The Nurses' Health Study Annual Newsletter Volume 10 • 2003

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Dear Colleagues,

As the principal investigators of the Nurses' Health Studies, we would like to thank you for your dedication to the study. Dr. Frank Speizer, the founding principal investigator, sends his regards from England, where he is on sabbatical continuing his research on lung dis-

ease. We are grateful for

your contributions and look forward to continuing our collaboration with you.

One important issue that we are currently addressing, with your help, is the use of postmenopausal hormones. Although we have been studying this topic for years, there is still much to learn. For example, we are exploring whether or not hormone use affects breast cancer risk even after the hormone therapy has been stopped. We are also evaluating various patterns of estrogen and progestin use to see if they impact breast cancer risk differently.

As we continue to advance our understanding of hormones and other health issues, we will also continue to share our findings so that you have the information you need to lead a healthier life. Thank you, as always, for your participation in the Nurses' Health Studies.

Sincerely,

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

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

The Impact of Weight on Cancer Risk

Most of us have been hearing about genetics and environmental pollutants for so long that we think cancer is beyond our control, but in fact, more than 50 percent of all cancers can be prevented with a healthy lifestyle. One of the most important steps you can take to lower your risk of cancer is to maintain a healthy weight. While most people are aware that a healthy weight can reduce the risk of heart disease and diabetes, few realize that it can also lower the risk of some of the most common types of cancer, including breast, colon, and endometrial cancer.

Breast Cancer

According to the Nurses' Health Study, women may be able to lower their risk of breast cancer by keeping their weight steady. Compared to women who gained less than five pounds during adulthood, those who gained more than 45 pounds had a 40 percent higher risk of developing breast cancer after menopause. This increase in risk is probably due to increased levels of estrogen. Although a woman's ovaries stop producing estrogen after menopause, her fat tissue continues to convert estrogen precursors to estrogen. The more weight a woman puts on after menopause, the more estrogen her body produces—and the higher her risk of breast cancer.

Among premenopausal women, the risk of breast cancer appears to decrease as weight increases. However, this does not mean that being overweight before menopause protects women against dying from breast cancer. Overweight women are often diagnosed with breast cancer at a later stage, when it is more difficult to treat. Furthermore, the large majority of breast cancers occur in postmenopausal women, and any weight gained before menopause will likely remain after menopause, when it can increase risk. *Continued on page 4*

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Recent Findings

This year, the Nurses' Health Studies 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 the **Publications** section of our website at www.NursesHealthStudy.org.

Obesity and Total Hip Replacement

New data from the Nurses' Health Study suggest that a woman's weight may be the strongest predictor of whether she will need a total hip replacement due to osteoarthritis. Overall, we found that being overweight at a young age was a greater predictor than being overweight later in life. Compared to lean women, those who were obese at age 18 had a fivefold increase in the risk of hip replacement, and those who were obese after menopause had a threefold increase in risk. (Karlson E et al. Am J Med 2003;114:93–8.)

Physical Activity and the Risk of Hip Fractures

A growing body of evidence suggests that leisure-time physical activity, including walking, may reduce the

risk of hip fractures. In the Nurses' Health Study, women who walked for at least four hours a week



had a 40 percent reduction in risk. For postmenopausal women who are not taking hormones, high levels of leisure-time activity can provide protection against hip

fracture that is equivalent to that provided by hormone use. Furthermore, for women who are sedentary, our results suggest that it is never too late to reap the benefits of an active lifestyle: sedentary women who increased their leisure-time activity to at least four hours a week lowered their risk of hip fracture by nearly 50 percent. (Feskanich D et al. JAMA 2002;288:2300–6.)

Dietary Fat and Breast Cancer Risk

Most of the research on dietary fat and the risk of breast cancer has focused on postmenopausal women. In the Nurses' Health Study II, however, we had the opportunity to assess this relationship in younger, mostly premenopausal women. What we found is that a high intake of animal fat (but not vegetable fat) may moderately raise a woman's risk of developing breast cancer. When we looked at sources of animal fat, we found that red meat and high-fat dairy foods both contributed to the increase in risk. (Cho E et al. J Natl Cancer Inst. In press.)

Calcium, Vitamin D, and the Risk of Hip Fractures



Calcium has been the primary focus of nutritional research on the prevention of osteoporosis. However, new evidence from the Nurses' Health Study suggests that intake of vitamin D may play a more important role for postmenopausal women than calcium does. We found a 40 percent lower risk of hip fractures among women who had vitamin D intakes of 500 IU per day, but neither milk nor a high-calcium diet appeared to reduce risk. Because vitamin D is not naturally found in many foods and women often consume less than the recommended amount, supplement use may be prudent. (Feskanich D et al. Am J Clin Nutr 2003;77:504–11.)

Progesterone Receptor Gene and the Risk of Endometrial Cancer

The development of endometrial cancer is linked to the balance between estrogen and progesterone. Consequently, genetic research on this disease has focused on genetic variants that affect the regulation or metabolism of these hormones. In the Nurses' Health Study, we have been studying variants in the progesterone receptor gene and have found that a specific variant may contribute to endometrial cancer risk, particularly among overweight women. Further studies are needed to better understand the role of the progesterone receptor in endometrial cancer. (DeVivo I et al. PNAS 2002;99:12263–8.)

Folate, Vitamin B₆, and Breast Cancer Risk

Folate has a number of established benefits, including protection against neural tube defects and colorectal cancer. Now data from the NHS suggest that folate may also offer protection against breast cancer. Using blood samples, we found a 25 to 30 percent reduction in risk among women who had the highest amounts of folate and vitamin B_6 in their blood. This benefit may be particularly important for women with higher alcohol consumption: alcohol is known to raise the risk of breast cancer, and folate may lessen this effect. Women can increase their folate intake by taking daily multivitamins or consuming more oranges, orange juice, and fortified breakfast cereals. (Zhang SM et al. J Natl Cancer Inst 2003;95:373–80.) \blacklozenge



Study Updates

The NHS Memory Study

Between 1995 and 2002, nearly 20,000 NHS participants completed two telephone interviews as part of our ongoing study of memory. During those interviews, women were given several standard assessments of cognitive function. By combining these assessments with the abundant questionnaire information that women have given us over the years, we hope to better understand how diet and lifestyle influence memory. We have already uncovered some important findings, with our most recent results highlighted below.

We are now completing third interviews with all of the women who completed the first two phone surveys, and we are grateful to the many women who have given their time to this important study. Everyone's participation remains critical since we are equally interested in women who have maintained their memories and women who are having some difficulties.

Nonsteroidal Anti-Inflammatory Drugs and Cognitive Function

According to the Nurses' Health Study, nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin, may influence cognitive function in women over age 70. We found that women

who took ibuprofen or aspirin regularly for at least eight years performed slightly better on several tests of cognitive function than women who never took the drugs. Although both drugs offered some benefit, the effect was stronger for ibuprofen. (Kang J et al. Neurology. In press.) •

The Growing Up Today Study

Seven years ago, we started the Growing Up Today Study (GUTS) with 17,000 children of women in the Nurses' Health Study II. Today, those children are 16 to 21 years old, and many are going off to college, joining the military, or living on their own. As they grow and mature into young adults, we are proud of the contributions they have made and look forward to continuing our work with them. We also greatly appreciate the encouragement that their moms have provided to keep them interested and involved. Below is one of our recent findings.

Physical Activity, TV/ Video Time, and Adolescent Weight Control

With obesity rates on the rise among adolescents, healthy weight strategies for this age group are becoming increasingly important. New data from the Growing Up Today Study suggest that a possible strategy is to replace one hour of television or video games each day with one hour of physical activity. We found that overweight adolescents who increased their TV/video time over a one-year period experienced modest weight gain, while those who increased their daily activity experienced modest weight loss. Although we looked at many different types of physical activity, walking and aerobics/dancing seemed particularly beneficial. (Berkey CS et al. Pediatrics 2003;111:836–43.) ◆

The NHS II Stress Study

In the Nurses' Health Study II, we are examining how intimate violence might affect women's health. Approximately 67,000 women answered a supplemental questionnaire to help us learn about this issue. Of these women, approximately 35 percent reported experiencing emotional, physical, or sexual abuse in their lifetimes. This number highlights not only the prevalence of the problem but also the importance of studying it. In the coming year, we will be looking at how violence impacts women's risk of asthma, hypertension, and gynecological disorders including fibroids. ◆

New Directions

Last year, we began a study of occupational exposures and pregnancy among Nurses' Health Study II participants. The goal of the study is to investigate how the demands of the nursing profession such as shift work, prolonged standing, and chemical exposures—might affect women's pregnancies. To date, more than 8,000 women have completed a



supplemental questionnaire about the occupational exposures they experienced during their most recent pregnancies. Such a response exemplifies participants' dedication to this important issue.



EIGHT & CANCER RISK

Continued from cover

Colon Cancer

Colon cancer is one of the most common types of cancer, but it is also one of the most preventable. Among the many ways that men and women can lower their risk of this disease is to maintain a healthy weight. In the Nurses' Health Study and Health Professionals Follow-Up Study, we found that obese adults were about 50 percent more likely than lean adults to develop adenomatous polyps and colon cancer. Adenomatous polyps are noncancerous growths in the colon that have the potential to become malignant.

The reason for the link between weight and colon cancer is not yet clear but may have to do with the effect of weight on insulin and other growth factors. Obesity can lead to higher levels of insulin in the blood, which might in turn promote abnormal cell growth in the colon.

Endometrial Cancer

Along with hormone use, weight is the most important factor influencing a woman's risk of endometrial cancer. This has been confirmed in a number of studies, including the Nurses' Health Study. We found that being overweight and gaining weight both raise the risk of endometrial cancer.

While the links between weight and endometrial cancer hold true for all women, they seem to be much stronger for postmenopausal women than for premenopausal women. For example, a weight gain of more than 40 pounds doubled the risk among premenopausal women but quadrupled it among postmenopausal women. The reason for this difference is likely related to estrogen levels. The more weight a woman carries after menopause, the more estrogen her body produces—and the higher her risk of endometrial cancer.

Warning: Too Much TV Time May Be Harmful to Your Health

TV time may be a major contributor to obesity, according to the Nurses' Health Study. For every two hours a day that women spent watching TV, their risk of obesity went up 23 percent. The good news, though, is that women can lower their risk by trading



TV time for light activity. For every two hours a day that women spent standing or walking at home, their risk of obesity went down 9 percent. (Hu F et al. JAMA 2003;289:1785–91.)

Are You at a Healthy Weight?

A healthy weight is defined by a body mass index (BMI) of 25 or lower. To calculate your BMI:

- I Divide your weight in pounds by your height in inches.
- 2 Divide the answer by your height in inches.
- **3** Multiply the answer by 703.

If your BMI is...

25 or lower: Try to keep your weight steady with a healthy diet and daily exercise.

Higher than 25: Do what you can to prevent weight gain. When you're ready, shedding some pounds and keeping them off will be important steps to better health.

Source: NutritionSource, Harvard School of Public Health www.hsph.harvard.edu/nutritionsource/weight.html

Kidney Cancer

Virtually every study that has examined the link between weight and kidney cancer has found that obesity raises the risk of this disease. Because the association is usually stronger among women than men, some researchers have speculated that the underlying mechanism might be related to hormonal changes. However, additional research is needed to evaluate this.

Esophageal Cancer

Esophageal cancer is divided into two main categories, squamous cell carcinoma and adenocarcinoma, and obesity is consistently linked to the latter. The reason for this is not yet known but may be related to the influence of obesity on gastric reflux, a condition in which stomach acids "back up" into the esophagus. Gastric reflux is an established risk factor for adenocarcinoma, and some studies have suggested that it is more common among obese adults.

Conclusion

While there are many risk factors for cancer that are beyond an individual's control, there are also many steps that people can take to lower their risk. Maintaining a healthy body weight is a key step that clearly impacts the risk of multiple cancers and also improves overall health. \blacklozenge

For more information on cancer prevention, visit: www.hsph.harvard.edu/cancer

Strategies for Maintaining a Healthy Weight



If you need to lose weight, set a realistic goal.

A good initial goal is to lose 5 to 10 percent of your current weight. Once you achieve that, keep aiming for another 5 to 10 percent until you're happy with your weight.



Make small, meaningful changes.

Cutting out just 100 calories a day (the equivalent of a single can of soda or a bedtime snack) or taking a brisk 30-minute walk each day can have beneficial effects on weight.

Exercise more.



The more you work your muscles—especially with strength training exercises—the more calories they burn even when you aren't active. If you already exercise, try to increase the duration or intensity. If you don't currently exercise, try a walking program. Start out with something simple: get off your bus a stop early, park your car at the far end of the parking lot, or take a brisk walk during lunch. Gradually increase your daily walking time until you do 30 or more minutes a day.



Keep track.

It's easy to eat more than you plan to. A daily food diary can make you more aware of exactly how much you are eating. Include everything, no matter how small or insignificant it seems. Even small snacks and juice add up to real calories.



Tame your blood sugar.

Eating foods that make your blood sugar and insulin levels shoot up and then crash may contribute to weight gain. Such foods include white bread, white rice, and other highly processed grain products. As an alternative, choose foods that have a gentler effect on blood sugar, like whole grains, beans, nuts, fruits, and vegetables.



Don't be afraid of good fats.

Fat in your diet helps you feel full. Good fats such as olive and canola oil can also help improve your cholesterol levels when you eat them in place of saturated fats, trans fats, or highly processed carbohydrates.



Reach for water when you're thirsty.

Drinking juice or sugared soda can add several hundred calories a day without you even realizing it.



Practice defensive eating.

In our society, food is everywhere—the mall and gas station, the ballpark and drug store. In the face of such plenty, it's important to learn strategies that help defend against eating too much:

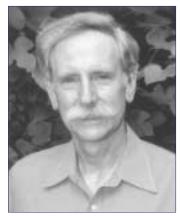
- Slow down, and stop before you're stuffed. Learn your body's signals and practice stopping before you feel full.
- Be selective. It's easy to eat food just because it's put in front of you. Be mindful of what you're eating, and make sure that **you** are choosing what to eat.
- Select small portions. If you're eating out with someone, try sharing an entrée. If you're eating alone, eat half and take the rest home for another meal.
- **Spoil your appetite.** Having a snack or appetizer can dull your hunger and help you eat less at a meal.
- Be aware of why you're eating. Sometimes we eat when we're bored or anxious. Dealing with feelings in other ways—talking to friends, taking a walk, or meditating—can help you relieve stress without gaining weight.



Source: www.hsph.harvard.edu/nutritionsource/weight.html (NutritionSource, Harvard School of Public Health)

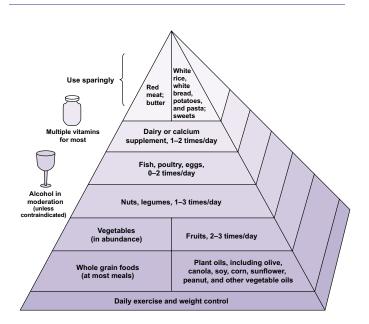
Focus on Our Research Team

More than 25 years ago, Dr. Walter Willett joined the Nurses' Health Study team to investigate how diet and nutrition affect women's health. Today, he is one of the nation's leading nutrition experts, using scientific evidence to challenge and reshape the definition of a healthy



lifestyle. His research has led to the unfolding of many a nutritional myth and has revealed that nuts are healthier than we once thought, that the type of fat we eat is more important than the amount of fat, and that all carbohydrates are not created equal. These findings, along with many others, are summarized in Dr. Willett's **Healthy Eating Pyramid** shown below.

As the principal investigator of the Nurses' Health Study II and Health Professionals Follow-Up Study, Dr. Willett oversees all of the research conducted within these large studies. He is also Professor of Epidemiology and Nutrition at Harvard School of Public Health and Professor of Medicine at Harvard Medical School. Though it's hard to imagine that Dr. Willett has spare time, he enjoys spending it on his bicycle, in his garden, or with his family.



The Healthy Eating Pyramid

Results from the Nurses' Health Study and Health Professionals Follow-Up Study suggest that people can significantly reduce their risk of chronic disease by adhering to the guidelines illustrated in this pyramid. (*McCullough M et al.Am J Clin Nutr 2002;76:1261–71*)

Rebuilding the Food Pyramid

Using decades of scientific research as his foundation, Dr. Willett has created a new food pyramid to replace the USDA version. His pyramid illustrates seven key changes that people can make to improve their diets and overall health:

• Watch your weight.

The only way to do this is to balance calorie intake with daily physical activity. (See page 5 for healthy weight strategies.)

- Eat fewer bad fats and more good fats. Good fats can be found in nuts, seeds, grains, fish, and liquid oils. Bad fats, like saturated and trans fat, are in red meat, butter, whole-milk dairy products, and hydrogenated vegetable oils.
- Eat fewer refined-grain carbohydrates and more whole-grain carbohydrates. Whole grains have a more mellow effect on

blood glucose levels than refined grains do. Refined grains include white rice, white bread, and pasta.

- Choose healthier sources of protein. The best sources are beans and nuts, along with fish, poultry, and eggs.
- Eat plenty of fruits and vegetables, but hold the potatoes.

Together with whole grains, fruits and vegetables serve as the basis of a healthy diet. Potatoes, though, have a dramatic effect on blood sugar and so should be eaten sparingly.

- Drink alcohol in moderation, if at all. This means less than one drink a day for women and up to two drinks a day for men.
- Take a multivitamin for insurance.

On top of a healthy diet, a multivitamin can provide added protection against chronic disease.

Pyramid and text source: Willett WC. *Eat, Drink, and Be Healthy: The Harvard Medical School Guide to Healthy Eating.* New York: Simon & Schuster, 2001.

Your Privacy

As a fellow health care provider, you are probably already aware that the **Health Insurance Portability** and Accountability Act (HIPAA) went into effect on April 14, 2003. The purpose of this federal law is twofold: 1) to protect health insurance coverage for workers when they change or lose their jobs, and 2) to protect the privacy of individuals' health care information. Although many states already have more stringent measures in place than those introduced by HIPAA, the Act guarantees basic rights and protections for all Americans.

The Privacy Rule under HIPAA promises to have a far-reaching impact on the health care field. However, we have not had to make any major changes in our privacy policies, and **we do not expect that HIPAA will affect your experience as a participant in the Nurses' Health Studies**. This is because we have always taken every available precaution to protect your privacy. We only allow authorized personnel to access your personal information, and we have always gotten your written permission to review any pertinent medical records. When we do share data with other scientists, we never include participants' names, Social Security numbers, or any other identifying information.

Because of these safeguards, the confidentiality of your NHS data has always been maintained. We remain committed to protecting your privacy as a study participant and will continue to take all of the necessary steps to shield your private information while advancing the study of women's health. As HIPAA goes into effect, we will keep you updated on how the new regulations might affect the Nurses' Health Studies. In the meantime, we appreciate your continued collaboration and are grateful for the trust that you have shown in us. •

What about DNA?

As with all of the data you provide to NHS, we are very careful about the blood and mouthwash samples you provide for genetic research. Genetic results are coded so that they are never stored together with individual identifying information. We will continue to make confidentiality our



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.

Feedback

Q: Why do the questionnaires ask about "physiciandiagnosed" illnesses? Many people have a nurse practitioner or other clinician as their primary care provider and rarely if ever see a physician.

A: This is a question we've been struggling with for many years. We realize that doctors are not the only health care providers to make diagnoses, and on several occasions we have considered changing the questionnaire to ask about "illnesses diagnosed by a health care provider." However, the Nurses' Health Studies are made up entirely of health care providers, and we do not want study participants to report selfdiagnosed conditions that have not been confirmed in a clinical setting. For this reason, we have continued to ask participants to report only "physician-diagnosed" illnesses.

Q: In the diet section of the questionnaire, the lowest category for each food is "never or less than once a month." Isn't it inaccurate to lump people who occasionally eat a particular food with those who never do?

A: Some nurses have told us that they don't like their answers being put in the same category as people who eat certain foods (often the meat or dairy categories). While we understand this, we think that adding a separate "never" category would make it more difficult to complete the questionnaires. In addition, we use the information you provide about various foods to better understand how diet affects women's health, and in this context, "less than once a month" is dietetically equivalent to "never."

Q: Can I get the results of the tests you've done so far on my blood samples? I'm especially interested in genetic markers for breast cancer.

A: There are several reasons why we cannot give participants their individual results. One is that the results may not be clinically relevant. Most of our research involves studying possible but not yet proven biochemical and genetic markers. As a result, the information is so preliminary that it has little value outside the research setting. We also store the blood samples over many years, and your individual results may not be relevant to you by the time they are analyzed. Another reason is that to contain costs, we only analyze a portion of samples for a given marker. Thus, a participant should not assume that a specific test was conducted on her blood. We will continue to keep you updated on the overall results of our genetics research (for example, see page 2). ◆

Update on the Cadet Nurse Corps

Last year we reported that a bill had been introduced in the U.S. House of Representatives to grant veteran status and benefits to nurses who served in the Cadet Corps during World War II. Following our report, over 3,500 women contacted Ruth Sartori, RN, who is heading up the effort to pass this legislation. While that bill did not succeed in 2002, it has been reintroduced, now with 25 co-sponsors, as the US Cadet Nurse Corps Equity Act of 2003 (HR-476).

If you are a former member of the Corps or wish to help promote the new version of the bill, please send a business-size self-addressed stamped envelope with your name and phone number to:

Ruth Sartori 196 Leonia Avenue Leonia, NJ 07605

(Telephone 201-944-8923)



Back of Beyond...

These are some observations that accompanied the 2002 questionnaire completed by a nurse living in the former Soviet republic of Kyrgyzstan.

I live in the middle of Central Asia and eat both Russian and Kyrgyz national dishes (we stay away from the head of a sheep). Fat is considered very good for you over here, and both Kyrgyz and Russians think Americans are crazy to worry so much about fat. For instance, the concept of skimming the fat off of chilled soup is unheard of. Of course, my national friends also think we are crazy to sit on cement (ruins the prostate and the ovaries), eat ice cream or drink anything cold with a sore throat (makes it worse) and, most especially, to open car windows on a hot day (a draft when it's hot will kill you for sure).

Life in the Back of Beyond is always interesting.

Take care of America, won't you please? We love her very much.

—M.N., Bishkek, Kyrgyzstan

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Collect calls are accepted; letters & feedback are welcome.

To report name or address changes, visit www.NursesHealthStudy.org & click Contact Us. Donations and bequests to the Friends of the Nurses' Health Study Fund at Harvard Medical School can be sent to the Channing Laboratory.

