



DESIRE A HEALTHY HEART?



Cardiovascular disease (CVD) remains the leading cause of death among all Americans, despite an overall decline in mortality in recent years. Several conditions fall under the umbrella of CVD, including heart attacks and stroke. Prevention is key—these conditions may be largely avoided with a healthy diet and lifestyle.

We have developed a freely available online calculator, called the Healthy Heart Score (www.healthyheartscore.com), that estimates long-term risk of developing CVD based on lifestyle habits. By answering the questions posed in the calculator, individuals can learn how their lifestyle habits affect their risk of heart attack and stroke and determine which lifestyle habits to maintain and which to improve.

BASED ON ORIGINAL RESEARCH

We developed the Healthy Heart Score using the best available evidence from all sources; a large part of this from the Health Professionals Follow-Up Study (HPFS) and the Nurses' Health Study (NHS). We tracked the development of CVD among healthy participants over a 24-year period, including 61,025 women (3775 developed CVD) and 34,478 men (3506 developed CVD).

Many factors may contribute to an individual's risk of CVD by either increasing or decreasing risk. We chose the nine most critical diet and lifestyle factors that best predict CVD development over the next 20 years:

- Smoking
- Weight
- Exercise
- Alcohol
- Fruits and vegetables
- Whole grains
- Nuts
- Sugary beverages
- Red and processed meat

The HPFS and NHS, with their large sample sizes and decades of data on diet and lifestyle, proved to be ideal populations to work with in developing this prediction model.



DEAR COLLEAGUES,
As we inch toward next year's 30th anniversary of the Health Professionals Follow-Up Study,

our study remains the largest detailed long-term study of men's health. Thank you for your tireless support over the years!

In this year's newsletter, our feature article highlights the creation of the Healthy Heart Score, our freely available online calculator. This calculator walks users through a series of questions to estimate individual risk of cardiovascular disease using variables that we can modify ourselves. The Healthy Heart Score uses data you have provided throughout the years.

We also dispel confusion about saturated fat, share complex research about genetic risk scores, and highlight the benefits of nut consumption.

Many thanks for your continued participation in our studies. We look forward to many more new and exciting discoveries to share with you!

Best regards,

Walter C. Willett, MD, DrPH
Principal Investigator,
Health Professionals Follow-Up Study

IN BRIEF

GENETIC RISK SCORES: UNDERSTANDING COMPLEX DISEASES

Over the past decade, genetic studies have identified many differences in DNA that may affect disease risk. One of these differences is known technically as a single nucleotide polymorphism, or “SNP.” Individual SNPs tend to be only very modestly associated with diseases. Because many individual genes work together to contribute to complex diseases, scientists are interested in examining SNPs in combination. For that reason, we have started to combine individual SNPs into genetic risk scores. These risk scores sum the number of mutations in relevant genes and give a fuller picture of the total genetic contribution to disease.

Indeed, studies that include genetic risk scores are useful for studying a variety of complex diseases, such as asthma, coronary heart disease, bladder cancer, and type 2 diabetes. For example, risk scores have been more strongly associated with type 2 diabetes than each individual SNP alone.

Genetic risk scores may be more broadly important too. For example, in the NHS and HPFS we found that a higher type 2 diabetes genetic risk score also is linked to higher cardiovascular disease risk. This result suggests that genetic risk scores could be helpful in discovering common genetic connections between different diseases that have been overlooked. Eventually, this may lead to new means of prevention or cure.

Genetic risk scores hold promise for future clinical practice, even though the improvement in risk assessment has been small so far, because they may help clinicians to better assess a patient’s risk of certain diseases. Ultimately, exploring genetic risk scores in complex diseases may advance basic and clinical research. (Qi Q et al. *Diabetes Care*. 2013;36(3):737-9)

NUTS FOR HEALTH

Nuts used to be considered bad for you because they are high in fats. Yet people who eat nuts on a daily basis may live longer than those who do not. In a recent study in the NHS and HPFS, we found that one daily serving of nuts was associated with a 20 percent lower mortality rate.



The benefit was also observed for most major causes of death. People who ate nuts five or more times a week had a 29 percent reduction in deaths from heart disease, and an 11 percent reduction in deaths from cancer. Our findings are consistent with a wealth of existing data to support health benefits of nuts on many chronic diseases.

We now appreciate that the specific fat types (unsaturated fats) and other nutrients in nuts (such as fiber, vitamins, minerals, and phytosterols) are beneficial. These benefits confer cardioprotective, anticarcinogenic, anti-inflammatory, and antioxidant properties.

Interestingly, in a subsequent study of women in the NHS II and their children in the Growing Up Today Study (GUTS), we found that increased nut consumption by pregnant mothers (who weren’t themselves nut-allergic) was associated with lower risk of nut allergy in their children. This finding may help to alleviate the widespread worry that eating nuts during pregnancy will cause the child to develop a nut allergy. (Bao et al. *N Engl J Med*. 2013;369:2001-11. Frazier et al. *JAMA Pediatr*. 2014;168(2):156-162)

BUTTER IS NOT BACK

The role of fats in our diet—particularly saturated fats—has stirred up controversial headlines lately.

While the media message has been confusing, our research results on fats and how they affect risk of coronary heart disease (CHD) are clear and consistent. Replacing saturated fat (found in butter, red meat) with polyunsaturated fat (found in nuts, vegetable oils) is associated with a lower risk of CHD.

In a recent meta-analysis, we reviewed 13 cohort studies that included more than 310,000 participants. We found that individuals who traded 5 percent of the calories they consumed from saturated fat sources for sources

of linoleic acid, a main type of polyunsaturated fat, lowered their risk of CHD by 9 percent. This same group lowered their risk of death from CHD by 13 percent.

One of the reasons this swap from saturated fat to polyunsaturated fat lowers CHD risk has to do with blood cholesterol. Polyunsaturated fats decrease “bad” LDL cholesterol. An increase in “bad” LDL cholesterol may hasten plaque buildup in arterial walls, resulting in CHD. (To estimate your risk of CHD and other cardiovascular diseases, please see our new online risk calculator at www.healthyheartscore.com.)

Since all fats are not created equal, it makes a difference which type is consumed. To achieve a lower risk

of CHD, the “swap” component is crucial—such as replacing butter or lard with vegetable oils, such as soybean oil, olive oil, canola oil, and corn oil.

For more information on the role of saturated fats, please read “Is Butter Really Back?” at www.hsph.harvard.edu/magazine-features/is-butter-really-back. Another helpful resource is The Nutrition Source at www.hsph.harvard.edu/nutritionsource. (Chowdhury et al. *Ann Intern Med*. 2014;160:398-406)



YOUR PRIVACY

Large studies will be the key to the success of these efforts to understand the role of genes. This highlights the importance of collaboration and careful data sharing with appropriate safeguards on participant confidentiality. Indeed, the National Institutes of Health (NIH) has mandated that data from studies of DNA and disease risk be deposited in a controlled-access database. Any data sent to this database will not contain any personal identifiers (e.g., your name, date of birth, address, zip code, or any trait information that could identify you).

Our participation in this NIH database will contribute to the large international effort to identify the genetic variants underlying the inherited predisposition to cancer, heart disease, diabetes, and other diseases. The goal is to develop more effective prevention and treatment strategies. However, we recognize that DNA sequence data are potentially sensitive. If you have any questions about these studies (called GWAS or sequencing studies), or you wish to withdraw from them in the future, please send an email to hpfs@hsph.harvard.edu or write to us at HPFS, 677 Huntington Avenue, Boston, MA 02115.

RESEARCH UPDATES

COFFEE CONSUMPTION AND DIABETES

Previous studies have found that higher coffee intake is associated with a lower risk for type 2 diabetes, but no studies have examined how changes in coffee consumption habits influence subsequent risk of diabetes.

Using data from the NHS I, NHS II, and HPFS, we found that participants who increased their coffee consumption by more than one cup per day over a four-year period had an 11 percent lower risk of type 2 diabetes in the subsequent four years compared to those who made no changes in consumption. Those who lowered their daily coffee consumption by more than one cup had a 17 percent higher risk for diabetes. Changes in decaffeinated coffee consumption and caffeinated tea consumption were not associated with changes in risk for type 2 diabetes, possibly because of the low amounts of consumption. (Bhupathiraju et al. *Diabetologia*. 2014 Jul;57(7):1346-54)

EATING HABITS AND CORONARY HEART DISEASE

It is commonly stated that breakfast is the most important meal of the day, though up until now there have been no evidence-based recommendations for adults regarding eating habits. Thus, we recently conducted the first large prospective study of eating habits (the timing and frequency of snacks, meals, and caloric beverages) and risk of coronary heart disease (CHD).

We used data from 26,902 HPFS participants and adjusted for demographic, diet and lifestyle factors. Participants who skipped breakfast had a 27 percent higher risk of CHD as compared to participants who ate in the morning. Participants who reported eating late at night (defined as “eating after going to bed”) had a 55 percent higher risk of CHD compared to those who did not. These associations between eating habits and CHD were influenced in part by body mass index (BMI), hypertension, hypercholesterolemia, and diabetes. Our results support previous short-term intervention studies that have documented cardio-metabolic disturbances with different eating habits. (Cahill et al. *Circulation*. 2013;128(4):337-343)

YOGURT AND PREVENTION OF TYPE 2 DIABETES

Type 2 diabetes affects approximately 26 million Americans, and more than 500 million people worldwide. Diabetes, along with its complications such as cardiovascular disease, is difficult to manage and treat. Since prevention is key, we decided to study the relationship between different types of dairy and the risk of developing type 2 diabetes among men and women in the HPFS and NHS. We found no association between total dairy consumption (high fat and low fat alike) and risk of diabetes, but the results differed when we looked at yogurt in particular. We found that a daily serving of yogurt was associated with an 18 percent lower risk of diabetes, after taking into account of other dietary and lifestyle factors.

While the exact mechanisms behind this study are yet to be understood, we speculate that the presence of probiotics in yogurt may help improve insulin sensitivity and reduce inflammation. Of course, this hypothesis will need to be tested in clinical trials. From public health recommendations, yogurt can be included as a part of healthy diet, although weight control continues to be the most important way to prevent diabetes. (Chen et al. *BMC Med*. 2014; 12(1): 215)

COLONOSCOPY SCREENING AND CANCER PREVENTION

Accumulating evidence demonstrates that colonoscopy and sigmoidoscopy can reduce colorectal cancer incidence and mortality. However, there is uncertainty about the effectiveness of each procedure in the prevention of colon cancer in the proximal, or first and middle, part of the colon. Unlike colonoscopies, sigmoidoscopies typically don't involve the entire colon, but only the area near the end, the sigmoid region and rectum.

Our study, including data from the HPFS, found that colonoscopy is effective against cancers found throughout the colon, while sigmoidoscopy alone is insufficient for preventing proximal cancer. Additionally, our finding

supports existing guidelines that recommend people with average risk of colorectal cancer have a colonoscopy every 10 years. We estimated that if all participants in the study had a colonoscopy, 40 percent of colorectal cancer cases would have been prevented. (Nishihara et al. *N Engl J Med.* 2013 Sep 19;369(12):1095-105)

"OBESITY PARADOX" REFUTED

Previous studies of body weight and mortality among patients with type 2 diabetes have reported conflicting findings, with some suggesting a survival advantage for those who were overweight or obese at the time of their diabetes diagnosis. A recent analysis among the NHS and the HPFS indicated that there was no such advantage to being overweight or obese.

We analyzed data from over 11,000 women and men who had type 2 diabetes. The "normal weight" group (body mass index, or BMI, 18-25 kg/m²) includes lean and healthy participants, as well as smokers and patients with existing or undiagnosed illnesses (both of which can lead to weight loss). This can make the group including "normal" weight individuals appear worse off than overweight or obese individuals in terms of survival. However, after accounting for smoking and underlying health in our study, it was clear that having a body weight within the normal range at time of diabetes diagnosis was associated with the best survival.

We concluded that having a healthy weight not only predicts better survival from diabetes but also lowers the risk of developing diabetes in the first place. (Tobias et al. *N Engl J Med.* 2014;370(3):233-44)

KIDNEY STONES AND HEART DISEASE

Kidney stones are on the rise among men and women. In the U.S., nearly 9 percent of individuals have had a kidney stone, and men are more than twice as likely as women to get one. Kidney stones can cause severe pain while passing, but have not traditionally been seen as a critical risk to long-term health.

Using data from the NHS and HPFS, we found that women with a history of kidney stones were about 30 percent more likely to develop heart disease, have a heart attack, or undergo a procedure to open blocked heart arteries. No increased risk was seen among men with a history of kidney stones.

The underlying cause of this increased risk is still unclear. Even though we took into account known shared risk factors including dietary intake, obesity, hypertension, and diabetes, there may exist a shared predisposition to the increased risk. This study does suggest that a kidney stone may be a marker for future risk of heart disease, though more research is needed. (Ferraro et al. *JAMA.* 2013;310(4):408-15)

ADOLESCENT MILK CONSUMPTION AND HIP FRACTURE

For years, drinking milk during childhood and adolescence has been recommended to maximize bone mass and thus offset the expected bone loss at older ages that can eventually result in osteoporosis. But does higher milk consumption in early life lead to lower risk of osteoporotic hip fractures?

In postmenopausal women in the NHS and in older men in the HPFS, we found that risk of hip fracture was not lower in those who drank milk four or more times per day during their teenage years compared with those who rarely drank milk. In fact, in men, hip fracture risk was higher in the teenage milk drinkers, increasing by 9 percent for each additional glass of milk per day.

One explanation for these findings is that milk consumption at young ages promotes greater height; each additional inch of attained height was associated with a 12 percent higher risk of hip fracture. (Feskanich et al. *JAMA Pediatr.* 2014;168(1):54-60)



HOW TO USE THE CALCULATOR

The Healthy Heart Score is a brief and simple online quiz, and takes just a few minutes to complete. Once finished, users receive a quick snapshot of their overall CVD risk [low (green), moderate (yellow), or high (red)] along with information on individual lifestyle habits that need focused preventive action (yellow and red) and practical tips for maintaining or improving lifestyle factors. The quiz is user-friendly and easy to follow.

At the end, individuals receive a printable, personalized assessment with heart healthy recommendations based on the answers provided, complete with tips on how to achieve the recommended goals. Helpful resources are linked throughout the quiz for more detailed information.

TARGET AUDIENCE

Anyone can use the online calculator, though the results may be especially useful to men and women who are 40 years or older and who are free of hypertension or high cholesterol—known risk factors for developing CVD.

Clinical practice already focuses on primary prevention, which targets the prevention of cardiovascular events through treatment of clinical risk factors, such as hypertension and high cholesterol. However, many adults

who develop CVD are not at high risk by conventional standards. The Healthy Heart Score hopes to pinpoint this group of otherwise healthy individuals by addressing lifestyle habits before these risk factors develop.

APPLICATIONS FOR USE

The Heart Healthy Score may serve as an important public health screening tool. As a free online calculator, it can reach a broad audience and have a major impact for prevention of CVD.

The Heart Healthy Score can be used in conjunction with the primary prevention strategies already in place in clinical practice, since each targets a different group. In this way, we hope to further minimize CVD risk, especially in the long term. (Chiuve et al. *J Am Heart Assoc.* 2014;3:e000954, originally published November 14, 2014)



BY THE NUMBERS

How many of the original health professionals are still participating in the study?



Still in contact with **28,915**

30,707 are alive today

51,529 health professionals in original cohort from 1986

FOCUS ON THE

RESEARCH TEAM



Dr. Eric Rimm and Dr. Stephanie Chiuve

When it comes to matters of the heart, Dr. Stephanie Chiuve knows her stuff—she helped develop the Healthy Heart Score, a web-based cardiovascular health calculator (see “Desire a Healthy Heart?,” page 1). She and other researchers are hoping to raise awareness about heart-healthy diets and lifestyle choices through this interactive online quiz, which is based on research from the HPFS and NHS.

Chiuve is a research associate at the Department of Nutrition at Harvard T.H.

Chan School of Public Health and an assistant professor of medicine at Harvard Medical School and Brigham and Women’s Hospital. Nutrition has long held her interest, from her childhood days as a competitive figure skater and then in college when she studied the role of diet on chronic disease. Through her first post-college job doing lab work she met Dr. Eric Rimm and other faculty members, and went on to complete her doctoral degree at the Harvard Chan School.

Outside of work, Chiuve enjoys spending time with her husband, two young children, and dog. She is an avid cook and loves to discover and prepare new heart-healthy recipes for her family. She is also a devoted Boston sports fan—go Red Sox!

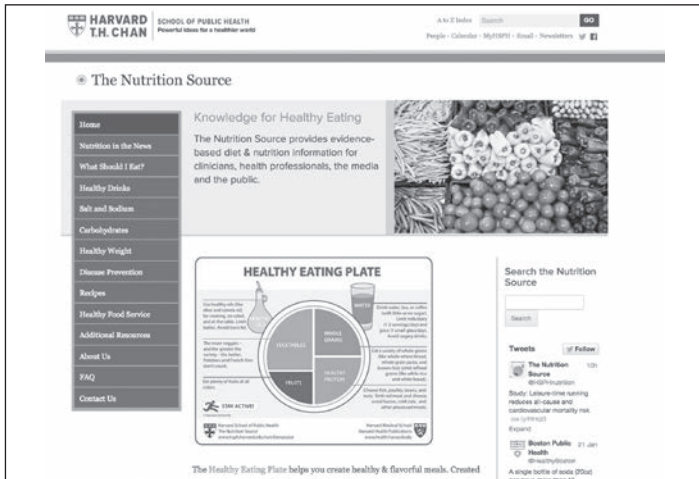
WEB SUBMISSIONS

To date, over 7200 participants have completed the 2014 HPFS questionnaire online. This is a 50 percent response rate from participants who have given us valid email addresses. As you can imagine, reducing the number of paper forms we receive, scan, and store helps in many ways: It reduces costs, streamlines form processing, and minimizes environmental impact.

Many participants who have replied online say they prefer this method of filling out the questionnaire. One participant wrote, “This is a more convenient way to respond to the follow-up questionnaire.” Another wrote, “Filling in all of these circles via computer is a joy and a pleasure! Thank you for all of the hard work you put into this study.”

Of course, whether you prefer to answer by web or paper, we value every completed survey and we will try to make your participation as convenient as possible.

INTERESTED IN NUTRITION UPDATES?



Much of what we now understand about diet and health comes from the Health Professionals Follow-Up Study, and we make a point of communicating through this newsletter the most important findings as they emerge. However, if you are interested in additional information on nutrition and health, we invite you to visit the website maintained by the Department of Nutrition at Harvard T.H. Chan School of Public Health called The Nutrition Source: www.hsph.harvard.edu/nutritionsource.

In addition to research from the HPFS, this site includes findings from other studies around the world, including our cohorts of women, the Nurses' Health Studies. The website also contains reviews on controversial topics in nutrition and helpful articles on how to put newfound knowledge into practice, such as replacing saturated fats and refined grains with polyunsaturated fats and whole grains. We also provide healthful recipes for foods served in our food service at Harvard, including those developed by the famous cookbook writer, Mollie Katzen.

In reading this website, please note that much of the information would not be available without your many contributions as a member of the Health Professionals Follow-Up Study.

Health Professionals Follow-Up Study

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To report name or address changes, please email the project coordinator at hpfs@hsph.harvard.edu or visit www.hsph.harvard.edu/hpfs. Letters and feedback are welcome.

Donations and bequests to the Friends of the Health Professionals Follow-Up Study Fund help to sustain our continued work.

Donations may be sent to the Harvard T.H. Chan School of Public Health. For information on how to give or to make a secure gift online, please visit www.hsph.harvard.edu/give and indicate that the gift is in support of the Friends of the Health Professionals Follow-Up Study Fund.