

NHHS News

Dear Colleagues,



As the Nurses' Health Study heads into its 26th year, Dr. Frank Speizer, the founding principal investigator, continues to guide the scope and direction of the study. I am honored to follow in his footsteps as the new principal investigator. Together with Dr. Walter Willett, the principal investigator of Nurses' Health Study II, we look forward to further collaboration with you.

As we continue to advance our understanding of women's health, we will also continue to share what we learn, so that it can be put into practice by the many women striving to lead healthier lives. That is one of the reasons we produce this newsletter each year: to provide you with scientifically sound information that you can use to improve your health. For example, the cover story this year summarizes what is known about diabetes and what you can do to prevent it. Feel free to share this newsletter with your family members and friends, so that they too can take advantage of the research you have long been a part of. Thank you, as always, for your continued dedication and commitment to the Nurses' Health Studies.

Sincerely,

Graham A. Colditz, MD, DrPH
Principal Investigator

Preventing Diabetes

With the sheer volume of health information out there – and so much of it contradictory – most of us find it difficult to know what steps we should be taking to lead a healthy life. Only occasionally is there an area where there are no mixed messages, and prevention of adult-onset, or type 2, diabetes is one of them. The evidence couldn't be clearer: the likelihood of developing type 2 diabetes is largely a function of *what we eat*, *how much we exercise*, and most importantly, *how much we weigh*. By taking control of these three factors, we can be assured we're taking the right steps to protect ourselves from one of the most common and serious conditions in the United States today.

Weight and Weight Gain

According to a recent analysis in the Nurses' Health Study, more than 60% of diabetes cases can be attributed to overweight or obesity. (Being overweight is typically defined as having a body mass index (BMI) of 25 to 29.9, while being obese is defined by a BMI of 30 or higher. See the chart on page 4 to find out how height and weight translate into BMI.) While obese women had the highest risk of diabetes in our study (nearly sixteen times that of lean women), we also observed an increased risk among overweight women and even women who were at the high end of the healthy weight range. Fortunately, the same analysis also yielded good news: losing weight can lower the risk of diabetes, and a woman's current weight seems to have a much greater impact on her risk of diabetes than her previous weight. This suggests that if a woman loses weight and keeps it off, she will lower her risk of diabetes substantially – and relatively quickly.



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Recent Findings

This year, the Nurses' Health Study produced a record number of publications on women's health. Below is a selection of our findings. A complete list of articles can be found by visiting www.NursesHealthStudy.org and clicking on **Publications**.



Fruit and Vegetable Intake and the Risk of Heart Disease

Researchers have long known that the nutrients in fruits and vegetables lower the risk of cardiovascular disease, but there has been less certainty about whether the foods themselves lower risk. When we examined this question recently in the Nurses' Health Study, we found that eating fruits and vegetables does offer modest protection against heart disease. Women who ate an average of three servings of fruits and vegetables a day were about 20% less likely to develop heart disease than women who rarely ate fruits and vegetables. A serving is a medium-sized piece of fruit, a cup of vegetables, or a six-ounce cup of juice. (Joshipura K et al. *Annals Internal Med* 2001;134:1106-1114)



Vitamin A Intake and the Risk of Hip Fractures

Taking vitamin A in large doses for extended periods of time – or ingesting a toxic amount on a single occasion – has previously been shown to have detrimental effects on bone. This has led researchers to investigate whether long-term consumption of diets high in vitamin A might contribute to osteoporosis and hip fractures. In the Nurses' Health Study, we recently examined this issue by studying the amount of vitamin A that postmenopausal women consume in the form of beta carotene and retinol. Although we found no association between beta carotene and hip fractures, we did see an association for retinol. The risk of hip fracture was almost doubled among those with the highest intakes of retinol (6,600 IU a day or more) compared to those with the lowest (less than 1,650 IU a day). Since retinol is consumed primarily in the form of vitamin supplements and fortified foods, this finding raises questions about whether the amount of retinol being provided is excessive. (Feskanich D et al. *JAMA* 2002;287:47-54)

Hepatitis B Vaccination and the Risk of Multiple Sclerosis

The hepatitis B vaccine has an excellent safety profile and is included in routine immunization programs in many countries. Nevertheless, concerns arose in the late 1990s when several cases of multiple sclerosis were reported after a mass immunization campaign in France. To address the possibility that the vaccine raised the risk of multiple sclerosis, we conducted a study among participants in the Nurses' Health Studies. We found no evidence of a link between hepatitis B vaccination and multiple sclerosis. These results are consistent with those of two other recent studies. (Ascherio A et al. *N Eng J Med* 2001;344:327-332)

Physical Activity and Mortality

New data from the Nurses' Health Study confirm what several other studies have shown: that the many benefits of physical activity translate into a longer lifespan. Regardless of their weight, active women in the Nurses' Health Study were less likely than sedentary women to die during a sixteen-year period of the study. Those who participated in moderate activity, such as walking, for at least one hour a week had a 20% reduction in mortality risk. (Rockhill B et al. *Am J Public Health* 2001;91:578-583)

CYP17 Genotype and the Risk of Endometrial Cancer

CYP17 is a gene that controls one of the enzymes involved in steroid hormone production. Previous studies have indicated that a variant of this gene might influence steroid hormone levels and affect endometrial cancer risk. When we assessed this in the Nurses' Health Study, we found that while the CYP17 genotype had only a modest effect on hormone production, it was associated with a decreased risk of endometrial cancer. (Haiman C et al. *Can Res* 2001;61:3955-3960)

The NHS Memory Study

Several years ago, we began a study of memory among NHS participants who were age 70 and older. The goal of the study is to investigate how lifestyle and diet influence women's ability to maintain their memories – a topic clearly important to all of us. The study involves calling participants and administering several standard assessments of cognitive function. To date, we have had great success with this and are grateful to the nearly 20,000 women who have completed telephone interviews. Our most recent finding is highlighted to the right.



We are now in the process of asking for second interviews from all of the women who completed the initial phone survey. Everyone's participation remains critical since we are equally interested in women who have maintained their memories and women who are having some difficulties.

Antioxidants and Cognitive Function

We recently examined whether two common antioxidant vitamins (vitamins E and C) influence women's cognitive function. Although we found no association for vitamin C, we did see an association for vitamin E. Women who took vitamin E supplements performed better in several areas of cognitive function than women who did not take supplements. Notably, this effect of vitamin E supplementation was greatest in women with the lowest dietary intakes of vitamin E. (Grodstein F et al. *Am J Epidemiol* 2001;S21)

The Growing Up Today Study

Established in 1996, the Growing Up Today Study (GUTS) includes approximately 17,000 young men and women, who are now 15 to 20 years of age. While the original goal of the study was to examine the impact of diet and exercise on adolescent weight gain, we have since expanded our focus to include such varied topics as sun protection, media influences, and the use of nutritional supplements. Below are some of our recent findings.

As with the Nurses' Health Studies, we take every possible precaution to protect the privacy of GUTS participants. We have a certificate of confidentiality from the Department of Health and Human Services, stipulating that in the case of a lawsuit or any legislative action, we cannot be forced to disclose any participant's identity. For more information about this, please see **Your Privacy** on page 6.

Risk of Overweight Among Adolescents Who Were Breastfed as Infants

Infants who are fed breast milk have a number of health advantages over those who are fed formula, including a lower risk of childhood infections and neurological conditions. Now data from the Growing Up Today Study suggest that they may also have a lower risk of being overweight in adolescence. Compared to infants who were formula-fed, those who were fed breast milk had a 22% lower risk of being overweight at ages 9 to 14. The longer the infants were breastfed, the lower their risk was of being overweight in adolescence. (Gillman M et al. *JAMA* 2001; 285:2461-2467)

Adolescents' Use of Sunscreen and Tanning Beds

New data from the Growing Up Today Study suggest that teenagers are not taking the necessary steps to protect their skin from ultraviolet light, either from the sun or tanning beds. Only 34% of adolescents reported using sunscreen regularly, and over 80% reported having had a sunburn the previous summer. Although girls were more likely than boys to use sunscreen, they were also more likely to use tanning beds, particularly in the oldest age groups. About 35% of 17-year-old girls reported using a tanning bed in the past year. Taken collectively, these findings are concerning, since childhood sun exposure can increase the risk of both melanoma and nonmelanoma skin cancer. (Geller A et al. *Pediatrics* 2002;109)



Continued from cover

Physical Activity

Even though being active can affect diabetes risk through weight, it can also have a more direct effect. We found that regardless of how much a woman weighs, she can reduce her risk of diabetes by being physically active. This is extremely important for overweight women, who have a greatly increased risk and can thus benefit most from activity. We also found that sedentary women can lower their risk of diabetes by becoming more active. Although a large increase in activity provides the most protection, even a very modest increase offers some benefit. Finally, we found that if it is done for an extended period of time each week, walking can be as protective against diabetes as vigorous activity. In the Nurses' Health Study, women who walked briskly for 3 hours a week reduced their risk of diabetes as much as women who exercised vigorously for 1½ hours a week. The more time women spent walking, and the faster they walked, the less likely they were to develop the disease. Taken collectively, these findings are encouraging. They suggest that, regardless of a woman's current weight or activity level, she can lower her risk of type 2 diabetes simply by walking more frequently or more quickly.



Diet

Although researchers are still trying to uncover exactly which aspects of diet influence diabetes risk, there is currently solid evidence around three factors: *glycemic index*, *fiber*, and *fat*.

Weight	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
Height																
5'0"	20	21	23	25	27	29	31	33	35	37	39	41	43	45	47	49
5'1"	19	21	23	25	26	28	30	32	34	36	38	40	42	43	45	47
5'2"	18	20	22	24	26	27	29	31	33	35	37	38	40	42	44	46
5'3"	18	19	21	23	25	27	28	30	32	34	35	37	39	41	43	44
5'4"	17	19	21	22	24	26	27	29	31	33	34	36	38	39	41	43
5'5"	17	18	20	22	23	25	27	28	30	32	33	35	37	38	40	42
5'6"	16	18	19	21	23	24	26	27	29	31	32	34	36	37	39	40
5'7"	16	17	19	20	22	23	25	27	28	30	31	33	34	36	38	39
5'8"	15	17	18	20	21	23	24	26	27	29	30	32	33	35	36	38
5'9"	15	16	18	19	21	22	24	25	27	28	30	31	32	34	35	37
5'10"	14	16	17	19	20	22	23	24	26	27	29	30	32	33	34	36
5'11"	14	15	17	18	20	21	22	24	25	26	28	29	31	32	33	35
6'0"	14	15	16	18	19	20	22	23	24	26	27	28	30	31	33	34

Determining Your Body Mass Index (BMI)

To estimate your BMI, identify your height in the left column. Then move your finger across the corresponding row, to the column with your weight at the top. This number is an estimate of your BMI. For example, if you are 5'7" and weigh 160 pounds, your BMI is 25.

BMI interpretation according to the National Heart, Lung, and Blood Institute:

Underweight	under 18.5	Overweight	25 - 29.9
Normal	18.5 - 24.9	Obese	30 & over

Glycemic Index Not all foods affect blood glucose levels in the same way. Some foods have what is called a high glycemic index, which means that they can raise blood glucose levels rapidly. Eating a lot of high glycemic index foods forces the body to produce insulin in large amounts to try to clear the high levels of glucose in the blood. Over time, this increase in insulin production can increase the risk of diabetes. In the NHS, we found that women who ate the most foods with a high glycemic index had a 50% greater risk of diabetes than those who ate the least. Examples of foods with a high glycemic index include baked potatoes and white bread, while foods with a low glycemic index include apples, beans, and whole grain pasta.

DIABETES

Fiber Fiber can essentially make a high glycemic index food act more like a medium or low glycemic index food. By slowing the conversion of these foods into glucose during digestion, fiber helps the body avoid spikes in blood glucose levels. This in turn reduces the demand for insulin, which lowers the risk of diabetes. In the Nurses' Health Study, we found that eating fiber lowered the risk of diabetes. Most of this benefit, though, seemed to come from one particular type of fiber: the kind found in whole grain foods (called cereal fiber). Compared to women eating



the least cereal fiber, those eating the most were nearly 30% less likely to develop the disease. Foods rich in cereal fiber include bran cereal, oatmeal, barley, and whole wheat bread.

Fat Recent data from the NHS suggest that it is not the amount of fat consumed but the type that can influence diabetes risk. We found that neither total fat, saturated fat, nor monounsaturated fat affected the risk of diabetes. However, *trans* fatty acids increased risk, and polyunsaturated fats reduced risk. *Trans* fatty acids are vegetable fats that are solid at room temperature and appear on food labels as "partially hydrogenated vegetable oils." They are found in many margarines, shortening, and most French fries and commercially baked products. Polyunsaturated fats, on the other hand, come primarily from plant and fish sources and are liquid at room temperature. Common sources of polyunsaturated fats include liquid vegetable oils, oil-based salad dressings, and fatty fish (like tuna and salmon).

Conclusion

Diabetes is a disease for which there is a clear prevention plan.

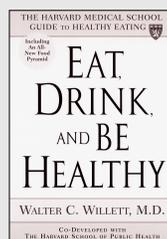
By keeping their weight in check, being physically active, and eating a healthy diet, women can lower their risk of diabetes by 90%. Notably, this is true for all women, even those with a family history of the disease. And the benefits don't stop at diabetes. Taking these steps is an important part of an overall healthy lifestyle that helps lower the risk of heart disease, stroke, cancer, and osteoporosis.



From the NHS Bookshelf

Walter Willett, Principal Investigator of Nurses' Health Study II, together with colleagues Edward Giovannucci, Patrick Skerrett, and Maureen Callahan, recently published a book called *Eat, Drink, and Be*

Healthy: The Harvard Medical School Guide to Healthy Eating. This book brings together current knowledge about diet and health from many sources, including the Nurses' Health Study.



Of particular interest are the many recipes and practical ways that the book offers for translating current science into enjoyable meals.

Looking for WWII Nurses

Congresswoman Nita M. Lowey (NY) has introduced a bill in the US House of Representatives called the *Cadet Nurse Corps Equity Act of 2001 (HR 1724)*. If passed, this legislation would grant veteran status and benefits to all nurses who served in the Cadet Corps during World War II. If you are a former member of the Corps and would like to help promote the bill, please contact:

Ruth Sartori / (201) 944-8923 / 196 Leonia Avenue, Leonia, New Jersey 07605

Focus on Our Research Team

Once again, we'd like to introduce you to one of our staff members whose behind-the-scenes work is essential to the successful conduct of the Nurses' Health Studies. Please meet **Shelagh Pearson, Human Studies Protocol Coordinator.**

Shelagh attended Emerson College, where she received a Bachelor's degree in Communications. She spent several years working as a paralegal and then became an administrator at Boston Medical Center. There, she coordinated research protocols and secured patient consent for clinical trials. Notably, this position also offered Shelagh her first introduction to the NHS: many of the nurses she worked with were participants and shared their annual newsletters with her.

Shelagh joined the Nurses' Health Study team in 1999 to help us manage the many policies and regulations that surround human research. In order for us to maintain our funding from the National Institutes of Health, our research protocols must undergo increasingly thorough reviews by the Institutional Review Boards at both Harvard School of Public Health and Brigham & Women's Hospital.



Your Privacy

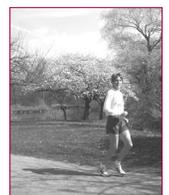
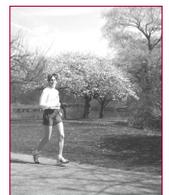
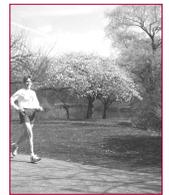
As a participant in the NHS, you have provided us with a wealth of data in the form of very personal information. Because of the trust you have shown in us, we are very careful to hold ourselves to the highest standards in the safekeeping and use of the data. **Our most recent step was to obtain an updated certificate of confidentiality from the Department of Health and Human Services.**

With this certificate, we cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. We will use the certificate to resist any demands for information that would identify you. Notably, this certificate does not prevent you from voluntarily releasing information about yourself or your involvement in the NHS.

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.**

These review boards act to protect the rights and safety of all participants in research studies. For example, when we conduct blood collections, the review boards examine our research protocols to ensure that we are taking the necessary steps to protect participants' privacy. Similarly, they make sure that we always provide participants with the name and telephone number of study personnel that they can contact if they have questions or concerns about our research. By serving as the crucial link between study investigators and the Institutional Review Boards, Shelagh helps to ensure the successful continuation of the Nurses' Health Study.

With 125 research protocols to maintain, Shelagh is often on the run, but keeping up with the pace of the job is no problem for this avid marathoner. She has completed two New York City marathons and is already training for her third.





Mothers Study

Given all the questions we have asked the NHS participants over the years, it was only a matter of time before we would ask to talk to their moms. After obtaining permission, we mailed a special questionnaire to each nurse's mom or to the nurse herself to administer to her mother. In these surveys, we asked the moms to recall their diets and lifestyles when they were pregnant with their nurse daughters. We also asked about breastfeeding, baby formula, and early childhood diet – things that only a mother would know. To date, we have received over 22,000 completed questionnaires from mothers and hope to use this information to learn more about how early life factors might affect the long-term health of offspring.

Stress Questionnaire



In the past, women in the Nurses' Health Studies have provided important information about the stress associated with caregiving and work. However, other stresses may also have important implications for women's health. For example, while personal relationships are often a source of strength and comfort, they can also be a source of conflict and stress for some women. To study this in more detail, we mailed supplemental questionnaires to Nurses' Health Study II participants to collect information about stress and support related to personal relationships. In addition, we asked for detailed information about each of their past pregnancies. There is increasing although inconsistent evidence that a woman's lifetime history of chronic stress before pregnancy (or acute stress during pregnancy) may affect her pregnancy outcomes, including her risk of miscarriage, preterm delivery, and fetal growth retardation.

The response to a single mailing of this questionnaire has been remarkable, with approximately 61,000 surveys returned thus far. Such a response exemplifies participants' dedication to the study and also provides us with the largest and most powerful data set ever assembled to address these issues.

Keeping Us Up to Date

As members of the Nurses' Health Study continue to age, some will unfortunately become disabled or develop conditions that make it difficult to respond to future mailings. Because we hope to examine these conditions and learn more about their causes, **we encourage you to discuss your participation in the NHS with your family and doctor.** Should you become disabled in the future, 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. By combining this information with the detailed medical and dietary histories you have provided over the years, we can identify possible causes of these conditions, along with ways in which they may one day be prevented.

Medical Record Review

Participants who report a new diagnosis 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



How do you use the genetic information you get from the saliva and blood samples you collect, and how is my confidentiality protected?

Both saliva and blood can provide DNA and thus help us to understand the role of genetics in promoting or preventing various diseases. In general, we only study genes about which little is known, and that is why we do not provide you with information on any of the genetic assays we conduct. The information is so preliminary that it has little value outside of the research setting.

Since the Nurses' Health Study is a unique resource, we are very careful about using any samples you provide. Even though national regulations about the use of scientific data could eventually change, confidentiality will always be extraordinarily important to us. We take every possible measure to ensure that individual results from genetic studies are never released, and we have special certification from the Department of Health and Human Services to protect participants' privacy. For more on this topic, please see **Your Privacy** on page 6.

There's a section on the questionnaire where you ask how we feel and how things have been with us. These seem like important questions, but why do you only ask about the past four weeks?

The four-week timeframe is a bit of a trade-off. If we asked how you felt in the past day, it might not be reflective of how you generally feel. For example, you might be an upbeat person, but if you had the flu on the day you filled out the questionnaire, your answers might not reflect your typical energy or outlook. On the other hand, if we asked about your feelings over a time period longer than four weeks, it could be difficult to accurately recall how you felt. In order to minimize the burden to you, while also obtaining the most accurate information possible, we focus these questions on the past four weeks.

What is the source of funding for the NHS?

Since 1976, the federal government has continuously funded the Nurses' Health Study through the National Cancer Institute (NCI) at the National Institutes of Health (NIH). They have also continuously funded the Nurses' Health Study II since its inception in 1989. This funding covers the studies' main activities, including the mailing and processing of questionnaires, data management, and the confirmation of cancers diagnosed in the cohorts. Other institutes at NIH have funded the sub-studies we've conducted on respiratory disease, diabetes, heart disease, fractures, eye disease, Parkinson's disease, and multiple sclerosis. Collectively, the NIH funds about 95% of our work.

The remaining 5% of our funding is made up of general gifts and project-specific support for non-NIH work. For example, we recently completed an analysis of vitamin A and fracture risk that was funded by Roche Vitamins, Inc. Before we accept such funding, we take a number of precautions to ensure that the funder will not interfere with the scientific integrity of our work. For example, we only accept funding for studies that we agree are scientifically justified, and the funder cannot interfere with the publication of results.

How long will the Nurses' Health Study 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.



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Collect calls are accepted;
letters & feedback are welcome.

To report name/address changes,
visit www.NursesHealthStudy.org
& click **Contact Us**.

Donations & bequests to
the Friends of the Nurses'
Health Study Fund at
Harvard Medical School
can be sent to the
Channing Laboratory.