



News and information for participants in the VITamin D and Omega-3 Trial (VITAL)

From the VITAL Study Directors

Dear VITAL participant,

Thanks to your collaboration, VITAL is fast becoming one of the most extensive resources in the world for the study of the health effects of vitamin D and omega-3 fatty acids. The primary goal of VITAL is to determine whether these supplements can prevent cancer, heart disease, and stroke, but a number of substudies—20 and counting—are focusing on other health outcomes or conditions. The newest substudy, which received funding from the National Institute of Diabetes and Digestive and Kidney Diseases in April 2015, will examine whether vitamin D and fish oil favorably affect kidney

function in men and women with high blood pressure. Two substudies that are already well underway are highlighted on page 2 of this newsletter. (Please note that VITAL participants who are eligible for certain substudies on the basis of their medical history receive separate invitation letters to join those substudies. Participation in substudies is *optional* and does not affect participation in the main trial.)

We very much appreciate your continuing support of VITAL. If you have any questions or comments, please feel free to contact us at 1-800-388-3963, vitalstudy@partners.org, or the postal address on page 4. Thank you!



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

VITAL Q&A

The Q&A column, a regular feature of the newsletter, takes center stage in this issue.

Q. A couple of my friends are taking high-dose vitamin D supplements (that is, more than 800 IU per day) or omega-3 fatty acids (fish oil), but I am not because I am committed to VITAL. Some of my friends think that vitamin D and/or fish oil have already been proven to be beneficial. What should I tell them?

A. The reality is that the jury is still out, and that is why VITAL is so important! No previous large

randomized clinical trials were designed to test whether vitamin D or fish oil supplements can prevent cancer, heart disease, and stroke in people without a history of these conditions. Many studies on vitamin D and omega-3 fatty acid supplements to date have been observational studies, comparing the health experience of people who self-select to take these supplements to the health experience of non-users. However, other factors in the lifestyles of people who choose to take these supplements may be responsible for the apparent health benefits of vitamin D or omega-3 fatty acids seen in some observational studies. Press reports, particularly headlines, often do not make this clear. Only a large randomized trial such as

VITAL can provide clear answers as to whether vitamin D or fish oil are beneficial or are merely markers for healthier lifestyles.

Q. I'm in good general health, eat a balanced diet, and do not have osteoporosis, but my doctor has recommended that I take a vitamin D supplement (1000 IU per day) for "insurance," saying that "it can't hurt and it might help." Your thoughts, please?

A. VITAL guidelines permit the use of non-study supplemental vitamin D in doses of up to 800 IU per day, which is consistent with the current recommended dietary allowance (RDA) of 600-800 IU per day for adults. If your doctor feels strongly that you should be taking a higher

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VITAL receives a lot of media coverage. For a sample, please take a look at the recently updated "VITAL in the News" section of the VITAL website, www.vitalstudy.org.

Spotlight on VITAL Substudies

VITAL substudies provide exciting opportunities for VITAL participants to help advance scientific understanding of the potential role of vitamin D and omega-3 fatty acid supplements in other health outcomes and conditions besides cancer and cardiovascular disease, which are the focus of the main VITAL study.

Autoimmune Diseases, Blood Markers of Inflammation, and Joint Pain

The possible role of vitamin D and omega-3 fatty acids (fish oil) in preventing certain types of autoimmune disorders, decreasing inflammation, and relieving joint pain has received much recent attention in the medical literature and popular press. There are many types of autoimmune disease, including multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, and autoimmune thyroid disease. These conditions are characterized by high levels of inflammation in the body. Some data suggest that low vitamin D intakes or blood levels may be associated with an increased risk of developing multiple sclerosis, but the relation between low vitamin D and the risk of developing other types of autoimmune

disease has received less study. Fish oil has been shown to reduce inflammation and joint pain in people suffering from rheumatoid arthritis, but whether it can lower the risk of developing rheumatoid arthritis (or other autoimmune diseases) in the first place, or alleviate joint pain from other causes, is unknown. Moreover, rigorous clinical trials of both vitamin D and fish oil for the prevention of autoimmune disease are lacking.

VITAL investigators are collaborating with Dr. Karen Costenbader at Harvard Medical School to determine whether vitamin D and fish oil can prevent or delay the onset of various types of autoimmune disease. We are also collecting follow-up blood samples in a randomly selected group of 1,000 participants who provided a baseline sample to determine whether these supplements can reduce levels of inflammatory markers in the blood. Finally, we are following 1,200 participants who reported severe knee pain at the start of the study to assess whether vitamin D and fish oil are effective at lessening this pain. The National Institute of Arthritis and Musculoskeletal and Skin Diseases is funding this research.

Infection

Infections are a leading cause of illness and mortality. Vitamin D and omega-3 fatty acids have promising but still unproven roles in this area. Although some randomized trials of vitamin D show benefit for acute respiratory infections, others do not; the role of vitamin D in preventing other infections (such as urinary tract infections) is also unclear. Prior studies on omega-3 fatty acids also show mixed results.

The VITAL team is partnering with Harvard colleague Dr. Carlos Camargo to test whether vitamin D and fish oil supplements can prevent infections, including upper respiratory infections (URIs) such as the common cold. We have enrolled 2,000 VITAL participants to receive three additional questionnaires about the occurrence, severity, duration, and use of treatments for URIs and to provide a one-year follow-up blood sample. We are also looking at other types of infections, including pneumonia and influenza, urinary tract infections, and skin infections. Approximately 1,250 participants who report these or other infections on their annual questionnaire are asked to answer a few questions about their illness. The National Institute of Allergy and Infectious Diseases is funding this research.

Just a Reminder: A New Look for the Large Study Capsules

The manufacturer of the large study capsules, which contain either omega-3 fatty acids (Omacor[®] fish oil, 1 gram) or placebo, has changed the color of the capsules from a reddish brown to a more transparent amber color. Please note that the formulation and dose of the study ingredients contained in the capsules, as well as the size of the study capsules, remains the same. If you were originally assigned to fish oil when you

entered the study, you will still receive fish oil. If you were originally assigned to placebo, you will still receive placebo. As before, the fish oil and placebo capsules look the same as each other. The transparent amber capsules started shipping in February 2015, and all participants should have them in hand by February 2016. You will receive the amber study capsules when you are due for a new shipment of calendar packs. In

the meantime, please continue to take your current supply of study capsules. Thank you!



Original (left) and new (right) look of the large study capsules

VITAL on the Go

... and tips from participants for remembering
to take the study capsules each day



“I managed to take my two pills each day, and I had several opportunities to discuss the importance of the VITAL study with folks we met along our journey.”

— Robert M. of Virginia, in St. Bees, England, in reference to a six-day family hiking trip through the Lake District National Park portion of the Coast to Coast Walk, which crosses England



“I’m so glad I was one of the chosen participants. I remember to take my study capsules every day by letting it be the first thing I do every morning, even before I brush my teeth—it works really well.”

— Bessie W. of North Carolina



“I have been in one or another of your studies for probably 20 years. I keep the [VITAL] calendar pack in the kitchen so every morning it is there ready for me to take the day’s pills. I have traveled extensively over the past 15 years and have so far

been to 141 countries. I keep the study pack with my toiletries and never forget to take the pills.”

— Alla C., RN, BS, MSN, of Georgia, at the Mansudae Grand Monument in Pyongyang City, North Korea



“My husband and I both take morning vitamins and pills. All we’ve had to change for the VITAL study was to add two more capsules to

the morning mix. The hardest is when we travel, which breaks up our breakfast routine. But by both being in the trial we can help remind each other, so we don’t miss taking our capsules.”

— Husband and wife participants Karl H. and Camille K. of Virginia, in Queenstown, New Zealand



“I remember my pills by cutting [the calendar packs] in week-long strips and always carrying them in my purse wherever I go. I also put the day (Mon., Tues., Wed., etc.) by the corresponding date (1st, 2nd, 3rd, etc.).”

— Charlotte J. of California, at the Oakland Bay Bridge in San Francisco



“Being a scientist myself, I have always been interested in well-conducted clinical trials. I find VITAL relevant to me and easy for me to incorporate into my daily schedule.”

— Dat D., PhD, of Maryland, at the Inca ruins of Machu Picchu, Peru



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amount of supplemental vitamin D, please call or e-mail to let us know (if you have not already done so) and also report the outside use on your next study questionnaire. In most cases, it is safe to continue taking your study capsules in addition to the supplement prescribed by your doctor. However, you should know that the medical community simply does not yet have the kind of evidence needed to determine whether the long-term use of vitamin D doses above the RDA confer any benefit, or what the overall balance of benefits and risks is. You and your doctor may find a recent article entitled “Vitamin D Clinical Practice and Research: At a Crossroads,” by Drs. JoAnn Manson and Shari Bassuk, to be of interest. A free link to this article, which appeared in the April 7, 2015 issue of *JAMA: the Journal of the American Medical Association*, can be found on the VITAL website, www.vitalstudy.org.

Q. How many participants are returning their annual study questionnaires? You always emphasize how important this is.

A. Our follow-up rate is excellent—well over 90 percent of participants have completed and returned all of their follow-up questionnaires. We attribute this achievement to the commitment and dedication of our participants. Thank you! For the validity of the study, it is essential that we are able to account for the health status of every person who was assigned to a treatment group at the beginning of the study. Therefore, even if you are not currently taking the study capsules, it is very important for us

to receive your completed health questionnaires. If you move, please do not forget to give us your new address so that you continue to receive study materials in a timely fashion.

Q. I stopped my study pills when I had surgery a few months ago and forgot to restart them. Is there any point in restarting them now?

A. Yes! We realize that it is not always easy to participate in a long-term clinical trial, as competing demands can interfere with your commitment to the study. If your health and circumstances allow you to start taking the study capsules again, we would very much appreciate your doing so. Although it may seem hard to believe, each day that a given participant takes his or her study capsules boosts the ability of the study to obtain definitive results. Even if you are unable to resume taking both types of study capsules, taking just one type is valuable to the study. Similarly, if you are unable to take the capsules every day, taking them just a few times per week is valuable. Even if you cannot restart either of the study capsules, filling out the yearly questionnaires is still valuable (see preceding question). We are grateful for whatever level of participation you can provide. If you wish to resume taking the study capsules and need calendar packs, please contact us at 1-800-388-3963 or vitalstudy@partners.org for a fresh supply.

Q. I just received another annual shipment of calendar packs but still have calendar packs left over from the last shipment. What should I do with the leftover calendar packs?

A. Please finish your current (already opened) calendar pack and then use any unopened calendar packs from the last shipment before starting the calendar packs in the new shipment. Some participants find it useful to keep old calendar packs around for a while to help them answer the pill-taking questions on the yearly questionnaire, but you do not need to hold onto the calendar packs once you're done filling out the questionnaire.

Q. I'm having a hard time getting the study capsules out of the calendar packs. Can the capsules be sent in a different type of packaging?

A. The capsules are sent in calendar packs and an aluminum pouch to ensure that they are in a dry environment and are protected from heat, humidity, and sunlight. Unfortunately, we cannot send the pills in different packaging. If the capsules are difficult for you to remove, you may wish to consider asking a family member or friend to help punch out a one month's supply of capsules to store in a bottle (keep at room temperature and away from moisture and sunlight).



**VITamin D and
OmegA-3 Trial
(VITAL Study)**

900 Commonwealth Avenue, Floor 3
Boston, Massachusetts 02215
Telephone: 1-800-388-3963
E-mail: vitalstudy@partners.org
Website: www.vitalstudy.org