



Division of Preventive Medicine
Department of Medicine

Please Reply to:

VITAL Study
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(800) 388-3963
(617) 731-3843 FAX
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Dear Healthcare Provider,

Your patient is participating in the nationwide *VIT*amin D and *Om*ega-3 *Tria*L (VITAL). We thought it would be helpful to tell you about this study, why the study is important, and how you can best support your patient's participation in the study.

Q. What is the VITAL study?

A. VITAL is a randomized clinical trial testing whether daily supplementation for 5 years with vitamin D (2000 IU) or marine omega-3 fatty acids (Omacor® fish oil, 1 gram) reduces the risk of developing cancer and cardiovascular disease in initially healthy midlife and older adults. A total of 25,875 men and women across the U.S. are participating. Participants were randomly assigned to one of four study groups: (1) daily vitamin D and fish oil (25% chance); (2) daily vitamin D and fish oil placebo (25% chance); (3) daily vitamin D placebo and fish oil (25% chance); or (4) daily vitamin D placebo and fish oil placebo (25% chance). At study's end, participants will be told their study group assignment.

The study is funded by the National Institutes of Health and is being conducted by Brigham and Women's Hospital, an affiliate of Harvard Medical School, in Boston, MA. Participants receive the study materials (study capsules and study questionnaires) via postal mail.

Q. Why is the VITAL study important?

A. Some studies suggest that vitamin D or omega-3 fatty acids (fish oil) supplements can prevent cancer and cardiovascular disease, but available results are far from definitive. Many times in the past, promising preliminary findings were not confirmed when rigorously tested in large randomized clinical trials.

Vitamin D: In 2010, the prestigious Institute of Medicine (IOM) conducted a comprehensive literature review and concluded that it remains unclear whether taking moderate or high doses of supplemental vitamin D lowers the risk of cancer, cardiovascular disease, and other non-bone conditions. Given the current lack of evidence for non-bone benefits, the IOM set the recommended dietary allowance (RDA) for vitamin D on the amount required for bone health only—600 IU/day for adults aged 70 and younger and 800 IU/day for adults aged 71 and older. These amounts are sufficient for $\geq 97.5\%$ of U.S. and Canadian residents, including those living in the north during the winter, and correspond to a vitamin D blood level of 20 ng/ml. Many labs consider a level of 30 ng/ml to be optimal, but little research supports this claim. The IOM's report challenges the notion that vitamin D deficiency is common and cautions against the need for widespread blood tests. It calls for more rigorous studies, particularly large randomized trials such as VITAL.

Omega-3 fatty acids: The effect of fish oil supplementation on risk for cancer and cardiovascular disease also remains uncertain, as there are no large randomized trials of fish oil for the primary prevention of these outcomes in a population at usual cardiovascular risk. Given the widespread use of fish oil for CVD prevention in the U.S., as well as preliminary data suggesting both benefits and risks for site-specific cancers, a definitive determination of the overall benefit-risk balance in the general U.S. population is critically important.

Q. How can I support my patient's participation in the study?

A. Unless there is a compelling medical reason not to do so, we would appreciate your encouraging the patient to follow study guidelines, which do not allow the use of (a) nonstudy vitamin D supplements of more than 800 IU/day, (b) calcium supplements of more than 1200 mg/day, and (c) nonstudy fish oil supplements of any dose. The reasons for these restrictions are (1) to ensure that the study will be able to determine whether vitamin D and fish oil supplements prevent cancer and cardiovascular disease and (2) to ensure the safety of participants. The risks of consuming high doses of supplemental vitamin D (more than 4000 IU/day) or fish oil (more than 3 grams/day) on a long-term basis are not completely known. Also, large amounts of supplemental calcium (above the amount we allow) may combine with supplemental vitamin D to increase the risk for kidney stones.

VITAL participants are allowed to take up to 800 IU/day of vitamin D in nonstudy supplements if they wish. Together with intake from food (which averages 200-300 IU/day), participants can opt to consume at least 1000 IU/day of vitamin D on their own, which is actually *more* than the RDA (see above). Thus, no participant will become vitamin D deficient due to participation in VITAL, even if assigned to the placebo group. Moreover, no participant assigned to the vitamin D group will get too much unless a nonstudy supplement containing significantly more than the 800 IU/day allowed is also taken. Participants in the vitamin D group who follow the study requirements will consume vitamin D in amounts well below the conservative safety limit of 4000 IU/day set by the IOM. Thus, neither group should have safety concerns from participation.

VITAL participants are also allowed to take up to 1200 mg/day of supplemental calcium. Together with intake from food (which averages about 700 mg/day), most participants can opt to consume almost 2000 mg/day. This is not only higher than the current RDA for calcium but is also close to the IOM's safety limit of 2000 mg/day. No one will become calcium deficient as a result of participating in VITAL.


Finally, although use of outside fish oil supplements is discouraged, there are no restrictions on how much fish can be eaten during the study. Patients should feel free to follow current recommendations from the federal government and the American Heart Association to eat fish, particularly fatty fish, at least twice per week.

Thank you for taking the time to read this letter and for your support of VITAL. For more information, please visit the VITAL website at vitalstudy.org or contact us by telephone (1-800-388-3963) or e-mail (vitalstudy@partners.org). We would welcome the opportunity to address any questions or concerns you may have.

Sincerely,



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