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# Vitamin D and Omega 3 Field Study on Progression of Type 1 Diabetes

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## Abstract

**Chronic inflammation has been linked to the progression of type 1 diabetes (T1D). Supplementation with vitamin D and omega-3 fatty acids, which have anti-inflammatory properties, may slow or stop the progression of T1D. A field study is underway to assess the relationship between these nutrients and T1D progression among auto-antibody positive individuals who have not been diagnosed with T1D.**

**The T1D Prevention Field Study is currently recruiting participants to complete online health surveys and home blood-spot tests for 25-hydroxyvitamin D [25(OH)D], Omega-3 Index, AA:EPA Ratio, high-sensitivity C-reactive protein, and HbA1c every three to four months for 5 years. Participants (or their parents/guardians) are given information about the importance of achieving a 25(OH)D level between 40-60 ng/ml and an AA:EPA Ratio between 1.5-3.0 to reduce inflammation. However, participants are free to choose their own supplement or dietary regimens. Data analysis will focus on associations between vitamin D and omega-3 status and progression of T1D. Initial enrollment in the T1D Prevention Field Study includes 103 participants from fifteen countries; total enrollment is expected to reach at least 400 participants by the end of 2022.**

**The field study approach allows for cost-effective research that capitalizes on new technologies for recruitment, data collection, and blood level testing from home. However, some challenges have arisen. Many individuals are reading the open source protocols and some choose to supplement and test on their own so incentives may be needed to increase enrollment. Additionally, some participants do not have access to auto-antibody testing or are unable to get access to their test results; therefore, there is a need to provide blood spot auto-antibody testing through the field study.**

## Introduction

Type 1 diabetes (T1D), which is a chronic autoimmune disease characterized by the destruction of insulin-producing pancreatic beta cells, affects approximately 1.25 million people in the U.S[1]. Almost 18,000 new cases of T1D are diagnosed each year among those aged less than 20 years[1]. Complications related to T1D include cardiovascular disease, blindness, and kidney failure[2]. The estimated yearly cost of T1D in the United States in terms of medical costs and lost income is $14.4 billion[3].

Studies have linked vitamin D and omega-3 status with T1D risk. Incidence rates of T1D were found to be higher in countries further from the equator, which have lower UVB irradiance from the sun[4]. Vitamin D and omega-3 intake and increased nutrient levels have been associated with a lower risk of developing autoimmunity against insulin-producing (islet) cells of the pancreas, or islet autoimmunity, and T1D diagnosis[5-11]. Also, studies have shown that use of Cod Liver Oil, which contains both vitamin D and omega-3 fatty acids, is associated with a lower risk of T1D[10,11]. Therefore, improving both vitamin D and omega-3 status may prevent T1D.

Chronic inflammation has also been associated with the development and progression of many

chronic diseases including T1D[12-15]. Therefore, the mechanism for the association of vitamin D and omega-3s with reduced risk of T1D may, in part, be related to the known anti-inflammatory properties of vitamin D and omega-3 fatty acids[16-19]. A recent randomized clinical trial demonstrated that co-supplementation with vitamin D and omega-3s has beneficial effects on inflammation biomarkers among those with diabetes[20]. The T1D Prevention Field Study was initiated to further evaluate the combined effect of vitamin D and omega-3 on inflammation and T1D prevention, with specific regard to nutrient levels rather than intake amount due to the significant variability in dose-response[21,22]. In accordance with the Open Source Movement, this paper describes the T1D Prevention Field Study in an effort to make participation as openly available as possible and allow protocol modifications if needed.

## Type 1 Diabetes (T1D) Prevention Field Study

GrassrootsHealth, a non-profit public health research organization, has been running a field study on nutrient levels and health outcomes since 2008. This field study is a long-term (5+ years), real-world prospective cohort study with a large worldwide participant population (N=10,000+). Participation includes completing online health surveys and home blood-spot 25-hydroxyvitamin D [25(OH)D] test kits. This field study has no inclusion or exclusion criteria and participants are allowed to achieve the nutrient status of their choice.

In July 2018, a T1D prevention sub-study was initiated and is currently recruiting auto-antibody positive individuals who have not been diagnosed with T1D to assess the relationship between vitamin D and omega-3 status with T1D progression. Participants complete online health surveys, which collect demographics, auto-antibody status, T1D diagnosis, supplement intake, and other health-related information. Blood-spot tests for serum 25(OH) D and Omega-3 Index, the physiological measures of vitamin D and omega-3 status, are completed at home every three to four months for a duration of 5 years. The AA:EPA Ratio, which is a measure of the primary pro-inflammatory omega-6 (arachidonic acid, AA) to the primary anti-inflammatory omega-3 (eicosapentaenoic acid, EPA), is also measured along with HbA1c levels and high-sensitivity C-reactive protein (hs-CRP), a biomarker of inflammation. Participants do not have any in-person visits with project staff or medical professionals as part of the field study. This study is neither designed nor intended to replace any communication or treatment from the participant's physician(s).

Different from a clinical trial, participants in this field study are not assigned to treatment and control groups or required to take a specific dose or achieve a specific nutrient level. Participants (or their parents/guardians) receive their blood-spot test results and information about the importance of achieving 25(OH)D levels between 40-60 ng/ml, an Omega-3 Index at or above 8%, and an AA:EPA Ratio between 1.5-3.0 to reduce chronic inflammation and improve health. However, they are free to choose their own supplement or dietary regimens and nutrient status targets. Due to non-supplemental inputs (e.g. diet, sun exposure) and inter-individual variability in dose response, participants are able to personalize their supplement doses based on their test results and desired nutrient status. Participants also receive information about islet auto-antibodies, anti- and pro-inflammatory foods, and other T1D-related information. The dissemination of test results and information allows participants to take ownership over their health and creates a more interactive and dynamic study environment compared to other observational study designs.

Participants have been recruited via social media, websites, and conferences for T1D families. Initial enrollment in the T1D Prevention Field Study includes 103 participants from fifteen countries; total enrollment is expected to reach at least 400 participants by the end of 2022. Data analysis will focus on associations between vitamin D and omega-3 status and progression of T1D. Specifically, the individual and combined effects of 25(OH)D, Omega-3 Index, and AA:EPA Ratio on hs-CRP levels, HbA1c levels, auto-antibody status, and diagnosis of T1D will be assessed. All participants provide informed consent and this study was approved by the Western Institutional Review Board (Olympia, WA, USA).

## Discussion

Families with children who have a high risk of developing T1D have asked for a less invasive, less expensive, and more convenient way of intervening in the progression of T1D. Vitamin D and omega-3 testing and supplementation are safe and affordable and could be a key tool to slow or stop T1D progression. Given the opportunities created by Open Source, such as through support groups and social

media, many are aware of the possible benefits of vitamin D and omega-3 and have been supplementing for many years. Anecdotal evidence from these individuals indicates that the T1D status of some has been updated to "non-progressor" or "reverter." The T1D Prevention Field Study allows for the collection of data from individuals across the vitamin D and O3 status ranges so that the relationship between nutrient status and T1D progression can be determined and quantified.

A field study approach allows for more cost-effective and generalizable research than most clinical trials. New technology can be utilized to increase research efficiency and participant involvement in the study. This includes internet-based recruitment, enrollment, and data collection; at home blood spot testing; and a personalized and interactive nutrient health system for participants. A field study with this new technology can easily collect measurements for multiple co-nutrients and data on many risk factors and health outcomes, which can be used to identify associations and synergistic effects between nutrients. Data collected from the field study may be used to help inform clinical trial hypotheses and promote collaborative research.

Some challenges have arisen during the first year of the T1D Prevention Field Study. Since many individuals are reading the open source protocols, some have chosen to supplement and test on their own. Incentives could be helpful to increase enrollment in the T1D Prevention Field Study. For example, providing supplements at no charge could increase enrollment and ensure supplement quality. Additionally, some participants do not have access to auto-antibody testing or are unable to get access to their test results. Providing blood spot auto-antibody testing through the field study could increase data completion and provide valuable information to participants about their status. Also, there has been concern that supplementation within or outside of the field study may interfere with pharmaceutical drug trials. However, we suggest that vitamin D and omega-3 supplementation and measurement may have an important role in any T1D clinical trial because the reduction of chronic inflammation and immunomodulation could be critical to the success of any other clinical intervention strategy.

While the T1D Prevention Field Study focuses on individuals who are auto-antibody positive without a T1D diagnosis, additional sub-studies are being planned to also assess the effect of vitamin D and omega-3 status among those who have an increased genetic risk but are not yet auto-antibody positive and those who have already been diagnosed with T1D. Preliminary findings from other research studies suggest that this therapeutic approach may halt autoimmunity, preserve residual beta-cell function, and reduce exogenous insulin requirements in patients with T1D[23-25]. Importantly, even a partial level of beta-cell function is associated with reduced risk of chronic complications[26], hypoglycemia, and diabetic ketoacidosis[27]. The relative contribution of vitamin D and omega-3s to reduce inflammation and autoimmune responses is being investigated by the ongoing POSEIDON trial, a phase I/II trial enrolling T1D children (6-17 years) and adults (18-65 years) with both new-onset (<6 months of disease duration) and established disease (>6 months and up to 10 years of disease duration)[28,29]. Participants are randomly assigned to receive vitamin D in a dose that achieves 40 ng/ml and omega-3 fatty acids in a dose that achieves an AA:EPA Ratio of 1.5-3.0, or vitamin D alone. As the additional GrassrootsHealth sub-study for those already diagnosed with T1D is established, participants who are unable to participate in the POSEIDON trial may enroll this alternative study, which will focus on the potential benefit of vitamin D and omega-3s beyond prevention.

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**Conflict of Interest:**
The Authors declare that they have no conflict of interests.

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