No. 3

VITAL Signs

News and information for participants in the *VIT*amin D and Omeg*A*-3 Tria*L* (VITAL)

Update on vitamin D research

In our first VITAL newsletter, we highlighted a recent report from the respected Institute of Medicine (IOM) that made recommendations about the amount of vitamin D that most Americans should consume. The IOM recommended 600 international units (IU) of vitamin D per day from food and/or supplements for people aged 1 to 70 and 800 IU per day for those aged 71 and older. To develop its recommendation, the IOM reviewed nearly 1000 scientific studies of vitamin D in relation to not only bone health but also other health outcomes such as cancer, heart disease, stroke, diabetes, and memory loss. It concluded that there is clear evidence that vitamin D has bone benefits but that current research is inconclusive as to whether higher vitamin D intake can decrease the risk for other chronic diseases. In other words, we simply don't know whether vitamin D supplements are beneficial in preventing diseases beyond osteoporosis or other bone disorders—nor do we know the amount of vitamin D that might be necessary to do so. That's why we're doing the VITAL study—to help get these answers.

Since the IOM released its report in late 2010, the role of vitamin D in preventing cancer, heart disease, and stroke—the primary outcomes of interest in VITAL—has remained unclear. Recent observational studies—that is, studies in which researchers track study participants with high intakes or blood levels of vitamin D but do not assign them to take vitamin D supplements as is done in randomized trials such as VITAL—have produced inconsistent results, with some studies reporting benefit and others not.

VITAL is designed to answer the question of whether vitamin D doses above the intakes recommended by the IOM can prevent cancer, heart disease, stroke, and other nonbone diseases, and its results are expected to shape future guidelines for supplemental vitamin D use. Study participants who

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> "[W]e … don't know whether vitamin D supplements are beneficial in preventing diseases beyond osteoporosis or other bone disorders …"

From the VITAL Study Directors

Dear VITAL participant,

We wish to thank each of you for your continuing commitment to the ***VIT***amin D and Omeg***A***-3 Tria***L*** (VITAL). We are grateful that you are participating in this important research study to clarify the health effects of vitamin D and marine omega-3 fatty acid (fish oil) supplements. Your participation in the study, along with that of 20,000 other men and women throughout the country, will allow us to determine whether these supplements lower the risk for cancer, heart disease, stroke, and other disorders (see Ancillary Studies box on page 4). We expect that the results of this landmark clinical trial will shape future clinical recommendations regarding the use of these supplements for the prevention of these health conditions.

A diverse group of men and women with respect to age, state of residence, and race/ethnicity has enrolled in VITAL. Future newsletters will provide a detailed description of the study population. To date, our youngest enrollee is age 50 and our oldest is age 97, and participants hail from all 50 states, as well as the District of Columbia and Puerto Rico!

Thank you again for your commitment to VITAL.

JoAnn Manson, MD

Julie Buring, ScD

JoAnn Manson, MD
Professor of Medicine
Harvard Medical School
Brigham and Women's Hospital

Julie Buring, ScD
Professor of Medicine
Harvard Medical School
Brigham and Women's Hospital

Educational Corner

Exercise: How much, how often, and how to keep motivated

Being physically active on a regular basis is perhaps the single most important thing you can do to maintain or improve your health. Exercise not only reduces the risk of developing or dying from heart disease, stroke, and diabetes, it also prevents certain cancers (including colon and breast cancer), lifts mood, builds bones, keeps joints functioning well, lowers the risk of falls and fractures, and helps to control body weight. Recent evidence also suggests that exercise boosts brainpower, or the ability to perform tasks that require attention, organization, and planning.

New research is identifying the biologic processes that underlie the diverse health benefits of exercise. Regular physical activity has been shown to improve cholesterol profile and reduce triglycerides (a type of blood fat); lower blood pressure and inflammation; promote a more relaxed nervous system, thus cutting the risk for deadly heart rhythms; stimulate the growth of new blood vessels; and lead to fat loss in the belly, all of which reduce the risk for heart disease and stroke. Exercise may also improve immune system function and keep insulin and estrogen levels in check, which along with its ability to lower inflammation, may reduce the risk for cancer. In addition, exercise boosts the body's production of substances called neurotrophins that favorably affect nerve and brain development, perhaps accounting at least in part for exercise's beneficial effect on memory and cognition.

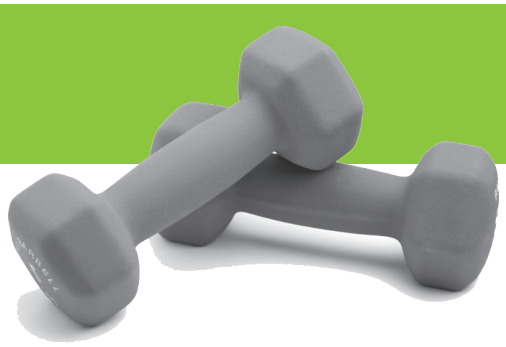
You don't need to run marathons to get most of the health rewards of exercise. National guidelines recommend moderate aerobic activity such as brisk walking for at least 30 minutes per day on five or more days of the week. (Somewhat more activity—45 minutes to 1 hour per day—may be necessary to reduce cancer risk and to lose weight without also cutting calories.) More vigorous activities are also an option for those who prefer to break a sweat, but they aren't essential for good health. In the Nurses' Health Study, a long-term study of more than 70,000 U.S. female nurses aged 40 to 65 years, women who walked briskly for 3 hours per week (averaging to about 30 minutes per day on most days of the week) received the same heart benefit as women who exercised more strenuously for 1½ hours per week; both groups were 30% to 40% less likely to suffer a heart attack over an 8-year period than were inactive women. Other studies have found that higher intensity exercise provides only slightly more benefit than moderate-intensity exercise.

A national survey indicates that only 28% of U.S. women and 31% of men exercise enough to meet the 30-minute guideline, and 40% of adults get no aerobic exercise at all. Lack of time and motivation are likely responsible for these dismal numbers.

If you're crunched for time, it may be helpful to know that you can splite your activity into two (or more) 15-minute sessions per day without diminishing its health benefits. In a long-term study of male Harvard alumni whose average age was 66 years, exercising in 15-, 30-, or 45-minute bouts all offered similar protection against cardiovascular disease, given an equivalent amount of total calories burned per week.

Besides walking or other aerobic activities, resistance exercise (strength training) to preserve bone and muscle mass is critical for midlife and older adults. National guidelines recommend resistance exercise at least two times per week, but only 17% of U.S. women and 22% of men meet this guideline. Aim for a 15-minute workout twice per week, with 1 or 2 sets of 8 to 12 repetitions using light arm and leg weights to exercise major muscle groups. In a 12-year study of more than 44,000 male health professionals aged 40 to 75 years, men who trained with weights for at least 30 minutes per week were 23% less likely to develop coronary heart disease than those who did not train with weights, suggesting that not only aerobic but also resistance exercise benefits the heart, although existing data are mixed and more research is needed.

Becoming—and staying—physically active can't be done unless you make it a top priority. A pedometer can be helpful for determining your baseline activity level, monitoring your progress, and bolstering your motivation. Aim to work up gradually to 10,000 steps per day. Write exercise into your calendar, scheduling it for a regular time of the day. Many people find that the morning works best for ensuring that other life demands won't interfere. Don't let small setbacks such as a cold or travel derail your overall plan; resume exercising as soon as possible. In addition to scheduling discrete blocks of exercise time,



incorporate walking into your daily routine—for example, take the stairs rather than the elevator whenever possible, don't go for the closest parking space, get off the train or bus one stop early, and plan active vacations.

Although at first glance regular exercise and avoidance of a sedentary lifestyle appear to be one and the same, recent studies suggest that, surprisingly, it's important not only to get sufficient exercise but also to avoid prolonged sitting—a challenge for many of us. For example, in a large study conducted by the American Cancer Society, women and men who reported sitting for 6 or more hours per day were 37% and 18% more likely, respectively, to die than their counterparts who sat for less than 3 hours per day. The link between sitting and death remained strong even after factoring out the effect of exercise.

It's never too late to reap the health benefits of boosting your physical activity level. For example, among initially inactive women in the Nurses' Health Study, those who became more active in mid- to late life were about 20% to 35% less likely to develop coronary heart disease over the subsequent 8 years than those who stayed inactive, and other studies have found similar results. Indeed, studies of people in their 80s and 90s show that regular aerobic exercise and strength training produces major improvements in physical and mental health over short periods of time.

Always consult your doctor before starting a moderate or vigorous exercise program, especially if you haven't

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VITAL Q&A

Q. I know that VITAL participants are not allowed to take (a) nonstudy vitamin D supplements of more than 800 international units (IU) per day, (b) calcium supplements of more than 1200 mg per day, or (c) nonstudy supplements containing fish oil while they are in the study. Are there multivitamins and calcium supplements that I can take and still meet guidelines (a) and (b)?

A. Pharmacists or other staff at your local drugstore, nutritional supplement store, supermarket, or big-box store should be able to help you find brands of multivitamins or calcium supplements that do not contain high doses of vitamin D and/or calcium. For additional guidance, please feel free to contact us. However, you should be aware that manufacturers change the formulation of their supplements on a frequent basis. Please check the labels of your supplements at each purchase to make sure that their contents have not changed and are still within study guidelines.

Q. What is the recommended dietary allowance (RDA) for calcium?

A. The current RDA for calcium, which was set by the Institute of Medicine in 2010, is 1000 mg per day for men aged 51 to 70 and 1200 mg per day for women aged 51 to 70 and for both men and women aged 71 and older. You should aim to meet this guideline by eating calcium-rich foods. Good dietary sources of calcium include milk and other dairy products; canned oily fish with bones, such as sardines or salmon; calcium-fortified orange juice and cereals; and broccoli, collard greens, and kale. Most individuals should consider calcium supplements only if their dietary calcium intake falls short of the recommended amount. Too many people are taking calcium supplements at higher doses than they need, especially in view of concerns that such supplements raise the risk for cardiovascular disease and kidney stones. Most people do not need to take more than 500 to 800 mg per day in calcium supplements to reach a total calcium intake (diet plus supplements) of 1000 to 1200 mg per day.

Q. Why do you ask for date of birth on every questionnaire?

A. In a study as large as VITAL, there are usually one or more participants with the same name. In addition to your name and study ID number, your date of birth serves as a unique identifier.

Q. I misplaced one of my VITAL newsletters. May I get another copy?

A. All newsletters are posted electronically on the VITAL website, www.vitalstudy.org. Please note that the newsletters are in PDF format, so you will need to use Adobe Acrobat reader (available for free at www.adobe.com) to access them. If you are unable to access the newsletter and would like us to mail you another copy, please let us know.

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take large amounts of supplemental vitamin D or fish oil outside the study greatly weaken the study's ability to detect benefits of these nutrients, should such benefits exist. Moreover, the risks of consuming very high doses of supplemental vitamin D (more than 4000 IU per day) or fish oil (more than 3 grams per day) on a long-term basis are not completely known. VITAL is designed for optimal safety for study participants. The study does not limit dietary intake (i.e., intake from food) of either vitamin D or fish, and it allows the use of vitamin D supplements up to 800 IU per day. Thus, no one should become deficient in either vitamin D or omega-3s even if receiving placebo in the trial. Thank you for adhering to VITAL study guidelines.

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recently been active or if you have health problems. Although national guidelines are useful for the population as a whole, they are not right for everyone. The amount of exercise you need depends on your genes, your diet, how much muscle and fat you have, your overall health, and how fit you are. If you are not physically fit, the amount and intensity of exercise necessary to improve your health may be modest. Your doctor can help to prescribe the most appropriate level of exercise for you.

VITamin D and OmegA-3 TriaL (VITAL Study)
900 Commonwealth Avenue East
Boston, Massachusetts 02215
Telephone: 1-800-388-3963

E-mail:
vitalstudy@rics.bwh.harvard.edu

Website:
www.vitalstudy.org

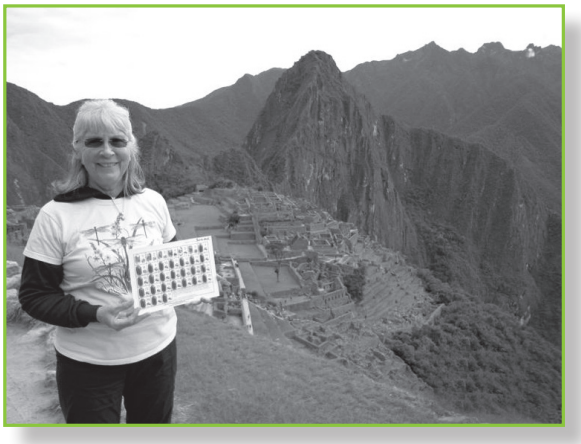
Ancillary Studies

Although the main goal of VITAL is to test whether vitamin D and/or omega-3 fatty acids can prevent cancer, heart disease, and stroke, we will also assess whether these supplements provide other health benefits, such as lowering the risk for:

- diabetes
- high blood pressure
- memory loss or cognitive decline
- autoimmune conditions such as thyroid disease, rheumatoid arthritis, and lupus
- bone fractures
- anemia
- eye problems such as macular degeneration and dry eye syndrome
- other conditions, including infections, asthma, depression, chronic knee pain symptoms, kidney disease, atrial fibrillation, and physical disability and falls.

If your early questionnaire responses indicated that you were eligible for one or more of these ancillary (add-on) investigations, you may have received separate mailings about these optional studies and may now be participating in them. In addition, participants who live within driving distance of Brigham and Women's Hospital in Boston, Massachusetts have been invited for optional clinic visits to have more detailed studies, including tests of blood sugar, lung function, physical function, bone density, and heart structure.

VITAL on the Go



VITAL participant **Yvonne R.** of California recently visited Peru. This photo was taken at Machu Picchu, a fifteenth-century Inca site.

A Call for Photos

Do you have a photo (of you holding your calendar pack, of course!) that you would like to share with other VITAL participants? If so, please send your photo, along with a short note stating where it was taken, to vitalstudy@rics.bwh.harvard.edu or our postal address (see contact information in box to the left). Digital photos are preferred. We plan to include as many photos of dedicated participants as possible in future newsletters. Please note that no participant photo will be published without the participant's express written consent.