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Vitamin D and fish oil supplements and risk of autoimmune disease

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A question most physicians hear almost daily is “Doctor, which vitamins or supplements do you recommend that I take?” This was a question that my colleagues and I set out to answer in the Autoimmune Disease Prevention ancillary study in the VITAL trial.¹ Now, when my patients, colleagues, or friends ask me, I can point to our research findings, which suggest that for women age 55 years and older, and men 50 years and older, marine omega-3 fatty acids (fish oil) 1000 mg a day, and vitamin D 2000 IU a day—the doses used in VITAL—lead to a 22% reduction in all autoimmune diseases with vitamin D, and a 15% reduction in the same with fish oil supplementation over 5.3 years of randomised follow-up. In the trial, these supplements were prescription grade and underwent rigorous quality testing. They were safe and well tolerated and no increase in adverse events was found. For individuals obtaining these supplements over the counter, I also recommend that they check the safety seals for quality assurance as these products are not always as well tested.

Autoimmune diseases are a family of 80 or more related illnesses that share pathogenesis, a breach of immune tolerance and an immune-mediated attack on the body's own tissues.² Together, they are very common, prevalence increases with age, and they have substantial morbidity, expense, and mortality.² While there is marked heterogeneity among these diseases, they all develop insidiously over time, with the breakdown in tolerance and up regulation of inflammatory pathways usually taking months to years. They also share many underlying genetic and environmental risk factors, and most are more common in women.³ Prior and ongoing trials of immunomodulators have targeted prevention of one disease or another in high-risk groups (e.g. rituximab or abatacept for rheumatoid arthritis prevention in those with early symptoms or autoantibodies, or for prevention of Type I diabetes in children).^{4–6} The VITAL autoimmune disease trial is unique, not only because of the positive results, but also because it targeted the general public, not a specifically high-risk group, and did not test these two supplements for prevention of only one disease. As VITAL enrolled community-dwelling older adults from across the US, we anticipated that rheumatoid arthritis, polymyalgia rheumatica, psoriasis, autoimmune thyroid disease, and inflammatory bowel disease would be the most commonly observed incident diseases. Our prediction was borne out except that incident inflammatory bowel disease was uncommon.

Post-intervention observation of VITAL participants is ongoing and there are still many questions to be answered by it and hopefully other similar large trials: 1) Will the effects be sustained over time? The

Kaplan-Meier curve for vitamin D suggested increased preventive effect after two years and we wonder if the curves will continue to separate; 2) Is there heterogeneity of the effects of these agents? We saw a suggestion that vitamin D was perhaps more effective at reducing the incidence of new onset psoriasis, while fish oil was perhaps more effective at reducing autoimmune thyroid disease. We are anxious to see if this will be borne out; 3) What are the genetic and lifestyle risk factors, and comorbidities, that interact with the autoimmune disease prevention effect of either supplement (allowing targeting of these non-toxic supplements to specific populations)? We observed that fish oil's preventive effect was stronger among those with a self-reported family history of autoimmunity. Thus, it may be that this supplement at least is more effective among people with an underlying genetic or environmental propensity for autoimmune disease and we hope to investigate this hypothesis. We also saw that vitamin D had a stronger preventive effect among those with low vs. high body mass index, potentially due to uptake in adipose tissue leading to lower bioavailability, and we intend to pursue this as well; 4) At least one important question cannot be answered by VITAL itself and will await another trial, that of the effectiveness of these agents in preventing autoimmune disease among younger individuals. Many autoimmune diseases occur and have similar pathogenesis across the age spectrum, such as psoriasis and rheumatoid arthritis, while others, such as type I diabetes, systemic lupus erythematosus, and multiple sclerosis, have their peak onsets much younger than the VITAL age range, and, lastly, diseases such as polymyalgia rheumatica and giant cell arteritis, and myasthenia gravis are not seen in children and young adults. Susceptibility to autoimmune diseases in children is thought to have a strong genetic component, and thus these supplements may not be as effective in preventing diseases that arise in youth.

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