Omega-3 Index – Beyond Heart Health

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Omega-3 Index - a new risk factor for death from coronary heart disease?
- a biomarker of cardiovascular health

**EPA + DHA**
% total fatty acids in red blood cells

**Greatest cardiovascular protection**

- **GISSI-P²**: ≈ 9-10%
- **CHS³**: 8.8%
- **DART⁴**: ≈ 8-9%
- **SCIMO⁵**: 8.3%
- **5 epi. studies**: ≈ 8%
- **PHS⁶**: 7.3%
- **Seattle⁷**: 6.5%

**Least Protection**
- **PHS⁶**: 3.9%
- **SCIMO⁵**: 3.4%
- **Seattle⁷**: 3.3%

Australians ~5%

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*Harris & von Schacky, Preventive Medicine 2004*
Effects of consuming fish or fish-oil on Omega-3 Index


Consuming LC n-3 enriched foods (~800mg/d) increases Omega-3 Index

Could the Omega-3 Index concept be applied more broadly?

In addition to cardiovascular protection, increased consumption of LC n3 PUFA may also deliver anti-inflammatory, metabolic and mental health benefits, e.g.

- **Polyunsaturated fatty acid status in attention deficit hyperactivity disorder, depression, and Alzheimer's disease: towards an omega-3 index for mental health?** Milte CM, Sinn N, Howe PRC. Nutr Rev 2009;67:573

- **Association between erythrocyte n-3 PUFA and biomarkers of inflammation and oxidative stress in patients with (n=80) and without (n=80) depression.** Baek D & Park Y. PLEFA 2013 Omega-3 Index: 8.62 ± 0.24% 9.48 ± 0.20% P<0.006

- **The association between n-3 polyunsaturated fatty acid levels in erythrocytes and the risk of rheumatoid arthritis in Korean women.** Lee AL & Park Y. Ann Nutr Metab 2013;63:88
In the Health Professionals Follow up Study (>40,000 men), higher fish intake was associated with a lower incidence of overweight (He K et al. JAMA 2002;288:3130).

In the Nurses Health Study (>79,000 women), higher fish intake and higher n-3 intake were associated with higher body mass index (BMI) (Iso H et al. JAMA 2001;285:304).

Such studies are limited by crude estimations of n-3 intake (FFQ). Biomarkers of intake may be more reliable. In a small study (124 adults) Micallef et al. showed that plasma n-3 levels were inversely related to BMI and waist circumference (Br J Nutr 2009; 102:1370).
Higher erythrocyte LCn-3 PUFA content is associated with a healthier body composition

**Aim**: to investigate relationships between Omega-3 Index, BMI and body composition

**Study Design**: opportunistic cross-sectional analysis of baseline measurements of erythrocyte fatty acids, BMI, waist circumference and body fat (DEXA) from 476 adults participating in 5 dietary intervention trials.

![Graph showing BMI and waist circumference across different Omega-3 Index quartiles with statistical significance markers.](image-url)
Body Composition and Omega-3 Status - split by gender

**Men**: median Omega-3 Index = 5.0

- BMI (kg/m²)
  - Quartile 1: 31.7
  - Quartile 2: 31.7
  - Quartile 3: 31.1
  - Quartile 4: 31.3

- Waist (cm)
  - Quartile 1: 112.0
  - Quartile 2: 110.5
  - Quartile 3: 109.2
  - Quartile 4: 108.1

- Body Fat (%)
  - Quartile 1: 35.4
  - Quartile 2: 35.7
  - Quartile 3: 34.1
  - Quartile 4: 33.0

**Women**: median Omega-3 Index = 5.1

- BMI (kg/m²)
  - Quartile 1: 37.3
  - Quartile 2: 34.2
  - Quartile 3: 32.2
  - Quartile 4: 32.6

- Waist (cm)
  - Quartile 1: 114.3
  - Quartile 2: 108.4
  - Quartile 3: 98.7
  - Quartile 4: 100.6

- Body Fat (%)
  - Quartile 1: 51.2
  - Quartile 2: 48.3
  - Quartile 3: 46.7
  - Quartile 4: 46.6

*P* < 0.001 for all comparisons.
## Linear Correlations

<table>
<thead>
<tr>
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<th>BMI</th>
<th>WC</th>
<th>% Body Fat</th>
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<tr>
<td>EPA</td>
<td>-0.08</td>
<td>-0.16*</td>
<td>-0.17 **</td>
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<tr>
<td>DPA</td>
<td>-0.05</td>
<td>-0.13</td>
<td>-0.14 *</td>
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<tr>
<td>DHA</td>
<td>-0.28**</td>
<td>-0.35**</td>
<td>-0.33 **</td>
</tr>
<tr>
<td>Omega 3 Index</td>
<td>-0.24**</td>
<td>-0.32**</td>
<td>-0.31 **</td>
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**n = 476**

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**n = 291**

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<tr>
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<td>-0.04</td>
<td>-0.13</td>
<td>-0.19 *</td>
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</table>

**n = 185**

* P<0.05    ** P<0.01
Curvilinear Regression analyses

This analysis demonstrates a possible sigmoidal relationship between the Omega-3 Index and markers of adiposity, particularly in women, indicating that there is less influence around the median level of the Index but larger effects at the lower and possibly upper ends of the range.

Women (291)  Men (185)

BMI (kg/m²)

- r = -0.26  P < 0.0001
- r = -0.10  P > 0.05

Waist circumference (cm)

- r = -0.36  P < 0.0001
- r = -0.18  P > 0.05

Body fat (%)

- r = -0.37  P < 0.0001
- r = -0.23  P > 0.05
Gender difference: is DHA more efficacious in women?

Changes in platelet aggregation in 41 men and 53 women after 4 weeks supplementation with placebo, EPA or DHA.
Clinical correlates and heritability of erythrocyte eicosapentaenoic and docosahexaenoic acid content in the Framingham Heart Study

Harris WS et al Atherosclerosis 2012;225:425-431

3196 Framingham Study participants (2005-8); mean Omega-3 Index = 5.6%.

In multivariable regression models, age, female gender, higher education, dietary EPA+DHA intake, fish oil supplementation, aspirin use, LDL cholesterol and lipid lowering drugs were directly associated with Omega-3 Index.

Heart rate, waist girth, triglycerides and smoking were inversely associated with Omega-3 Index.

The total explained variability in the Omega-3 Index for the fully adjusted model was 73%, which included major components due to heritability (24%), EPA+DHA intake (25%), and fish oil supplementation (15%).

Erythrocyte omega-3 fatty acids increase and linoleic acid decreases with age: observations from 160,000 patients

Harris WS et al PLEFA 2013;88:257
Conclusions

• A higher Omega-3 Index is associated with a healthier body composition
• DHA appears to be a more significant predictor than EPA or DPA
• This relationship appears to be stronger in women than men
• Influences of omega-3 fatty acids on other health parameters are likely to be specific for individual fatty acids, gender and possibly age
• Such information should be forthcoming from large databases of erythrocyte fatty acid analyses
• Routine measures of omega-3 fatty acids in erythrocytes could provide a future guide to health status
• However, causality must be established