Predicting the effects of supplemental EPA and DHA on the omega-3 index

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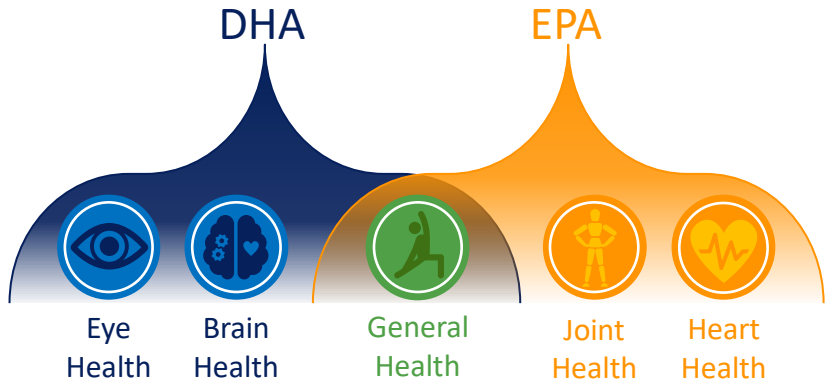
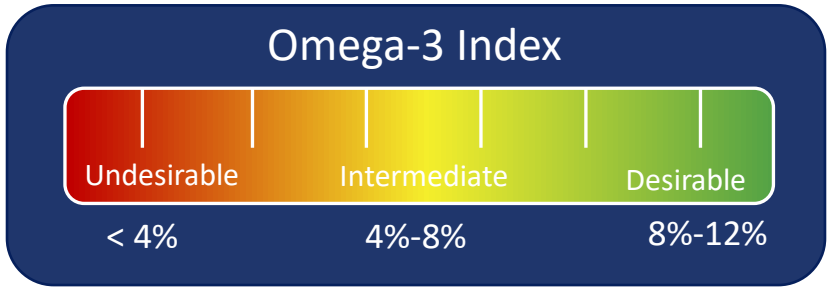
BACKGROUND

- The O3I is EPA + DHA expressed as a weight-% of total fatty acids (FAs).
- It was first proposed in 2004, as a potential risk factor for coronary heart disease (CHD) death.
- Several cross-sectional and prospective studies have supported its clinical utility.
- Results from studies show that an O3I of 8% or more is protective against fatal CHD.
- The O3I is also inversely correlated with major depressive disorders and inflammatory biomarkers.





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O3I AND SUPPLEMENTION

An individual's O3I response to supplementation could be affected by:

- Supplementation dose
- Body weight
- Baseline O3I
- Sex
- Age
- Chemical formulation of EPA and DHA [ethyl ester (EE) or triglyceride (TG)]
- Genetic factors
- Smoking
- Dietary fat content of accompanying meal

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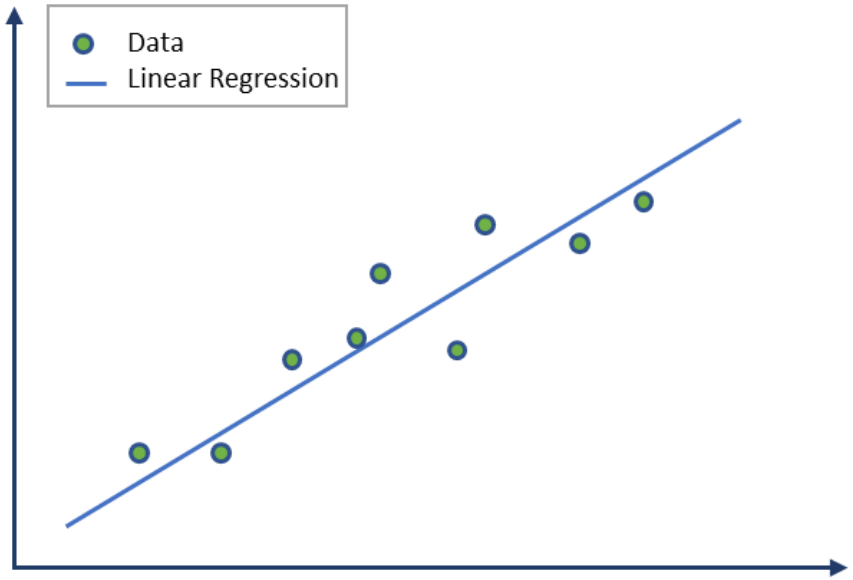
AIM AND METHODS

Aim:

The aim of the study was to build a regression model to predict O3I response to dose.

Methods:

Data from 14 published intervention studies (subjects n = 1422) in which EPA + DHA was given, were used to predict changes in the O3I.



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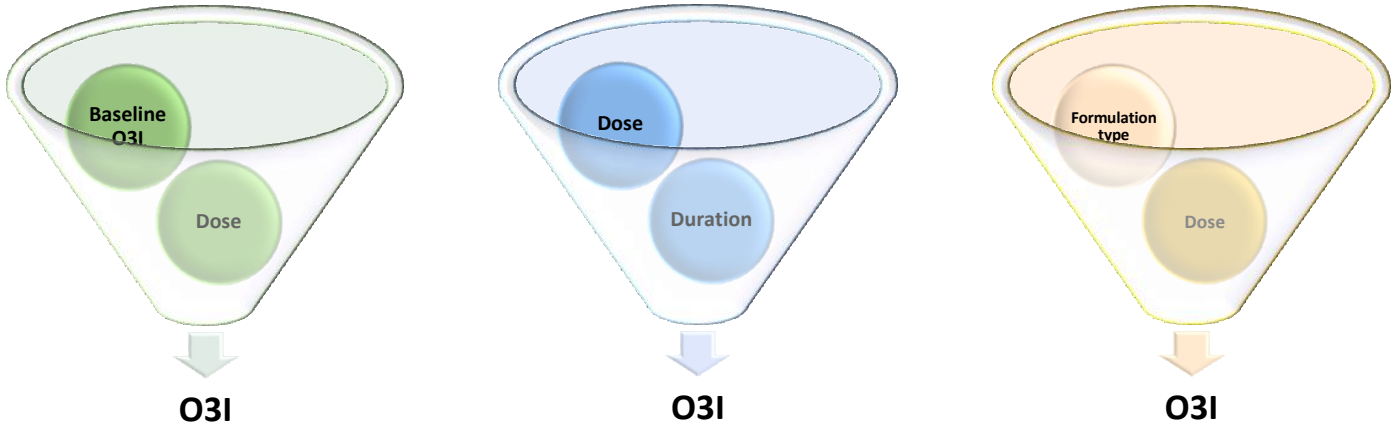
STATISTICAL ANALYSIS / MODELING

For absolute change in the O3I, eight predictor variables were considered:

- EPA + DHA dose (mg/d)
- Sex
- BMI (kg/m2)
- Duration of treatment (weeks)
- Baseline O3I (%)
- Age
- Race (Asian, black, Hispanic, other, white)
- Type of chemical formulation (EE or TG)

For absolute change in the O3I, the following three, potential statistical interaction terms were considered:



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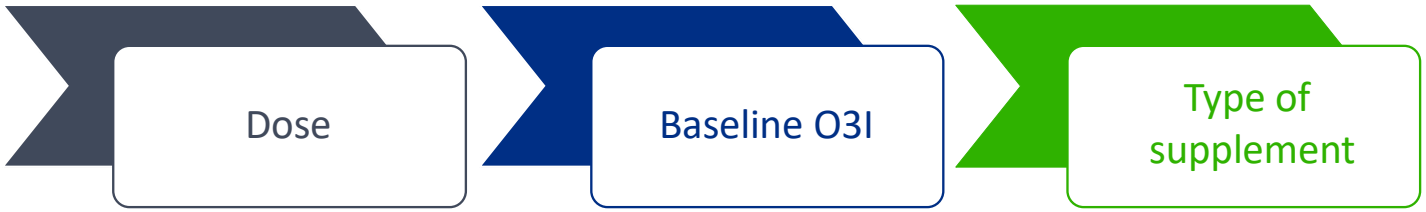
MODELING RESULTS

The model equation developed can be used to estimate the final O3I (and 95% CI) of a population given the n3 FA dose and baseline O3I. In order of importance, the major determinants of the O3I response were:



TG formulations produced ~ 1% greater increase in the O3I for the same EPA + DHA dose than an EE formulation.

Equation example:
In order to achieve a mean O3I of 4% in 13 weeks, the approximate EPA + DHA doses are:

- For triglyceride form: 1500 – 1750 mg/d
- For ethyl ester form: 2500 mg/d

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SUMMARY / COCLUSION

- In order to achieve a desirable O3I (≥8%) from a baseline of ~4%, roughly 2000 mg/d EPA + DHA would likely be required.
- This recommendation is applicable to individuals that resume their habitual diet.
- In clinical settings, direct testing of the O3I would be the preferred approach to assess EPA + DHA status.

Lifetime O3I:

- The daily dose needed over a lifetime to maintain an O3I of ~8% is likely much lower (i.e. average EPA + DHA intake in Japan is 800 – 1000 mg/d and the mean O3I in Japanese is 8%).
- Especially if EPA and DHA are supplied in the triglyceride form lower daily amounts of EPA + DHA (< 1 g/day) will likely be sufficient to maintain an O3I of ~8%.

Predicting the effects of supplemental EPA and DHA on the omega-3 index

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ABSTRACT

Background: Supplemental long-chain omega-3 (n–3) fatty acids (EPA and DHA) raise erythrocyte EPA + DHA [omega-3 index (O3I)] concentrations, but the magnitude or variability of this effect is unclear.

Objective: The purpose of this study was to model the effects of supplemental EPA + DHA on the O3I.

Methods: Deidentified data from 1422 individuals from 14 published n–3 intervention trials were included. Variables considered included dose, baseline O3I, sex, age, weight, height, chemical form [ethyl ester (EE) compared with triglyceride (TG)], and duration of treatment. The O3I was measured by the same method in all included studies. Variables were selected by stepwise regression using the Bayesian information criterion.

Results: Individuals supplemented with EPA + DHA (n = 846) took a mean ± SD of 1983 ± 1297 mg/d, and the placebo controls (n = 576) took none. The mean duration of supplementation was 13.6 ± 6.0 wk. The O3I increased from 4.9% ± 1.7% to 8.1% ± 2.7% in the supplemented individuals (P < 0.0001). The final model included dose, baseline O3I, and chemical formulation type (EE or TG), and these explained 62% of the variance in response (P < 0.0001). The model predicted that the final O3I (and 95% CI) for a population like this, with a baseline concentration of 4.9%, given 850 mg/d of EPA + DHA EE would be ~6.5% (95% CI: 6.3%, 6.7%). Gram for gram, TG-based supplements increased the O3I by about 1 percentage point more than EE products.

Conclusions: Of the factors tested, only baseline O3I, dose, and chemical formulation were significant predictors of O3I response to supplementation. The model developed here can be used by researchers to help estimate the O3I response to a given EPA + DHA dose and chemical form. *Am J Clin Nutr* 2019;110:1034–1040.

Keywords: n–3 fatty acids, omega-3 index, dietary supplements, EPA, DHA, statistical models

Introduction

The literature supporting the benefits of long-chain omega-3 (n–3) fatty acids (LC n–3 FAs; i.e., EPA and DHA) in cardiovascular disease (CVD) has been mixed (1). A 2018 meta-analysis concluded that the current evidence did not support a

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Supplemental Tables 1 and 2 and Supplemental Materials are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: BIC, Bayesian information criterion; CHD, coronary heart disease; CVD, cardiovascular disease; EE, ethyl ester; FA, fatty acid; LC n–3 FA, long-chain n–3 fatty acid; O3I, omega-3 index; RCT, randomized controlled trial; TG, triglyceride.

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