Health Study, suggests that avoiding very low intakes of calcium can help reduce the risk of colorectal cancer.

Vitamin D. Although vitamin D is consumed through multivitamins and fortified foods, it is also generated through exposure to sunlight. The skin contains a natural form of this vitamin that, when activated by sunlight, can be circulated and stored in the body. Using blood samples from the Nurses' Health Study, we measured circulating levels of vitamin D among hundreds of women and found a reduced risk of colorectal cancer among those with the highest levels.

Fruits, Vegetables, and Fiber. The evidence on fruits, vegetables, and fiber has been inconsistent for colorectal cancer. Most recent studies, including the NHS, have not seen a relationship between dietary fiber and the risk of developing colorectal cancer. However, we still encourage women to eat plenty of these foods as part of an overall healthy diet.

Aspirin

Like most medications, aspirin has both benefits and risks. Three large clinical trials, as well as our own evaluation in the NHS, have shown that regular aspirin use reduces the risk of colorectal cancer and polyps. High doses seem to be most effective, especially when taken for at least a decade, but these same doses can also increase the risk of gastro-intestinal bleeding. Because of these competing risks, we cannot currently recommend routine aspirin use for colorectal cancer prevention.

Conclusion

By getting regular checkups, keeping their weight in check, being physically active, and eating a healthy diet, women can substantially lower their risk of developing colorectal cancer. And the benefits don't stop there. Taking these steps will also help lower the risk of heart disease, stroke, and other types of cancer.

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.

Night Work, Melatonin, and Breast Cancer Risk

Many women in the Nurses' Health Studies work night shifts, allowing us the unique opportunity to study how these shifts affect women's health. Rotating night shifts are of particular concern because exposure to light at night suppresses the body's production of melatonin, a hormone that could influence the risk of cancer. In our studies, women who worked rotating night shifts for more than 20 years had an 80% higher risk of breast cancer than women who did not work such shifts. To determine whether this association could be related specifically to melatonin levels, we evaluated urine samples provided by about 450 women and found that lower melatonin levels were associated with an increased risk of breast cancer. Factors (in addition to light exposure at night) that reduce melatonin levels include older age, greater body weight, and possibly smoking. (Schernhammer E et al. *J Natl Cancer Inst* 2005; 97:1084, *Epidemiology* 2006; 17:108, and *J Pineal Res* 2006, 40:116)

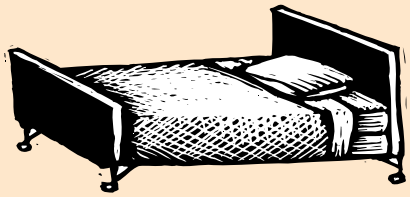
Dietary Fat and Risk of Cataract

Age-related cataract, a clouding of the eye's lens, is found in 90% of people over age 65 and is the leading cause of blindness worldwide. However, we know very little about preventing cataracts, and the treatment usually involves surgical removal. Finding a way to delay cataract development would reduce disability for millions of people and also reduce the costs associated with cataract surgery. To this end, we examined the association between dietary-fat intake and cataract surgery in the Nurses' Health Study. We found that a higher consumption of certain omega-3 fatty acids, mostly from fish, was associated with a reduced risk of cataract extraction. Women who consumed "fatty" fish, such as salmon or mackerel, at least once per week were significantly less likely to require cataract extraction than women who rarely consumed fatty fish. (Lu M et al. *Am J Epidemiol* 2005; 161:948)

Insulin Levels and Memory

Substantial weight gain can lead to increased insulin resistance and subsequent elevations in insulin levels. Insulin resistance is known to have adverse effects on cardiovascular health, and now our data suggest that high insulin levels might also impair memory. We measured levels of insulin secretion in the blood and found that higher levels were associated with greater memory problems, even in women who didn't have type 2 diabetes. Fortunately, women can avoid rises in insulin through weight maintenance, physical activity, and a healthy diet. (Okereke O et al. *Arch Intern Med* 2006; in press)

Sleep Patterns and Cognitive Function



Many women, especially those who are postmenopausal, have trouble sleeping or getting enough sleep. Studies have shown that inadequate amounts of sleep can lower immune function and possibly increase the risk of cardiovascular disease. In the Nurses' Health Study, we found that poor sleep patterns were associated with lower scores on a series of cognitive-function tests. For example, women who slept less than 6 hours a night had cognitive-function scores similar to those of women 5 years older than them. Furthermore, women who had difficulty sleeping had more memory problems than those who slept well. Snoring, however, was not related to memory. (Tworoger S et al. *Alzheimer Dis Assoc Disord* 2006; 20:41)

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

The NHS Memory Study

For almost 10 years now, we've been studying how older women in the Nurses' Health Study might maintain memory. To date, we've identified several important ways that memory loss might be prevented (or at least delayed), including regular physical activity and long-term use of antioxidant vitamins. We're now conducting our fourth round of memory interviews over the phone and are grateful to all the participants who continue to contribute to this important area of research.

As part of the memory study, about 70 nurses have undergone full neurologic consultations, and about 50 have had optional brain scans with magnetic resonance imaging (MRI). In the coming year, we hope to expand the number of participants in this substudy. In the meantime, we'll continue to keep you updated as we learn more about maintaining memory into older age.

The Growing Up Today Study 2

The Growing Up Today Study 2 (GUTS2) is now in its third year and going strong. Modeled after the original Growing Up Today Study, GUTS2 includes more than 11,000 children of NHSII participants. The children are now aged 11 to 17 and will be receiving their GUTS2 questionnaires this June. As with our other studies, we'll be sending out GUTS2 questionnaires every other year to track participants' activity, diet, and growth.

In an effort to learn even more about adolescent growth, we started a pilot study last summer with more than 8000 GUTS2 mothers who agreed to measure and record their children's height and weight for us every six months. This pilot study is clearly a cooperative effort between the GUTS2 participants and their mothers, and we appreciate all the extra effort that goes into accurately completing the forms.

NHS Joining National Genetics Efforts

The National Cancer Institute (NCI) recently launched a new initiative to identify common, inherited gene mutations that increase the risk for breast cancer, either directly or indirectly through interaction with environmental exposures. As part of this project, the NCI is collaborating with a number of research groups, including NHS investigators led by Dr. David Hunter. The hope is that such collaboration will speed the identification of important genetic mutations. For more information about the Cancer Genetic Markers of Susceptibility (CGMS) project, please visit http://cgems.cancer.gov/.

NHS Data in Action

Researchers at the Harvard Center for Cancer Prevention have used findings from NHS and other important studies to help people learn about chronic disease risk factors and disease prevention. They have developed an interactive, web-based tool called Your Disease Risk: (**www.yourdiseaserisk.harvard.edu**)

Your Disease Risk offers visitors the chance to find out their risk of five of the most important diseases in the United States and get personalized tips for preventing them. Together, these diseases (cancer, heart disease, stroke, diabetes, and osteoporosis) have a staggering impact on the nation's health. Available in both English and Spanish, the website offers personalized risk assessments and strategies for making healthy lifestyle choices, along with general information about disease prevention. The site also has a host of other resources, such as scientific articles, podcasts, webcasts, and expert commentary.

Your Disease Risk is one more example of the far-reaching effects of the NHS. Your efforts are helping people around the world discover new ways to stay healthy.

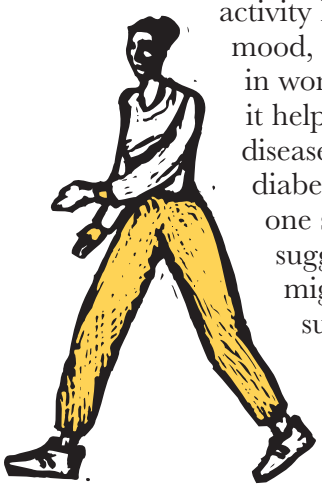
Physical Activity and Survival After Breast Cancer

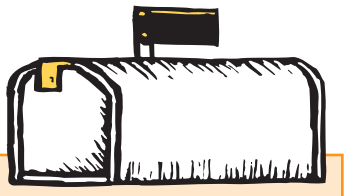
Studies have shown that physical activity can reduce a woman's risk of developing breast cancer, but what are the benefits in women who have already had breast cancer? Can physical activity help prevent recurrence or improve survival in these women?

To address this question, we tracked the activity patterns of nearly 3000 women who had previously been diagnosed with stage 1, 2, or 3 breast cancer. We evaluated the types of recreational activities they did and the amount of time they spent exercising each week. Overall, we found that moderately active women (those who walked 3 to 5 hours per week at an average pace or did an equivalent amount of exercise) were 50% less likely to die from breast cancer than sedentary women. Engaging in more exercise — or in more-vigorous exercise — didn't appear to offer any additional benefits.

We're not sure why physical activity improves the odds of surviving breast cancer, but we think the answer could be related to hormone levels. Being active might lower certain hormone levels in the body, thereby suppressing cancer growth and recurrence. Although we didn't measure hormone levels in this particular study, we did find that physical activity had the strongest effect in women whose cancer was known to be susceptible to hormone levels. Notably, about 80% of the women in our study had this type of cancer (known as "hormone-receptor-positive" cancer).

What should women do with this information? First, keep in mind that exercise is not a replacement for standard breast cancer treatment. All of the women in this study received standard treatments that are known to extend life, and being active was an additional way — not an alternative way — to help ensure their long-term health. That being said, women have little to lose and much to gain from exercise after a breast cancer diagnosis. Physical activity has been shown to improve mood, body image, and self-esteem in women with breast cancer, and it helps prevent other common diseases, like heart disease, diabetes, and osteoporosis. Going one step further, our findings suggest that physical activity might also boost the chances of surviving breast cancer.





NHS MAILBOX

"It is clear to anyone who reads about health issues that the collated, collected information from this grand-scale study is the only one of its kind. As anyone would guess, it takes a group of helping, altruistic individuals like nurses to be so involved. Thank you for all your work and for keeping all the participants involved and informed." — C.J.
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"I am so honored to be a part of this study! I look forward to the surveys and the results. My sons were selected for GUTS2, and I have told them how fortunate they are to be "part of science" and have made them promise to answer all your surveys as they grow older. Thank you for all that you do!" — J.T.
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FOCUS ON OUR RESEARCH TEAM

When Jennifer Bealer became the Research Coordinator for our blood lab, she needed no introduction to the Nurses' Health Studies. Long before she became part of our research team, her family was involved in the Nurses' Health Studies. Her mother has been a member of the Nurses' Health Study II since its inception in 1989, her brother has been part of the Growing Up Today Study since he was in middle school, and her grandmother participated in the NHS Mothers' Study a few years ago.

Jennifer's contribution to our research is a bit different than her family members' but just as important. She oversees the preparation of thousands of specimen samples for biochemical assays and genetic research. This requires coordination between study investigators, data managers, and the external labs that analyze the samples. Furthermore, Jennifer maintains a detailed database to keep track of the more then 800,000 samples we have stored in liquid nitrogen.

When blood samples are to be sent out for analysis, Jennifer typically creates pairs of samples, from two women who have reported similar lifestyle habits and demographic information. One sample will be from a nurse who has developed a disease such as breast cancer, and the other will be from a nurse who has remained healthy. By comparing these sample pairs, we can identify the specific characteristics that contribute to disease.

Jennifer may be the third generation involved with the Nurses' Health Studies, but she insists that her family's devotion to medical research is nothing out of the ordinary. The labs are dependent on nurses who diligently send back their surveys year after year, and the staff have received many letters from nurses expressing appreciation for the work that's been done so far. Jennifer emphasizes, "This is really about the nurses. Without them, I wouldn't be here!"

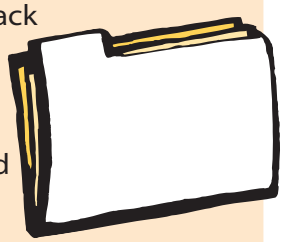
Keeping Us Up-To-Date

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.

I received a letter from the NHS inviting me to participate in a sub-study about a particular medical condition that I have. If I choose not to participate in the substudy, will I still be a part of the Nurses' Health Study?

Yes, of course. Many participants are asked at one time or another to answer questions about a particular condition or to provide a sample for analysis. Your decision to participate or not participate in any substudy or sample collection has no bearing on your participation in the Nurses' Health Studies.

I just completed and returned my Nurses' Health Study questionnaire, but I've received another one in the mail. What should I do with it?

We send an initial mailing to all participants, and then, some months later, we send another one to those nurses who have yet to respond. Because these are sent via bulk mail, they sometimes take a few weeks to get to their destination (and back to us). In the meantime, you may have completed and returned yours. If you are unsure whether you filled out your questionnaire, please feel free to call. If you are certain you have sent yours in, go ahead and discard the mailing.

How many of the original nurses are still participating in the Nurses' Health Studies?

When it began in 1976, NHS included121,701 nurses. More than 100,000 (about 85%) are alive today, and we are still in contact with around 95,000 of them. When NHSII started in 1989, it included 116,608 nurses. Around 115,000 (roughly 99%) are alive today, and nearly 113,000 are still active in the study.

Our Far-Flung Correspondents...

I am currently living on a 46 foot sailboat and have been sailing in Mexico and to Hawaii and Alaska. We are currently in Ixtapa, Mexico and will be heading south to Ecuador shortly and then on to the Galapagos and then the South Pacific. My husband and I sailed about 12,000 miles last year. Amazing how far you can go at six miles an hour. -J.F.

(reprinted with permission)

I am a full-time rancher now in a very remote region of Utah. My chores involve walking up and down a 12% grade for 50 feet twice a day, which accounts for the weight loss over the past two years. Tossing around 80- to 100-pound bales of hay twice a day helps. I also live in primitive circumstances, so I don't have many of the modern conveniences most of my peers enjoy, such as electricity other than a small solar plant. Running water depends on how well the pickup is running to get it. Other than missing a washing machine, I enjoy my life. - D.R.

THE NURSES' HEALTH STUDY

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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.

With sincere thanks,
Frank E. Speizer,
Founding Principal Investigator