Fall 2010

PHYSICIANS' Health Study

NEWSLETTER

HARVARD MEDICAL
Department of Medicine
BRIGHAM AND WOMEN'S HOSPITAL
A Teaching Affiliate of Harvard Medical School

A New Chapter: No More Pill Packs

Since 1982, you've downed a lot of pills in the name of science. More than 15 million aspirin. More than 25 million vitamin C pills. Not to mention all the beta carotene, vitamin E, and multivitamins—plus the placebos. In June, the pill taking will stop for good. It's time to run the numbers on the last treatment standing—the multivitamin—to determine whether taking one every day for more than a decade has any effect on the risk of cardiovascular disease or cancer, eye disease, or cognitive decline. (See Q&A on page 3 for information about when PHS II participants will be unblinded.)

Whatever the results, they will likely affect many Americans' decision about continuing to take a daily multivitamin. Whether or not you're among the 8,067 still participating in the multivitamin arm of the trial, you have already influenced numerous other epidemiologic debates. Most recently, PHS II participants' adherence to taking vitamins C and E—or placebo—for eight years added significant weight to the no-benefit column when it comes to whether these popular supplements have the power to stave off CVD or cancer. Going back to 1996 and PHS I, with an amazing 13 years of pill taking—more than 32 million pills in all—you demonstrated that beta carotene supplements are also incapable of fending off CVD and cancer.

And it all started with the aspirin results,
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Gordon John Weir, MD, of Singers Glen, Virginia, made sure to keep his pill pack dry during a 12-day trip on the Colorado River through the Grand Canyon.

Dear Doctor,

Those of you who've been part of the study since the beginning will mark your 30th anniversary as participants in 2012. For those who joined the PHS II in 1997, it will be 15 years. The "modern" gift for a 30th wedding anniversary is a diamond. For the 15th anniversary, a watch. We wish we could be this generous in thanking you for your tireless dedication to PHS. Soon, even our standard "gift"—pill packs—will stop coming to PHS II participants, as we close out the treatment phase of the trial on June 1, 2011.

If you are taking pills, please keep doing so through June 1. If you are due to receive more, we will be sending enough to take you through that date. As the treatment phase ends, you can also expect to receive an endpoint questionnaire, and shortly thereafter, a risk factor questionnaire. All PHS II participants will be unblinded soon after this and will receive a letter telling them whether they have been taking a multivitamin or placebo for more than a decade. Once the final analysis is completed and its publication is imminent, we will post the findings on the PHS Web site at **http://phs.bwh.harvard.edu/**.

Dr. J. Michael Gaziano (front row, center) and members of the PHS staff, several of whom have been with the study for 25 years.

As always, we want to encourage you to continue filling out the questionnaires, which we plan to keep sending. We don't want to lose touch with you and sincerely appreciate your taking the time to complete them because a wealth of information can be—and has been—garnered with your long-term follow-up and through ancillary studies. Those of you who are PHS I participants but who did not join PHS II are still being followed in an observational cohort. And some of you have already participated in one or more of these additional studies. As always, we offer our eternal gratitude for your amazing commitment, and hope that you will continue our "relationship" by responding to our questionnaires and queries, as you have so faithfully done in the past. ✻

With best regards,
Dr. J. Michael Gaziano, Principal Investigator

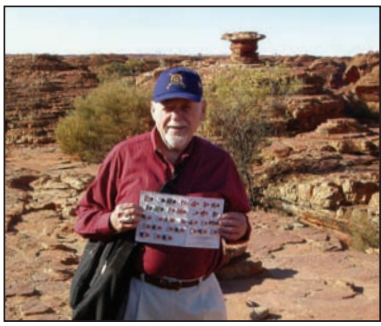
Participant profile

Average age: 75.7 Youngest: 60 Oldest: 104	
Current smokers:	2%
How many participants . . .	
WOULD RATE THEIR GENERAL HEALTH AS:	
Excellent?	31%
Very good?	40%
Good?	22%
Fair or Poor?	7%
EXERCISE VIGOROUSLY ENOUGH TO SWEAT?	
1–2 days/week?	21%
3–4 days/week?	46%
5–7 days/week?	29%
GET THIS MUCH SLEEP EACH NIGHT?	
Less than 6 hours	25%
7 hours	41%
8 hours	26%
9 or more hours	8%
HAVE EATEN FAST FOOD IN THE LAST YEAR?	
Never or less than 1 time/month	54%
1 to 3 times/week	32%
1 time/week	8%
2 or more times/week	5%
WORE SUNSCREEN DURING THE PAST SUMMER?	
Never	29%
25% of the time	21%
50%–75% of the time	30%
100% of the time	13%

Meyer Lifschitz, MD, previously from San Antonio, Texas, now lives in Israel. The holiest site in Judaism, the Kosel (Western Wall) is in the background of this photo in Jerusalem's Old City.

Barry Bershow, MD, made the trip from Chanhassen, Minnesota, to Equador, where he took in the flora and fauna of the Galapagos.

Hitting the links regularly—though not usually with pills in hand—is an enjoyable pastime for Lee Liggett, MD, of Kerrville, Texas.



Raymond C. Jess, MD, recently traveled to Kings Canyon in the Australian outback (above) and also to Nepal from his home in Lake Jackson, Texas.

Recent Findings from the PHS

Elevated blood insulin and cognitive change in older men without diabetes.

Type 2 diabetes has been associated with diminished cognition in later life, but little is known about the relationship between insulin level and cognition in those without diabetes. This study of nondiabetic PHS II participants whose mean age was 71 found that higher fasting insulin and greater insulin secretion may be related to overall cognitive decline, even in the absence of diabetes. *Neuroepidemiology.* 2010;34(4):200–207.

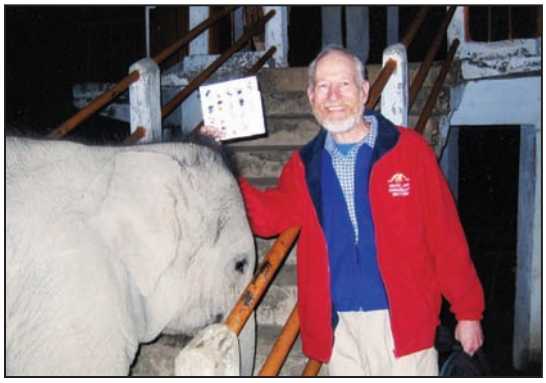
Alcohol consumption and functional outcome after stroke.

In this study, which examined the relationship between alcohol consumption prior to stroke and its effect on one's functional outcome shortly *after* a stroke, men who drank one drink per week appeared to benefit modestly from this minimal amount of alcohol, compared with nondrinkers or near teetotalers. However, there was not a strong association between alcohol consumption and functional outcome. *Stroke.* 2010;41(1):141–146.

A 25-year study of adiponectin and leptin concentrations and prostate cancer risk and survival.

Obese individuals often have a low level of one hormone, adiponectin, and a high level of another, leptin. In the PHS, higher prediagnostic concentrations of adiponectin predisposed men to a lower risk of developing high-grade prostate cancer and a lower risk of subsequently dying from it. The leptin level had no effect on developing lethal prostate cancer or dying from it. *Clinical Chemistry.* 2010 Jan;56(1):34–43. *(Continued on page 4)*

Pediatrician Allan LaReau, MD, traveled from his home in Michigan to Leogane, Haiti, as part of a medical mission after the earthquake in January.



During a trip to India, Peter M. Martin, MD, had a chance to meet a young elephant, who seemed game to try his pills, in Kaziranga National Park. Dr. Martin spends part of the year in Virginia and part in New Hampshire.

Information about Genotype Data Sharing

The biological samples that you have generously provided are an important part of research being done today. In recent years, our involvement in genetic studies such as genome-wide association studies (GWAS) has led to many exciting findings. In a GWAS, we study at one time many thousands of gene variants to identify chromosomal regions associated with the risk of various diseases. Due to the value of pooling data from multiple studies, the National Institutes of Health (NIH) has mandated that we submit genotype data from the PHS to the database of Genotypes and Phenotypes (dbGaP), which archives and distributes the results of genetic studies. Rest assured that any data we send to this database is completely devoid of personal identifiers (e.g., your name, year of birth, address, etc.). In addition, the NIH restricts access to qualified researchers who can show an appropriate scientific use for the data. More information about dbGaP can be found at **www.ncbi.nlm.nih.gov/gap**. If you have questions about data sent to dbGaP, or wish to have your data excluded from this database, please call us at **1-800-633-6907**, or e-mail us at **phs@rics.bwh.harvard.edu**. You can also write to us at **PHS, Brigham and Women's Hospital, 900 Commonwealth Ave. East, Third Floor, Boston, MA 02215**.

Questions & Answers

Q: Once the multivitamin treatment phase ends next year, how will I know whether I've been taking a vitamin or placebo?

A: The answer will be contained in a letter we'll send you a few months after the treatment phase ends in June 2011, so make sure to open any correspondence you receive from the PHS. We will begin the process of unblinding participants after the treatment ends. You can expect to receive: an endpoint questionnaire first, a risk factor questionnaire, and then the letter unblinding you.

Q: How will I know what the results are from the multivitamin arm of the trial?

A: We will post the information on the PHS Web site, **http://phs.bwh.harvard.edu**, at the same time the information is released through publication in a journal. This will likely be about one year after the treatment phase ends.

No More Pill Packs

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which translated, with much fanfare, into a check mark in the benefit column. A 44 percent reduction in the risk of a first MI from a 325-mg tablet every other day was front page news in *The New York Times* in January 1988. These findings are the "biggies," the primary endpoints, but with more than 350 journal articles based on ancillary studies and other PHS data now in print, the scientific contributions from this study have far exceeded the original expectations of the PHS research team. A total of 29,071 physicians have participated in the study since it began, 72 percent of whom are still alive. All of you continue to contribute to PHS' scientific causes by sending in the questionnaires—about 800,000 of those to date—which have the power to influence subsequent generations with clinically relevant health information that will guide public health practice for years to come

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Recent Findings from the PHS *(Continued from page 2)*

PCB levels and risk of non-Hodgkin's lymphoma.

Exposure to PCBs and to p,p'-DDE, a byproduct of the banned pesticide DDT, has been associated with the risk of non-Hodgkin's lymphoma (NHL). The baseline levels of these two substances were measured in 205 men who were later diagnosed with NHL and in 409 controls. A positive association was found between PCB exposure and development of NHL, but no association was observed for p,p'-DDE exposure. *Epidemiology*. 2010 Mar;21(2):172–180.

Nuts and risk of type 2 diabetes.

Is there a connection? In a word, no. In PHS participants, no statistically significant association between eating nuts and diabetes was found, in either lean, overweight, or obese men. *European Journal of Clinical Nutrition.* 2010 Jan;64(1):75–79.

Vigorous exercise and risk of atrial fibrillation.

Limited data suggest that athletes may have a higher risk of developing atrial fibrillation (AF). In this large prospective study of 16,921 apparently healthy men, the frequency of vigorous exercise was associated with an increased risk of developing AF in men under 50 and in joggers. This risk decreased with age and was offset by the known beneficial effects of vigorous exercise on other AF risk factors. *American Journal of Cardiology* 2009;103(11):1572–1577.

Normal systolic blood pressure and risk of heart failure in U.S. male physicians.

Cases of incident heart failure (HF) in PHS participants over a 16-year period were examined. A linear relationship emerged between normotensive systolic blood pressure (<120 mmHg) and HF risk; there was a 35% increased risk of HF among those with systolic pressures of 130–139 mmHg compared with men who had normal SBP (<120 mmHg). *European Heart Journal*. 2009 Dec 11(12):1129–1134. ✻

YOU CAN HELP. We are committed to seeking grants that would allow us to follow up with Physicians' Health Study participants. In addition, private support is also appreciated to achieve this goal.

If you are interested in contributing to the Physicians' Health Study, please contact Dr. Gaziano at **(800) 633-6907**, or **phs@rics.bwh.harvard.edu**. ✻