



NHSII NEWS



A RECORD 40 YEARS

If you've ever gotten a letter from us, asking for more information about something you

reported on the questionnaire, chances are it came from Barbara Egan's group. Back in 1978, two years after the start of the Nurses' Health Study, we needed someone to assist with the process of confirming reports by the nurses of cancer and cardiovascular disease. Having raised her 5 children, Barbara was looking for a career. Original investigators Dr. Frank Speizer and Dr. Charles Hennekens took Barbara on to help collect medical records to confirm new cancer cases.

Now 40 years later, having risen through the ranks, Barbara is retiring from the Nurses' Health Study. Her compassion for the study participants has been a model for everyone here because she has always regarded "our nurses" as invaluable partners in this research. She has been like a mother to hundreds of students, fellows and co-workers who have worked alongside her over the decades. As Barbara leaves to spend more time with her family and enjoy her house on Cape Cod, her experience and her passion for the study will be sorely missed.

NEW COLLECTION UNDERWAY

Update on the Microbiome in Nurses Study

The Massachusetts Life Sciences Center has funded us to collect tens of thousands of stool and saliva samples from NHSII. This collection started in July, 2018 and will continue for approximately 24 months.



The robotic freezer can store over 3 million samples at -80°C. Any individual tube can be automatically accessed from anywhere within the 10 different freezer compartments.

In 2017, we asked you and other members of NHSII about your willingness to participate in this collection; over 80% have agreed. We are thrilled with this overwhelmingly positive response.

Why collect stool and saliva?

Collectively, the ecosystem of microorganisms living on and in us is called the microbiome. The overall goal of collecting stool and saliva is to begin to describe what makes up a healthy microbiome and also to define when it may be unhealthy. It is essential to better understand the ways in which the microbiome influences our health and how lifestyle, environment, diet and early life factors can modify the effectiveness of the microbiome in helping to keep us healthy. In addition, learning how people can alter the composition of their microbiome may afford opportunities to harness these microorganisms to improve human health.

What to Expect

If you told us on the last questionnaire that you would be willing to participate, you should eventually receive an email or letter from us requesting your official consent. Once we have your consent, you will then be queued-up to be mailed a collection kit.

Recent Findings

The Genetics of Breast Cancer

Much is still unknown about genes and breast cancer risk. The NHS and the NHSII contributed to an international consortium along with more than sixty other studies to more fully understand the genetics of breast cancer. With 137,000 participants with breast cancer (21,000 with estrogen-receptor negative disease) and 119,000 participants without breast cancer, we discovered 65 previously unsuspected genetic variants that

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contribute to breast cancer risk. We also located 10 genetic variants associated with the less-well understood estrogen-receptor negative disease. While any individual genetic variant alone only has a small effect on breast cancer risk, these new genetic variants, along with previously identified variants together explained 18% of familial breast cancer.

These findings can be used in the future to identify women with higher genetic risk who may benefit from more intensive screening or prevention strategies.

Changes in Diet

We have previously identified healthy diets that are linked with a lower risk of major chronic diseases and death, but little is known about how changes in diet over time impact subsequent risk of death.

In the NHS and the male Health Professionals Follow-Up Study, we examined the association between changes in diet quality among nearly 74,000 adults over a 12 year period, and their risk of death. Those who improved their diets by eating more whole grains, vegetables, fruits, nuts, and fish and less red and processed meats and sugary beverages, had a 9%-16% lower risk

of death. On the other hand, those with a decline in diet quality had a 6%-12% higher risk of death.

Our findings highlight the long-term health benefits of improving diet quality. A healthy eating pattern can be achieved in numerous ways and can be adopted according to an individuals' food and cultural preferences and health conditions.

The Benefits of Maintaining a Healthy Weight

Weight gain during adulthood could influence health risks later in life. Participants in the NHS and the Health Professionals Follow-Up Study were asked to recall their weight from early adulthood (age 18 for women, 21 for men) and to report their weight at age 55.

Women gained an average of 22 pounds over early-to-middle adulthood, and men about 19 pounds. Over an 18 year period, after age 55, each 11-pound weight gain was associated with a 30% higher risk of type 2 diabetes, 14% higher risk of hypertension, 8% higher risk of cardiovascular disease, 6% higher risk of obesity-related cancer, 5% higher risk of dying prematurely (among never smokers), and 17% lower odds of achieving healthy aging.

Although most people only gain a small amount of weight per year, the cumulative weight gain over adulthood can be large. Our findings will help health professionals counsel patients regarding the health consequences of even small increases in weight.

Disinfectants and COPD

Past research has linked exposure to disinfectants among healthcare workers with breathing problems such as asthma. In NHSII, we examined whether use of

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nurses were diagnosed with COPD. Nurses who used disinfectants to clean surfaces at least once a week had a 22% higher risk of developing COPD. There was

disinfectants may increase the risk of developing chronic obstructive pulmonary disease (COPD).

Among 55,000 nurses active in nursing, 37% reported weekly use of disinfectants to clean surfaces. During 8 years of follow-up, 663

also a suggestion of a higher risk with weekly use of disinfectants to clean instruments, but this was not statistically significant.

High level exposure to specific disinfectants, such as glutaraldehyde, bleach, hydrogen peroxide, and quaternary ammonia compounds (also known as “quats”), was associated with a 24% to 32% higher risk of developing COPD.

Although these preliminary findings need confirmation, they emphasize the urgency of integrating occupational health considerations into guidelines for cleaning and disinfection in healthcare settings.

THE COMPLEX HISTORY OF HORMONE REPLACEMENT

Early evidence from the Nurses’ Health Study indicated that menopausal hormone therapy use was associated with a lower risk of coronary heart disease. The Women’s Health Initiative (WHI), a large-scale randomized trial, was designed to test the effect of using hormones on development of coronary heart disease and other health outcomes. Because coronary heart disease is uncommon in early menopause and the risk increases with age, the WHI enrolled older women, aged 50-79 years. The WHI trials were terminated earlier than planned due to an increased risk of breast cancer in the estrogen plus progestin group and an increased risk of stroke in the estrogen alone group. Discrepancies in the findings of NHS and WHI for some outcomes, particularly coronary heart disease where no benefit of hormone therapy was observed in WHI, generated an intense debate, with some researchers discrediting the NHS findings. However, upon closer examination, the results of NHS and WHI were found to be very similar, and any differences appeared to be due to the younger age of NHS participants at the time they started taking hormones, which more closely corresponds to the use of hormone therapy in actual practice.

In the NHS, women using hormone therapy were generally below age 55 years and started hormone therapy within 2–3 years of the onset of menopause. Conversely, women in the WHI were older with an average age of 63 years and most were 10+ years past menopause when they started taking hormones. In the two studies, when we re-examined associations within comparable age groups (e.g., 50-59 y), results for hormone therapy were highly similar in NHS and WHI. In both studies, the results were more favorable when hormone therapy was started in early menopause. Therefore, the NHS and the WHI both found right answers but to different questions. While NHS examined the role of menopausal hormone therapy when started primarily in early menopause, the WHI examined the effects of hormone therapy in an older cohort, more distant from the onset of menopause.

Endometriosis Research

Endometriosis is a chronic condition that occurs when endometrial-like tissue, usually lining the walls of the uterus, grows outside the uterus. This disease can severely impact quality of life by causing severe, painful menstrual periods, chronic pelvic and bowel pain, sexual dysfunction, and infertility. Approximately 10% of reproductive age women have endometriosis. The NHSII has collected information on endometriosis since 1993, which has allowed our cohort to become a leader in endometriosis research.

Breastfeeding and Endometriosis Risk

In NHSII, we found that among women who had children, those who breastfed for longer periods of time had a significantly lower risk of being diagnosed with endometriosis. Lead author, Leslie Farland, ScD noted, “These findings offer new insights into a condition for which there are very few known, modifiable risk factors.”

In the NHSII, over 3,000 women had been surgically diagnosed with endometriosis after their first pregnancy. We found that for every three additional months that mothers breastfed per pregnancy, women experienced an 8% reduction in endometriosis risk. Women who breastfed exclusively for 18 months or more across their

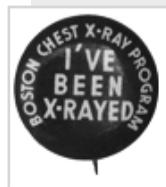
reproductive lifetime had a nearly 30% lower risk. We found that postpartum amenorrhea – the temporary absence of menstrual periods that occurs when a woman is breastfeeding – accounted for some – but not all – of the association, suggesting that breastfeeding may lower endometriosis risk through other mechanisms as well. Breastfeeding changes many of the hormones in a woman’s body, including oxytocin, estrogen, gonadotropin-releasing hormone and others for which there is evidence of a role in endometriosis pathophysiology.

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Endometriosis and Cardiovascular Disease Risk

Using the detailed, long-term follow-up data contributed by the NHSII participants, we found that women with endometriosis may have a higher risk of heart disease. In the entire NHSII cohort, endometriosis was confirmed in over 11,000 women. During 20 years of follow-up, women with endometriosis had a 52% higher risk of heart attack, and a 91% higher risk of developing angina or chest pain compared to women without endometriosis. Moreover, among women aged 40 or younger, those with endometriosis were three times more likely to develop heart disease, compared to women without endometriosis. Removal of the uterus or ovaries may partly account for the greater risk of heart disease. As observed previously in NHS and NHSII, surgically induced menopause may increase the risk of heart disease, and this elevated risk may be more evident at younger ages. “It is important for women with endometriosis to adopt a heart-healthy lifestyle, be screened for heart disease, and be familiar with symptoms, because heart disease remains the primary cause of death in women,” said senior study author Stacey Missmer, ScD. The team’s findings were selected for an American Heart Association press release and were the year’s most highly cited for the journal *Circulation: Cardiovascular Quality and Outcomes*.



FROM THE MAILBOX

NHS nurse Nancy W. sent us this unusual pin. “No idea which of my forebears picked it up, but it falls to me to dispose of it. Medical?

Health? Ah, of course, send it to the Nurses’ Health Study and let them find a home for it.”

It turns out that the pin comes from a 1949 anti-tuberculosis campaign to get chest X-rays for every adult in Boston. Twenty mobile X-ray units were loaned to the project by the US Public Health service. At the time, the death rate from TB in Boston was nearly twice that of the rest of the US.

Hearing and Vision

Many of the results from the Nurses' Health Study relate to cancer or cardiovascular disease. However, we have done some interesting work relating to issues that, in the past, were often not considered an area for epidemiological study: hearing and vision.

Hearing

Hearing loss is common, often disabling, and can adversely affect communication, quality of life, and health. Some evidence suggests that hearing loss may

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Greater adherence to healthy dietary patterns...was associated with a 30% lower risk of self-reported moderate or worse hearing loss.

be associated with faster cognitive decline among older adults. Two-thirds of women in their 60's and over 60 million adults nationwide suffer from hearing loss. Although commonly considered an unavoidable companion to aging, hearing loss may not be inevitable.”

The Conservation of Hearing Study (CHEARS) is an ongoing investigation of hearing in the Nurses' Health Studies to identify preventable contributors to hearing loss, such as diet and lifestyle factors that can be modified to reduce risk. Our recently published study among 71,000 NHSII women demonstrated that greater adherence to healthy dietary patterns, such as the Mediterranean diet or the DASH diet, was associated with a 30% lower risk of self-reported moderate or worse hearing loss. Using detailed information from the Hearing Study Supplemental Questionnaire that was completed by over 33,000 participants, we found an even greater reduction (37%) in risk among women who consumed a healthier diet. We also found eating more of certain foods, such as fish, and nutrients, such as beta-carotene, beta-cryptoxanthin and long chain omega-3 fatty acids, was associated with lower risk. Studies in CHEARS have revealed that maintaining a healthy weight and staying physically active may help lower the risk of hearing loss, while frequent use of analgesics, such as ibuprofen and acetaminophen,

and longer duration of use of postmenopausal hormone therapy were associated with a higher risk.

We have also been conducting the largest, most geographically diverse longitudinal study using audiometry to measure change in hearing. Over 3,700 NHSII women across the US completed baseline clinical hearing tests in the CHEARS Audiology Assessment Arm and 84% have completed 3 year follow-up testing. As most hearing loss is irreversible, we hope that evaluating hearing loss at earlier stages will identify ways to prevent hearing loss and delay its progression.

Vision

Vision is our most valued sense. Everyone wants to age with their senses fully intact, but few of us do. About 75% of us who live long enough will develop cataracts that have to be surgically removed, and about 15% will have their vision impaired by age-related macular degeneration (AMD). Although cataracts are treatable, there is no remedy for most types of AMD.

Problems with cataracts often start as eye lenses begin turning brown, resulting in far greater sensitivity to glare and making driving more difficult. Remembering the basic science that sugars that are oxidized or react with proteins turn brown, we asked if high carbohydrate intake might be associated with risk for AMD and cataract. We found indications that higher glycemic diets (think sugar, soda, rice and white bread) are associated with increased risk for AMD and cortical cataract, much the same as diets that increase risk for cardiovascular disease and diabetes. We calculated that by lowering dietary glycemia through changes in diet by only 8%, 100,000 people could be spared from AMD.

In experiments using animals, we found evidence that changing the diet from high to lower amounts of high glycemic foods may arrest or reverse the progress of AMD-like retinal damage at early stages. Together these findings are leading to new insights on the causes of these blinding diseases and potentially new approaches for the prevention, early detection, and treatment of these conditions.

Our Environment and Risk of Developing Breast Cancer

In the early 2010s, national agencies called on researchers to examine potential environmental risk factors for breast cancer. In response, we linked residential histories of study participants to maps of environmental exposures to assess breast cancer risk.

Air Pollutants

Various air pollutants that cause cancer or have other adverse health effects, including particulate matter (PM) and hazardous air pollutants (HAPs), are monitored by the Environmental Protection Agency. In the NHS, we previously showed that each increase of 10 micrograms of particulate matter smaller than 2.5 microns (PM_{2.5}) per cubic meter was associated with a 13% higher risk of death.

The good news is, among NHSII participants, higher ambient PM exposure and exposure to various HAPs during adulthood was not associated with elevated breast cancer risk. Because air pollution data were not available until the mid-1980s, we were not able to investigate air pollution exposure during childhood, which may be the more important time period. This merits further study, such as in the NHS3.

Outdoor Light at Night

We previously showed that rotating shift-work is associated with breast cancer risk. This may be driven by exposure to light at night, which can decrease melatonin secretion and disrupt circadian and sleep patterns. Although outdoor light at night is not a perfect measure of individual exposure to light at night, our findings suggest that this may modestly increase

breast cancer risk. Compared to areas with the lowest light at night, we observed 14% higher risk of breast cancer for women residing in areas with the highest levels of outdoor light at night. This finding is consistent with the only other prospective study to investigate this topic. Further work is required to confirm these results and clarify the potential mechanisms.

Radon

Radon is a naturally occurring radioactive gas found in soil, rocks, air, and water. The primary source of radon exposure is from the gas entering homes through cracks in foundations. In the NHSII, county-level estimates of radon were measured from state and nationally-representative surveys of household radon. We observed that county-level radon exposure was not associated with risk of estrogen-receptor positive (ER+) disease. In contrast, higher county-level radon was associated with a 38% higher risk of developing estrogen-receptor negative and progesterone-receptor negative (ER-/PR-) breast cancer, and a 52% higher risk of triple negative (ER-/PR-/HER2-) breast cancers after accounting for important breast cancer risk factors. Household radon levels vary within a county, thus future work on residential and workplace exposure to radon would provide more precise estimates of exposure and breast cancer risk.

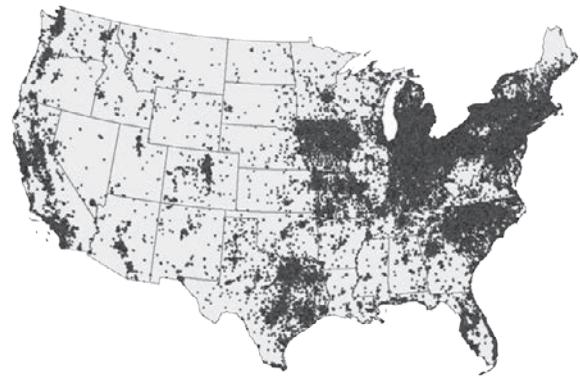


Diagram showing the location of participants in Nurses' Health Study II. Detailed mapping of the study members can be compared with data on air pollution, light exposure and radon.



Let's Be Social!

Want to stay in touch? Like our Facebook page at facebook.com/nhs3.org

We post news on the latest NHS results a couple times a month and feature updates on recruitment for Nurses' Health Study 3 and other topics of interest. Come join us online!

Study Updates

GROWING UP TODAY STUDY

guts

The Growing Up Today Study (GUTS) has been following offspring of Nurses' Health Study II participants since 1996. Today over 27,000 GUTS participants in their twenties and thirties are helping us study young adult health. We will be launching a new GUTS questionnaire online this fall, and we hope to hear from as many GUTS participants as possible! We will be sending email invitations once the questionnaire has launched.

Long-term research of this kind is only possible thanks to the generous commitment of both GUTS and NHSII participants. If your kid(s) are in GUTS, we ask that you remind them that their continued participation is always important to this exceptional research. Even if it has been a few years since your son or daughter last participated, we'd love to hear from them in 2018! Participants will be able to complete the online GUTS Questionnaire at gutsweb.org. For assistance or to provide updated contact information, please email us at guts@channing.harvard.edu.

NURSES' HEALTH STUDY 3

Nurses' Health Study 3

Recruitment of reproductive aged male and female nurses into the Nurses' Health Study 3 is still ongoing. As of June 2018, more than 45,746 women and 648 men have joined the study. Unlike Nurses' Health Studies I&II, NHS3 participants tend to be younger at enrollment- the average age is 33 years (range 17-52 years) and most are premenopausal (88%). We also have a slightly higher recruitment of minority races (15%). Much of our ongoing research in NHS3 is focused on reproductive health. To date we have had over 7,000 pregnancies reported during follow-up (with an average of 1,000 new pregnancies reported per year). For most pregnancies, we have collected information on exposures experienced pre-conception as well as during the second trimester of pregnancy, including a full diet assessment. In addition to pregnancy outcomes, with follow-up for 5+ years, we have also started to accrue cases of hypertension, asthma, high cholesterol, and benign breast disease which will pave the way for future research focused on chronic disease risk. We have also recently started a mobile-health sub-cohort where we will be passively collecting data from wrist worn devices, which can be used to assess physical activity, sleep, and detailed location information. Please help spread to the word! For more info or to join, male or female nurses born after January 1, 1965 can visit www.nhs3.org

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Collecting your samples is surprisingly easy and hygienic. You will be able to provide a sample at a time convenient for you. The kit will contain a "collector" to place on your toilet seat and 4 tubes for sample collection. Samples from the first two tubes will be used to measure the relative distribution of over 150 microbial species. The third is a special tube that will preserve the microbes in an anaerobic environment for future studies. Finally, samples collected in an oral swab tube will be used to assess the distribution of microbes in your mouth.

We are incredibly excited about this new collection in the Nurses' Health Study II. To get ready, we have acquired a robotic liquid handler for transferring samples into freezer-ready tubes and also a state-of-the-art robotic freezer that can store over 3 million samples at -80° C.

This project will set the stage for novel ground-breaking work, which will be the first ever of this size. Your contributions will greatly enhance our understanding of gut health and overall health for decades to come.

A Family Affair: Friends of the Nurses' Health Study

Every day, the Nurses' Health Study is discovering new ways to tackle many of the world's greatest challenges in women's health. Now, we are facing a new challenge when it comes to funding.

Our research relies on federal funding from the National Institutes of Health (NIH). Over the past several years, NIH funding for our work has been significantly reduced, making the future of our research less certain. This lack of stability means we must now focus on simply keeping the core of the studies moving forward. With additional funds, we could continue our research into how people can maintain their memory into old age; do more work learning how lifestyle and the environment interact with our genes to affect the risk of developing cancer, heart disease, and diabetes; and unravel more of the mysteries of ALS and Parkinson's disease.

Many participants and their families have asked how they might support the Nurses' Health Studies beyond the wonderful and generous donation that all participants make of their time and energy. In these uncertain times, we are deeply grateful for the expressions of support and donations made to the Friends of the Nurses' Health Study Fund. Your dedication allows us to continue finding answers to today's most pressing health questions.

Make a Tax-Deductible Donation Today:

To make a gift online: Visit nurseshealthstudy.org/donations

To donate by mail: Make your check payable to Friends of the Nurses' Health Study and mail to:

Nurses' Health Study
Channing Division of Network Medicine
181 Longwood Avenue, Room 350
Boston, MA 02115-5804

If you need assistance or would like to speak to someone about different options to financially support our work, please contact Danielle Hernon at 617-424-4334 or dhernon@bwh.harvard.edu

There are many ways that you can support the Nurses' Health Study:

- Donate cash or appreciated securities
- Make an IRA charitable rollover gift from a qualified retirement plan
- Name the Nurses' Health Study as a beneficiary of your will, trust, retirement plan, or life insurance policy
- Create a gift that provides you and/or a loved one with lifetime income

Thank you. Your support truly makes a difference.

Staying in touch

To report name or address changes, please visit www.nurseshealthstudy.org.

Letters and feedback are welcome!



CHANNING DIVISION OF NETWORK MEDICINE

181 Longwood Avenue

Boston, MA 02115

tel: 617-525-2279 **fax:** 617-525-2008

email: nhs@channing.harvard.edu