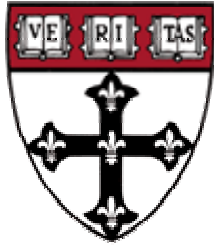


Winter 2005



# HPFS Newsletter

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## RESEARCH HIGHLIGHTS

### Special points of interest:

- Exercise and prostate cancer
- Alcohol and cardiovascular disease
- Drinking coffee and type 2 diabetes
- Measuring genetic markers
- Protecting your privacy

### Prostate Cancer

We are continuing our studies on prostate cancer on several fronts. The data you have provided continue to be a fruitful source of important findings. Sexual activity has been hypothesized to play a role in the development of prostate cancer, but there had been essentially no prospective study of this topic. We recently reported that high ejaculation frequency was associated with modestly lower risk of total prostate cancer. Compared with men reporting four to seven ejaculations per month at ages 40 to 49 years, men reporting 21 or more ejaculations per month had a 32% lower risk of prostate cancer. (JAMA. 2004; 291:1578-86).

We confirmed a previous finding that fish consumption may decrease risk of prostate cancer by now showing a similar protective association with omega-3 fatty acids from fatty fish such as salmon (Am J Clin Nutr.

2004 Jul;80(1):204-16). In contrast, we confirmed a previous surprising finding that men who consumed more alpha-linolenic acid, the major omega-3 fatty acid from terrestrial sources, experienced higher risk of prostate cancer. However, this finding has not been seen in some other studies. Important sources of this fatty acid are fatty meats and dairy products, and some oils such as canola oil. Because alpha-linolenic acid, similar to marine omega-3s, has benefits for cardiovascular disease, we must continue our study to further define the best dietary sources and the optimal intake of omega-3s for overall health.

We also found that eating cruciferous vegetables (broccoli, cabbage, brussel sprouts) frequently, about three to five servings per week, may reduce prostate cancer risk by 20 to 30% (Cancer Epidemiol Biomarkers Prev. 2003;12:1403-9). We also found that men who take supplemental zinc at

high doses, such as 100 mg/day for ten or more years, have two to three fold higher risk of aggressive prostate cancer (J Natl Cancer Inst. 2003;95:1004-7). Note that this level is much higher than the recommended intake for this mineral.

We showed that physical activity may lead to less aggressive prostate cancer and reduced mortality from the disease (Archives of Internal Medicine, in press). Although for many conditions even moderate amounts of activity confer some benefits, to achieve a benefit for prostate cancer, relatively vigorous exercise (for example, jogging rather than walking) for at least three to four hours per week appears to be necessary. While this may be difficult to achieve for all men, the payoff for prostate cancer and many other conditions may be important.

We have expanded our research by examining biomarkers from the blood samples that many of you have provided. We previously reported that high (Continued on pg. 2)...

### Inside this issue:

Research Findings	1-4
Study Updates	5
Your Privacy	5
Focus	6
Frequently Asked Questions	6

# HPFS Newsletter

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## RESEARCH HIGHLIGHTS (Continued from pg 1)

### Prostate Cancer (cont.)

intake of tomato products was associated with a lower risk of prostate cancer. We now examined blood levels of lycopene, a carotenoid found mostly in tomatoes such as in tomato sauce, and confirmed that men with higher levels of blood lycopene had a reduced risk of prostate cancer. (Cancer Epidemiol Biomarkers Prev. 2004; 13:260-9). We believe this finding further con-

firms a role for tomato products, but caution against consuming lycopene supplements that have now become available. We believe that the overall evidence is stronger in suggesting a role of tomatoes, which have many other compounds besides lycopene, than for pure lycopene.

We are also encouraged by the preliminary finding that men with prostate cancer who consumed higher amounts of to-

mato sauce and fatty fish, about two or more servings per week of each, appeared to have a reduced rate of progression of the disease, though these findings need to be confirmed. This is the first finding from this new component of the HPFS in which we are following men with prostate cancer for recurrences and progression. Over time, we believe that this study will provide critical new data.

### Colorectal Cancer

We continue to study the causes of cancers of the colon and rectum. One of our long-standing interests has been the hypothesis that high alcohol intake increases risk of colorectal cancer by acting against folate, a protective micronutrient. We recently have provided evidence for this hypothesis using a genetic approach. Specifically, we showed genetic variation in how individuals metabolize alcohol and folate influences their chances of developing colorectal cancer (Cancer Epidemiol Biomarkers Prev. 2003;12:970-9). In particular, some men who breakdown alcohol slowly and who metabolize folate in a certain way are at increased risk of colorectal cancer if they drink two or more alcoholic beverages per day and have

low folate intake. However, we do not believe that it is necessary for men to know their genetic makeup because regardless of this, their risk is minimized if they consume enough folate. The important question remaining is how much folate intake is needed for optimal health? The situation for folate has changed because beginning in 1998, grain products in the U.S. have been fortified with folate, so it is possible that we are all getting enough folate. For example, we do not know if getting additional folate from multivitamins and fortified breakfast cereals would provide additional benefits. For this and many other reasons, continued follow-up of the HPFS is critical to provide answers to such important practical questions.

Although for practical rea-

sons, we often study single nutrients and food items in relation to a disease, we know intuitively that diet is complex and many components work together or may act against each other. We have used new statistical approaches to better examine a whole dietary pattern. For colon cancer, these new approaches show that a dietary pattern characterized by higher intakes of red and processed meats, sweets and desserts, french fries, and refined grains is associated with an increased risk of colon cancer (Cancer Causes and Control, in press). The composite actions of these items may have a deleterious role on colon cancer, as well as other diseases such as coronary disease and diabetes, more than we would observe just by studying a single component.

### Cardiovascular Disease

Our research on coronary heart disease was one of the main reasons for initiating the Health Professionals Follow-up Study in 1986. During the

last few years, several interesting new findings have gained national attention. During the first twelve years of the study, we confirmed over 1,400 new cases of nonfatal myocardial infarction or fatal

coronary disease among men who were free of chronic disease at baseline. To expand on our initial study of average alcohol consumption and coronary heart disease published in 1991, we

## RESEARCH HIGHLIGHTS (Continued from pg 2)

### **Cardiovascular Disease (cont.)**

explored the role of drinking patterns. We found that men who consumed one to two drinks per day had about a 25% lower risk of developing heart disease than those who abstained. Interestingly, we found that drinking pattern was equally important. Our results suggest that light to moderate amounts of alcohol on most days per week is more beneficial to overall heart health compared to heavier consumption limited to a few days per week. The type of alcohol consumed (red wine, white wine, beer, or spirits) or the consumption of alcohol with meals was not associated with further benefit. We also found that men who drank lightly at the beginning of the study and who subsequently increased their consumption to moderate amounts had a lower risk of coronary disease compared to those who stayed light drinkers or those

who drank substantially more over the course of the study (N Engl J Med 2003;348:109-118). Our data do not suggest that all men who abstain or who are light drinkers should drink more alcohol. Obviously, the decision to drink alcohol or drink more alcohol is an individual decision and may depend on an individual's preference, religion, health status, or many other factors. If you do decide to make a substantial change in your alcohol consumption patterns, we urge you to discuss this with your personal physician.

In a second paper on coronary heart disease, we detailed the association between whole grain intake and risk of coronary disease. We created a new food database with detailed data on grams of whole grain for most foods from the U.S. food supply. We found that men who ate the greatest amount of

whole grains had an approximately 20% lower risk of heart disease compared to those who ate substantially less. We found that much of this benefit could be attributed to the bran content of the whole grain. When we looked specifically at intake of added bran, we found that men who added bran to their diet (at least 17 grams per day) had a 30% lower risk of coronary disease compared to men who had no added bran. This exciting new data suggests that, in addition to the fiber content, other components of bran such as phytochemicals, vitamins, or other naturally occurring compounds may be independently beneficial in lowering risk of coronary heart disease (Am J Clin Nutr, 2004;80(6):1492-1499). We hope to continue similar analyses on other chronic diseases now that we have created this new database on whole grain.

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### **Diabetes**

We recently found that participants who regularly drank coffee had significantly lower risk of type 2 diabetes, compared to non-coffee drinking participants.

Men who drank more than six cups of caffeinated coffee per day reduced their risk for type 2 diabetes by more than 50% compared to men in the study who didn't drink coffee. These effects were not accounted for by lifestyle factors such as smoking, exercise, or obesity. Decaffeinated coffee also appeared beneficial, but its

effects were weaker than regular coffee. The researchers note that caffeine, the best known ingredient in regular coffee, is known to raise blood sugar and increase energy expenditure in the short-term, but its long-term effects are not well understood.

Coffee (both regular and decaffeinated) has lots of antioxidants like chlorogenic acid (one of the compounds responsible for the coffee flavor) and magnesium. These ingredients can actually improve sensitivity to insulin and may contribute to

lowering the risk of type 2 diabetes. Although this is good news for coffee drinkers, it is still not clear why coffee is beneficial for diabetes and more research is needed.

*(Continued on pg. 4)...*

## RESEARCH HIGHLIGHTS (Continued from pg 3)

### Parkinson's Disease

More than one million people in North America have Parkinson's disease and the disease risk increases substantially after age sixty. We began investigating this disease approximately ten years ago with the hope to provide insights into healthy aging. We had previously reported that coffee consumption was associated with a lower risk of Parkinson's disease (*Ann. Neurol.* 2001; 50: 56-63) and that higher intake of dairy products was associated with a higher risk (*Ann Neurol.* 2002; 52: 793-801), although the dairy finding still needs to be confirmed in other studies. Intakes of dietary anti-

oxidants, fat, and folate or alcohol consumption were not related to the risk (*Neurology* 2002; 59: 1161-1169; *Am J Epidemiol* 2003; 157: 1007-1014; *Am J Epidemiol* 2004; 160: 368-375; *Ann Neurol* 2003; 54: 170-175).

Recently, we found that regular users of nonsteroidal anti-inflammatory drugs (NSAIDs) other than aspirin had approximately 45% lower risk of Parkinson's disease than nonusers (*Arch Neurol.* 2003; 60: 1059-64). This publication has helped to stimulate much research interest in the possible neuroprotective effects of those commonly used medications. We also found that men who were often involved in vigorous physical activities (such as running, jogging, biking, etc.) had a

substantially lower risk of Parkinson's disease compared with men who rarely exercised (*Neurology*, In press). Overall obesity was not related to Parkinson's disease, however, abdominal obesity that is often found in men was associated with a higher risk of Parkinson's disease among never smokers (*Am J Epidemiol*; 2004; 159: 547-55).



### Dental Research

The safety of amalgam restorations has been a controversial topic. A supplemental questionnaire was sent out to a random sample of 579 HPFS participants who provided toenail samples in 1987 to collect information on amalgam restorations and handling methods. In addition to amalgam restorations, our study (*Journal of Public Health Dentistry* 2003; 63(1): 52-60) also assessed factors associated with mercury levels among dentists, such as practice characteristics and mercury handling methods.

General dentists were found to have more than twice the level of mercury in toenails than non dental health profes-

sionals and 60% higher than dental specialists. No association was found between the mercury levels and the number of amalgam restorations placed or removed (per week) by general dentists. We also examined the amalgam handling practices among the general dentists: 21 % of the general dentists in the study reported using high-speed hand piece without water spray, but there was no evidence that dry cutting of amalgam was associated with high mercury levels. The combined use of disposable capsules and water storage of scrap amalgam appeared to reduce the risk of elevated mercury levels (odds ratio of 0.18 vs. combination of reusable capsules and non-water storage as a reference). In addition to

dental practices methods, we also explored other predictors of mercury. The consumption of tuna and saltwater fish was positively associated with toenail mercury levels regardless of professional status. However, our findings showed no relationship between the number of dental amalgams and toenail mercury levels. This suggests that although professional exposure may lead to higher mercury levels among dentists, the removal of amalgam fillings cannot be justified by the potential toxicity of mercury in dental amalgams.

## STUDY UPDATES

### Cheek Cell Collection

Many of you have provided cheek cell samples in the past. However, recent methods for DNA analysis have become much more efficient and simple;

*“This sample will allow us to study how differences in genes influence the risk of cancer...”*

genetic markers can now be measured by the simple procedure of processing a saliva sample. This sample will allow us to study how differences in genes influence the risk of cancer, cardiovascular disease and other diseases. We are therefore requesting saliva samples from all participants who did not provide a blood sample. The procedure is very simple; you need only to

rinse your mouth with a commercial mouthwash and then return to us a small cup filled with the mouthwash (all materials will be provided).

### Tissue Block Collection

Understanding the etiology and progression of cancer has been one of the main goals of the Health Professionals Follow-Up Study. To achieve this goal, we have been collecting and studying samples of cancerous tissue. These paraffin-embedded samples (called tissue blocks) contain molecular information. By combining this molecular information with the data provided on the questionnaire (including diet, lifestyle and medical history), we hope to gain further insights into how cancer develops and how it might be prevented.

The tissue block collection began in 1996 for colon pol-

yps, colon and prostate cancer. We have since expanded to pancreatic and bladder cancer. To date, we have received over 2067 specimens. We are very grateful to the many participants who have allowed us access to their specimens.

Because of confidentiality concerns with biological specimens, we are very careful and diligent with all samples and information you provide. We know that you have placed a great deal of trust in us by providing us samples with DNA, and we take this very seriously, and we will not violate this trust in any way. We take every possible measure to ensure that individual results from genetic studies are never released. For more information on our privacy measures, please see below.

## YOUR PRIVACY

As a HPFS participant, you provide us with very personal information through your questionnaires, medical records and biological samples. We are grateful for your contributions and for the trust you have shown us in providing this information.

We want to assure you that we protect your information in every possible way and hold ourselves to the highest standards in safekeeping and use of your data. For example, we only allow authorized personnel to access your personal informa-

tion, and we also code all of our genetic results so that they are never stored together with individual identifying information.

We also have a Certificate of Confidentiality from the Department of Health and Human Services, which means that under current laws we cannot be forced to disclose information that may identify you in any legal proceedings. Once again, we are continually grateful for your trust and contributions. Your trust is essential to the success of the study and we would never want

to do anything that would risk losing your trust in us. Thank you for your continued commitment.



# HPFS Newsletter

## FOCUS

With each newsletter, we like to introduce you to some of the researchers and staff members. This year we would like to introduce you to Betsy Frost-Hawes, Project Coordinator. She earned a Bachelor of Arts in International Relations from the University of Maine, Orono. Betsy has been with the Health Professionals Follow-Up Study since 1988 and is involved in just about every phase of the study, from the early stages of questionnaire design to the mailing and processing of the surveys to the final verification of the collected data.

Betsy also helps with the management of the Human Subjects applications. In order for us to maintain our funding from the National Institutes of Health, our research protocols must undergo increasingly thorough review by the Institutional Review Board at the Harvard School of Public Health. These review boards serve to



protect the rights and safety of all the participants in the research study. Betsy serves as a link between study investigators and the Institutional Review Boards to ensure successful continuation of the Health Professionals Follow-Up Study.

Betsy strives to live a healthy lifestyle. As a native Mainer, she enjoys nearly all outdoor activities, particularly, running, bicycling, and cross country skiing - but most importantly, she is savoring the Red Sox's World Series win!

## FREQUENTLY ASKED QUESTIONS

**Q.** Why don't you include more physical activity options, (i.e., basketball, skiing, dancing, yoga, etc.) in the physical activity grid?

**A.** Due to limited space on our questionnaires, our physical activity grid does not incorporate all possible physical activities. We suggest to our participants to try their best to categorize their activity into the available grids. For example, if you play basketball weekly you could categorize that as squash or rowing. If you are unsure how or where to categorize your activity, please feel free to attach a brief note and we will look at each questionnaire individually.

**Q.** Based on your results, what would you recommend as a

healthy diet for us?

**A.** The Department of Nutrition at the Harvard School of Public Health has a good website to use as a reference. This website contains information regarding the food pyramid, fats and cholesterol, carbohydrates, protein, fiber, fruits and vegetables, vitamins (just to name a few key points). You should also talk to your physician regarding a healthy diet.

You can find the website at:

<http://www.hsph.harvard.edu/nutritionsource>

The Health Professionals Follow-Up Study also has its own website at:

<http://www.hsph.harvard.edu/hpfs>

**Q.** I have retired. Would you still like me to participate?

**A.** Your participation is still

extremely important. We value your contribution regardless of your lifestyle change. If you have retired or changed professions, we still would like you to remain part of the HPFS. Please inform us of any new address change or contact information so that we can keep you abreast of any new information and send you the most recent questionnaire and newsletter.

Thanks again! You will receive the next HPFS questionnaire in 2006 (our 20 year anniversary)!