

# High-potency EPA increases omega-3 index and mental health score in healthy subjects

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## ABSTRACT

Omega-3 fatty acids are of interest in the management of mood disorders, such as depression. In particular, high-EPA interventions and higher plasma EPA may be associated with improved clinical outcomes. A typical dosage of 1-2g/d at an EPA:DHA ratio of 3:2 or greater has been recommended. Previous work associated with our group has yielded an 80% response rate in depressed adults managed with a combination of anti-depressant (fluoxetine, 20mg) and high-potency EPA (1g) for 8 weeks, compared to approximately 50% response to either treatment alone. However, less is known about how EPA intervention may affect mood in healthy subjects. Therefore, we investigated the influence of a high-potency fish oil supplement (1g/d, 3.3:1, for 120d) on HS-omega-3 index and mental health score, assessed using an SF-12 health survey, in 157 healthy adults who were already regular users of omega-3 supplements at baseline. We observed a significant increase in omega-3 index from 6.1% at baseline to 7.3%, with the proportion of subjects achieving a clinical target of 8% increasing from 5.6% at baseline to 24.8%. We also observed a small but significant increase in mental health composite score. To our knowledge, we are the first to report an increase in omega-3 index in regular consumers of fish oil by switching to 1g/d of high-potency EPA-rich oil. Maximizing the response to omega-3 supplementation may be a prudent clinical target for reducing certain risk factors and promoting healthy mood, although more work is needed.

## BACKGROUND

### Beneficial effects of Omega-3

- Higher intakes of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) benefit overall health and are associated with reductions in total and all-cause mortality, and are established to have cardioprotective and anti-inflammatory effects.<sup>1-4</sup>
- Growing body of evidence now supports a connection between omega-3 status and mental health and cognitive function.<sup>5,6</sup>
- Certain psychiatric diseases demonstrate similar mechanisms to cardiovascular disease (CVD) including endothelial dysfunction, increased inflammatory markers, and elevations in plasma homocysteine levels.<sup>7-9</sup>
- Population studies and preliminary clinical data have demonstrated omega-3 fatty acids may help elevate mood in depressed subjects.<sup>5,10</sup>
- Meta-analysis suggests higher EPA administration and higher plasma EPA, as compared to DHA, are associated with improved clinical outcomes in patients with major depressive disorder.<sup>6,11</sup>

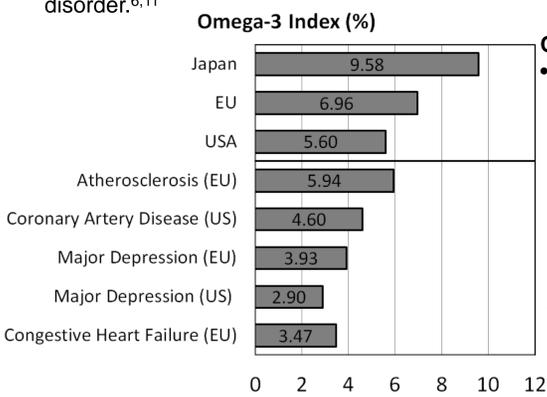


Figure 1: Mean HS-Omega-3 Index values in various populations. Adapted from von Schacky<sup>12</sup>

### Omega-3 Index:

- Standardized analytical procedure used to measure EPA and DHA in red blood cells. Research strongly supports a target reference value of 8% or greater, whereas lower HS-omega-3 index levels are associated with a poorer clinical condition (Figure 1).<sup>12</sup>

### Objective of present study:

- Assess whether a high-potency supplement can maximize omega-3 and health status in individuals who are presumed to have adequate omega-3 levels at baseline.

## MATERIALS AND METHODS

### Virtual contract research organization (CRO):

A proprietary, web-based CRO program, developed by Medicus Research (Northridge, CA) was used, enabling researchers to enroll subjects through inclusionary and exclusionary dialogue, monitor progress by survey tools and automatic prompts, and virtually follow up with subjects regarding completion of milestone events, adverse event reporting, and non-compliance issues.

### Subject recruitment and protocol:

Healthy subjects (ages of 18-70 years) working at health food stores in U.S. were recruited. Subjects ceased using their present omega-3 supplement for a two-week wash-out period before the study and during intervention. Subjects were provided with a high-EPA omega-3 supplement containing a total of 1,100 mg omega-3s with 756 mg EPA, 228 mg DHA, and 300 IU vitamin D3 in a single soft gel capsule (Minami Nutrition® MorEPA® Platinum, provided by Garden of Life, West Palm Beach, FL). Study duration was 120 days featuring a total of 5 virtual CRO visits, including a web-based SF-12 Health Survey. Subjects also received via mail an Omega-3 Index test kit to be completed on day 1 of the study, and another to be completed at the end of the study.

### Omega-3 status:

Omega-3 status was quantified using the HS-Omega-3 Index, a measure of the amount of EPA and DHA in red blood cell membranes expressed as percentage of total fatty acids. HS-Omega-3 Index was assessed through a self-administered finger-stick blood test (OmegaQuant, Sioux Falls, SD). Results were analyzed and reported by the manufacturer.

### SF-12 Health Survey:

The subjective assessment of mental and physical health utilized a shortened, validated version of the SF-36 health survey created by Quality Metric, in use since 1994. The composite scoring system applied was from Positive Aging Resource Center, and the reference range of scores had a cutoff of 50 for Physical Component Summary (PCS) and 42 for Mental Component Summary (MCS).

### Statistical Analysis:

All values are reported as the mean ± the standard error of the mean (SEM) or as a percentage of total subjects, and data were analyzed using SPSS (Chicago, IL). Paired T-tests were used to test significance for the HS-Omega 3 Index (baseline versus day 120), and analysis of variance (1 by 4) was used to determine time effect of the intervention of the SF-12 composite scores.

## RESULTS

Table 1: Baseline consumption rates of Omega-3 fatty acid supplements.

	Fish Oil Capsules	Fish Oil Liquid	Vegetarian Omega-3 Capsules
Total users <sup>1</sup>	66%	21%	19%
Frequency of use <sup>2</sup>			
1/d	51%	72%	36%
2/d	30%	3%	16%
3/d	5%	1%	-
4/d	2%	1%	-
5+/d	1%	1%	-
1/wk	11%	21%	47%
Dosage <sup>2</sup>			
<500mg	10%	25%	63%
500-1000mg	57%	42%	26%
>1000mg	33%	33%	11%

<sup>1</sup>Percentage (%) of total study population.

<sup>2</sup>Percentage (%) of omega-3 supplement users by column

The HS-Omega-3 Index increased from 6.1% (range of 3.1-11.8%) at baseline to 7.3% (3.7-13.3%) at 120 days ( $p < 0.001$ , Figure 1). This represents an approximate 20% increase over baseline. The baseline score of approximately 6% was higher than previously reported baseline scores of approximately 4%, as expected, reflecting regular use of omega-3 fatty acid supplements.<sup>13,14</sup>

Mental composite scores increased after 60 days and remained elevated through day 120 ( $p < 0.001$ , Table 2). There was no change in the physical composite score at any time point during the intervention.

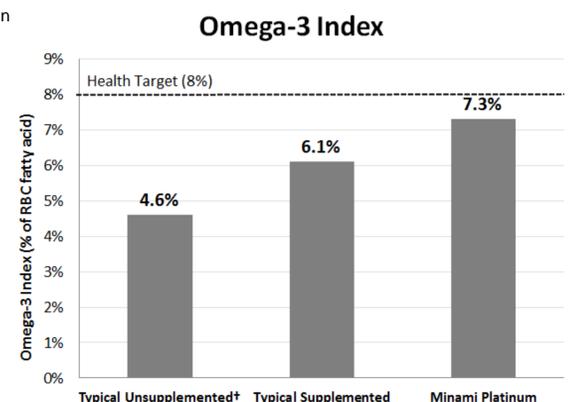


Figure 2: Omega-3 Index in general population†, healthy subjects at baseline, and following fish oil supplementation with high EPA omega-3. \* $p < 0.001$ . †data from Skulas-Ray<sup>13</sup>

Table 2: Mental and physical health composite scores in healthy subjects at baseline and following fish oil supplementation, \* $p < 0.001$  compared to baseline.

	Baseline	60	90	120
Mental Composite	49.5 ± 0.5	52.5 ± 0.5*	53.0 ± 0.6*	53.5 ± 0.5*
Physical Composite	53.2 ± 0.3	53.1 ± 0.4	53.2 ± 0.4	53.9 ± 0.3

## CONCLUSIONS AND DISCUSSION

- A high-potency EPA-rich fish oil supplement was effective in increasing omega-3 status in healthy adults.
- Assuming a clinical target of >8%, the percentage of subjects meeting this target increased from 5.6% at baseline to 24.8% of subjects following supplementation.
- Small but significant increase in mental health scores was observed as compared to baseline, based on the SF-12 mental health composite.
- Further studies are needed in both healthy populations and populations with mood disorders to research the effects of EPA on depression.
- Results contribute to establishing a clinical target for healthy omega-3 levels as related to the promotion of healthy mood and mental health status.

## FUTURE/ONGOING WORK

Ongoing studies include a 4-year research program in collaboration with the Institute of Nutrition and Functional Foods (INAF) investigating the anti-inflammatory effects and mechanisms of EPA and DHA in men and women with symptoms of metabolic syndrome (MetS).

Another study, in collaboration with the University of Washington, is investigating the use of high-dose EPA in patients with depression and coronary heart disease (CHD) in conjunction with and without antidepressant therapy. This study aims to establish whether a high-dose EPA can improve depression levels and cardiac risk markers in these patients when used alone or with antidepressants. Earlier data using a lower dose of EPA and lower EPA:DHA ratio showed cardiovascular benefits but not efficacy in depression, however, the use of a higher dose containing at least 1-2 g of EPA is now supported by other small trials showing improved efficacy of antidepressants with EPA.

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