



# Research

## Correlation of fish consumption and the Omega-3 index in healthy free living Sri Lankan subjects (Addenda-Case reports of effects of supplementation with flax seed oil and marine Omega-3 oil).

Ruvan A. I. Ekanayaka,<sup>1</sup> Ekanayaka, N. K. <sup>2</sup>, Waniganayake, Y. <sup>3</sup>

<sup>1</sup> Norris Clinic/ Nawaloka Hospitals PLC

<sup>2</sup> Department of Pathology, Medical Research Institute, Colombo.

<sup>3</sup> Institute of Cardiology, NHSL

Corresponding author: Ruvan A. I. Ekanayaka, .

Email: ruvan\_nishali.ekanyaka@yahoo.com

### Abstract

Fish consumption has been shown to correlate with reduced cardiovascular morbidity and mortality in humans. The Omega-3 index has been proposed as a parameter to stratify subjects into risk zones regarding the propensity for developing cardiovascular disease. We assessed the Omega-3 index in 45 healthy free living Sri Lankan subjects divided into three categories based on their fish intake. Vegetarians had the lowest Omega-3 index of 4.63 (SD 1.624, SEM 0.406) whereas the values for consumers of <250g fish/week and >250g fish/week were 6.96 (SD 1.568, SEM 0.419) & 7.93 (SD 1.455, SEM 0.403) respectively. The difference in the Omega-3 index observed between the vegetarians & fish consumers was significant ( $P < 0.05$ ). The Omega-3 index described a bell shaped distribution in all categories of subjects. Even in the category deemed to have adequate fish consumption, 61.54% of individuals did not achieve an Omega-3 index in the low risk zone. None of the vegetarians had an Omega-3 index in the low risk zone. This could be a risk factor contributing towards the high prevalence of coronary arterial disease in Asian communities which are predominantly vegetarian. This study highlights the value of assaying the Omega-3 index for accurate risk stratification.

## Introduction

Dietary Surveys conducted in many populations have demonstrated an inverse relationship between fish consumption and cardiovascular events. Coastal Eskimos who subsist on a diet consisting mainly of fish and seal have a demonstrably low incidence of ischemic heart disease [1, 2]. An inverse relationship between fish consumption and 20 year mortality from cardiovascular causes has also been demonstrated [3, 4].

In addition a low risk of sudden cardiac death associated with high consumption of fish has been demonstrated by several workers. In Japan, sudden cardiac death is virtually unknown in healthy individuals and this phenomenon has been correlated to their high consumption of fish [5]. On currently available data it appears possible to postulate a steep concentration risk dependence between fish consumption and cardiovascular deaths [6].

A beneficial association between high fish consumption and low incidence of strokes has been demonstrated by other workers [7, 8]. This finding, in conjunction with the benefit seen with regard to coronary disease, suggests that fish consumption has beneficial effects on atherosclerotic disease in general.

It is widely accepted that the content of Omega-3 fatty acids, namely 20:5n-3 (EPA, eicosapentaenoic acid) and 22:6n-3 (DHA, docosahexaenoic acid) are responsible for the protective action against atherosclerotic disease seen with increased fish consumption [9]. Harris et al concluded that the evidence to suggest an inverse relationship between 20:5n-3+22:6n-3 (EPA+DHA) intake and risk of fatal and possibly nonfatal ischemic heart disease was consistent [10]. In addition there seems to be some evidence to suggest benefit with regard to reduction of arrhythmias, specifically atrial fibrillation and ventricular fibrillation [11-13]. A meta analysis has confirmed that fish oil reduces the heart rate in humans [12]. This could be an important mechanism by which fish oils reduce cardiovascular events. Blood pressure, inflammatory response, endothelial function and cognitive development too seem to be benefited as well [14, 15]. However these claims need further supportive evidence. The effect of fish oils on malignancies remain unresolved and controversial [6]. Some workers have demonstrated a beneficial effect in carotid disease [17, 18] which confirms the assumption that fish oils have a beneficial effect in reducing the atherosclerotic burden in general.



Guidelines published by cardiac societies recommend intake of ~1g of fish oil /day for subjects suffering from ischemic heart disease. Whether a standard intake will benefit all individuals equally remains an open question as other dietary factors, genetic predisposition, body mass index and calorie expenditure are all factors likely to affect the Omega-3 status in a given individual [19]. Hence a reliable measure of the Omega-3 status of an individual would be clinically useful.

Harris has demonstrated that in heart transplant patients the content of Omega-3 in the red blood cells (RBC) and myocardium show a correlation. Hence the RBC Omega-3 content could be used as a surrogate for the cardiac 20:5n-3(EPA)+ 22:6n-3(DHA) content [20]. It is believed that 20:5n-3(EPA) and 22:6n-3 (DHA) are incorporated into the myocardium itself so that an effect is exerted on the functioning of the Na<sup>+</sup> and Ca<sup>2+</sup> channels. The Omega-3 fatty acids are thought to exert their beneficial effect by their actions on the cell membrane, which may include an interaction with ion channels, serving as ligands for nuclear transcription factors [21] and modulation of the eicosonid system towards vasodilatation and less towards inflammation[22,23] . Hence the content of fish oils in the membrane is probably more important rather than the serum level in the context of cardiovascular protection.

The content of 20:5n-3(EPA) and 22:6n-3(DHA) in the red cell membrane may be expressed as a percentage of its total fatty acid content. This has been termed the Omega-3 index. The Omega-3 index has been suggested to be considered as novel cardiovascular risk factor [24]. When the Omega-3 index is 6.5% in RBC, these individuals have a 90% less risk for sudden cardiac death (SCD) compared to individuals with a value of 3.3% [6]. Individuals with an Omega-3 index of 6.87% had 90% less risk for SCD compared to those with a value of 3.58%[6]. An Omega-3 index which is <4% carries a 10 fold risk of IHD compared with a value of >8%. Based on such data, risk zones have been determined for the value of the Omega-3 index as follows [10]:

- <4% :- High Risk
- 4% -8% :- Intermediate Risk
- >8% :- Low Risk

The highest protection seems to be afforded when the Omega-3 index is >8% and hence this value would be accepted by most workers as being the target value that should be achieved in clinical

practice. The Omega-3 index is of special interest as it is an easily modifiable risk factor [20, 21]. The Omega-3 index correlates well with other indicators of Omega-3 intake. However, as the Omega-3 index has a half life which is 4- 6 times longer than the serum levels of 20:5n-3(EPA) and 22:6n-3(DHA), it could be considered analogous to the HbA1c measurement with regard to blood glucose levels [19].

The important Omega-3 fatty acids in human nutrition are 18:3n-3(ALA, alpha linolenic acid), 20:5n-3 (EPA) and 22:6n-3 (DHA). All these are derived from plant sources as animals cannot synthesize 20:5n-3 (EPA) and 22:6n-3 (DHA) de novo. 18:3n-3 (ALA) is found in abundance in plant foods such as soya and canola.[9]. Conversion of 18:3n-3 (ALA) into 20:5n-3 (EPA) and 22:6n-3 (DHA) is poor. Retroconversion of 22:6n-3 (DHA) into 20:5n-3 (EPA) is well established but not 20:5n-3(EPA) into 18:3n-3 (ALA) [9].

It is well documented that consumption of foods rich in 18:3n-3 (ALA) can be correlated with reduced cardiovascular morbidity and mortality. In fact it is noted that the larger the study population and longer the duration of observation, the results shows better correlation [9].

In view of the importance of the Omega-3 index as a modifiable risk factor we decided to study the average Omega-3 index in healthy free living Sri Lankan subjects and investigate its correlation with fish consumption. This would provide useful information for clinicians when giving advice on fish intake in order to achieve adequate cardiovascular protection in primary & secondary prevention programs.

## Materials and Methods

Free living volunteers were randomly selected from the community for the study. They were enrolled in the study if the general medical examination confirmed normal health status. The subjects were required not to be on any nutritional supplements.

The study population was to be 45 subjects divided in to 3 categories based on their fish consumption as follows:-

- Category I: - Nil fish consumption (Vegetarian)



Category II: - Inadequate fish consumption (< 250 g fish/week)

Category III: - Adequate fish consumption (>250g fish/week)

Categorization was done on the basis that most recommendations give 150g-250g fish/week as the ideal level of consumption for healthy individuals.

Detailed data regarding fish consumption was obtained by a single investigator by weekly interview of subjects and spouses for 4 weeks. Information was obtained by recollection regarding the fish consumption and fish purchases for the week immediately preceding the interview. The average weekly consumption was computed from this data. The fish consumed by the study subjects are given in table 1. Fish sandwiches and fish burgers were not consumed by our study subjects.

**Table 1.** Types of fish consumed by study population

English name (Common Name)	Scientific name	Sinhala name
Spanish mackerel	<i>Scomberomorus commersoni</i>	Thora
Jack, Trevallies	<i>Caranx ignobilis</i>	Paraw
Skipjack tuna	<i>Katsuwonus pelamis</i>	Balaya
Yellowfin tuna	<i>Thunnus albacores</i>	Kelawalla
Sail fish	<i>Istiophorus platypterus</i>	Thalapath
Frigate tuna	<i>Auxis thazard</i>	Alagoduwa
Mackerel shark	<i>Isurus sp.</i>	Mora
Barracudas	<i>Sphyraena sp.</i>	Jeelawa
Trenched sardinella	<i>Amblygaster sirm</i>	Hurulla
White sardinella	<i>Sardinella albella</i>	Sudaya
Bigeye scade	<i>Selar crumenophthalmus</i>	Bolla

Subjects included in each category were comparable in terms of age & sex (Table 2)

The AHA recommends an intake of at least two servings of fatty fish per week. If each serving is taken to be 3.5 ounces of cooked fish or ¾ cups of flaked fish, this would approximate 150-250g of fish per week.

This is in agreement with the Canadian recommendation of 75g of fish x 2/per week. The National heart foundation of Australia gives a rather higher recommended intake namely 2-3 servings of 150g of oily fish per week. This would be 350g-450g of fish weekly.

Blood was sampled for the assay of the Omega-3 index using the finger stick blood collection kit, after a ten hours fast. As there is an inter laboratory variability in the Omega-3 index results, a laboratory using a standardized methodology for the assay was selected namely Omegamatrix GmbH-Germany. 26 types of fatty acids were assayed and the 20:5n-3 & 22:6n-3 levels were expressed as a percentage of the total, which gives the Omega-3 index.

## Results

The Omega-3 indices in the three categories are given in table 3

The average Omega-3 index was highest in category III which had adequate fish consumption (7.93, SD 1.455, SEM 0.403) and lowest in the totally vegetarian category I (4.63, SD 1.624, SEM 0.406). The difference between category I & III reached statistical significance (P <0.05). The Omega-3 index for category II which had suboptimal fish intake was 6.96 (SD 1.568 SEM 0.419) and when compared to category I, a statistically significant difference is demonstrable (P <0.05). Table 3 gives the significance of the differences seen between each category.

When Category II & III are considered as a composite, the Omega-3 Index is 7.43 (SD 1.565 SEM 0.301). When compared with vegetarian category I, a statistically significant higher value is seen in this composite category. When category III is compared against category II, although optimal fish consumption shows a trend towards a higher Omega-3 index, the difference does not reach statistical significance (P =0.111).



**Table 2:** Demographics & dietary data of study participants

	Category I (n=15)	Category II (n=15)	Category III (n=14)
<b>Demographics</b>			
Age (years)	61± 6.07	48.3 ± 13	47 ± 17.16
Female Sex	11 (68.7%)	9 (64.3%)	6 (46.1%)
Employment status			
<sup>2</sup> Salaried worker	03	11	11
<sup>2</sup> Retired	10	03	02
<sup>2</sup> Unemployed	03	-	-
<b>Life style</b>			
Current Smoking	-	06 (42.8%)	06 (46.1%)
Alcohol (units per week)	-	3.1	3.4
Physical activities (total MET/per week)	988	1018	1122
<b>Antropometrics</b>			
BMI (kg/m <sup>2</sup> )	21.13 ± 5.1	26.9 ± 4.9	28.03 ± 4.3
Waist circumference (cm)	116 ± 17	117 ± 13	117 ± 11
<b>Dietary Composition</b>			
Total energy intake (K cal)	1971± 171	1836 ± 202	1918 ± 188
Total fat (g)	42 ± 36	50 ± 20	56 ± 18
SFA (g)	10 ± 31	17 ± 11	22 ± 33
MUFA (g)	12 ± 30	14 ± 12	17 ± 11
PUFA (g)	15.1 ± 11		
Omega-3	0.21 ± 11	0.46 ± 0.18	0.88 ± 0.21
Carbohydrate (g)	294 ± 84	334 ± 88	348 ± 78
Protein (g)	33 ± 13	53 ± 12	56 ± 11
Total fiber (g)	21 ± 11	12.1± 5.1	12 ± 6
Fruits (g)	133 ± 37.43	110 ± 61.31	98 ± 46
Vegetables (g)	156 ± 78.11	126 ± 71	126 ± 31
<b>Clinical measurements</b>			
S Cholesterol (total ) (mg%)	214 ± 31.1	234 ± 43.4	241 ± 37.4
LDL (mg %)	108 ± 31.6	131 ± 18.6	132 ± 41.1
HDL (g)	43 ± 6.6	39 ± 12.3	39 ± 9.2
TG (mg%)	131± 68.6	153 ± 32.4	158 ± 78.9
FBS (mg%)	78± 11	76± 18	78 ± 17
<b>Blood pressure</b>			
Systolic (mm Hg)	118± 06	121 ± 88	122 ± 37
Diastolic (mm Hg)	78 ± 1.01	79 ± 07	79 ± 11



**Table 3.** Omega-3 index values for each category

Category	N <sup>1</sup>	Mean	Range	SD <sup>2</sup>	SEM <sup>3</sup>	Risk zone
I	16	4.63	2.27-7.89	1.624	0.406	High risk
II	14	6.96	4.54-9.84	1.568	0.419	Intermediate risk
III	13	7.93	5.78-10.28	1.455	0.403	Intermediate risk
II+III	27	7.43	4.54-10.28	1.565	0.301	Intermediate risk

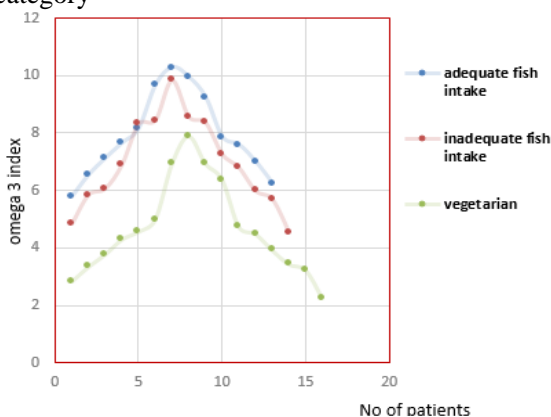
**Table 4.** Comparison of the Omega-3 indices between categories

	Mean difference	T value	Standard error difference	Significance (2 tailed)
Category I & category II	2.33	3.989	0.59	0.000433
Category I & Category III	3.29	5.694	0.58	0.000004
Category II & Category III	0.96	1.653	0.58	0.111

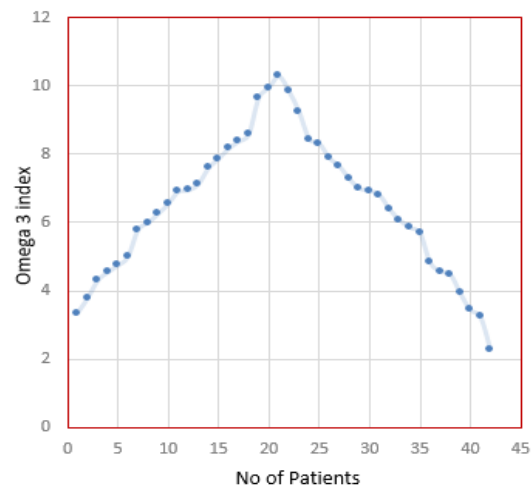
**Distribution of Omega-3 index within each category**

The mean Omega-3 indices in the 3 categories show a wide range within each category. When plotted as graphs, the distribution suggests a bell shaped curve (Figures 1& 2, table 5).

**Figure 1.** Distribution of Omega-3 indices in each category



**Figure 2** Distribution of the Omega-3 indices in the total study population



This is demonstrable even in the optimal fish consumption category where, 61.54% of subjects did not achieve the low risk zone value for the Omega-3 index.

<sup>1</sup> Number

<sup>2</sup> Standard deviation

<sup>3</sup>Standard error of mean



**Table 5.** Distribution of risk zones within each category

Category	Risk zone	%
I	Low	0%
	Intermediate	56.25%
	High	43.75%
II	Low	35.71%
	Intermediate	64.28%
	High	0%
III	Low	38.46%
	Intermediate	61.54%
	High	0%

When the total study population is considered the Omega-3 index distribution still describes a bell shaped curve (Figure 2).

## Discussion

Our study confirms that the Omega-3 index is heavily influenced by the quantum of fish consumed. The pure vegetarians have an Omega-3 index in the high risk zone which possibly could be one risk factor contributing towards the high prevalence of ischemic heart disease in the predominantly vegetarian populations in Asia.

It is calculated that the Sri Lankan free living subjects classified as having an optimal fish consumption would have had the diet providing >0.9 g of 20:5n-3(EPA) +22:6n-3(DHA). This compares well with the fact that in the USA the average diet supplies 0.1-0.2g/day of Omega-3 fatty acids. On the other hands Greenland Eskimos have a very high intake of 10.5g/day [2, 25].

The study reveals that considerable individual variation exists in incorporating dietary fatty acids in to cell membranes, in that only 38.46 % of individuals with optimal fish intake had Omega-3 indices in the low risk zone. This fact needs to be emphasized because assessment of the dietary intake of Omega-3 fatty acids would not on its own indicate the true status of membrane Omega-3

content. It is the cell membrane composition that is important as that would be the biochemical substrate which would finally confer benefit against atherosclerotic disease. In the vegetarian category none of the subjects had an Omega-3 index in the low risk zone. The data from the dietary questionnaire could not establish high intake of 18:3n-3(ALA) in Sri Lankan subjects.

The findings of this study serves to emphasize the importance of assaying the Omega-3 index, if the Omega-3 status is to be considered a modifiable risk factor. That the dietary intake does not seem to be a sufficiently strong predictor of the Omega-3 index has been demonstrated even in previous studies which showed that dietary intake of fish oil as assessed by food questionnaires does not give data which will accurately predict the Omega-3 index of erythrocytes. In fact, the predictive value appeared to be weak. [20,26].

### *Omega-3 intake & cardiovascular protection*

In order to give evidence based recommendations for the quantum of fish consumption required for cardiovascular protection it is necessary to consider the information which can be gleaned from published studies. The postulated clinical effects are given in table 6.

Definitive recommendations for fish consumption needed for protective action is as yet not determined probably because the relationship between dietary Omega-3 content and the Omega-3 index is non linear.

In the GISSI prevenzione trial, survivors of myocardial infarction were studied to whom 850g/day of fish were administered. A benefit with respect to sudden cardiac death and other major cardiac adverse effects was demonstrable commencing from the 10th- - 120th day of supplementation [43,44].

In the DART trial, oily fish was given to survivors of a first myocardial infarction amounting to two servings per week. After 2 years a benefit was demonstrable with respect to reduction in a second myocardial infarction. The intake of fatty fish was modest, approximating 300g per week [45].

In the study of Sisocovick et al, 5.5g of Omega-3 fatty acid per month was estimated to approximate one fatty fish meal per week [6]. This was associated with a 70% reduction in the risk for a primary cardiac arrest. Other studies too have confirmed that a modest intake of 22:6n-3(DHA)

**Table 6.** Clinical effects of fish oil.**Research**

<i>Data from human studies</i>	<p>Reduces blood pressure [28].</p> <p>Attenuates vasoconstriction of angiotensin II [29,30].</p> <p>Reduces level of systemic inflammation [31].</p> <p>Improves left ventricular diastolic filling [32].</p> <p>Reduces excitability of cells [33].</p> <p>Stabilizes unstable plaques [34].</p> <p>Improves endothelial function [35].</p> <p>Decreases LDL levels [36].</p> <p>Decreases triglycerides levels [36].</p> <p>Decreases platelet aggregatability [37].</p>
<i>Data from animal studies</i>	
In rats	<p>Reduces peripheral vascular resistance [38].</p> <p>Reduces myocardial oxygen consumption [39].</p> <p>Increases contractile recovery after reperfusion [39].</p> <p>Reduces hypertrophy in hypertensive animals [40].</p>
In non rodent animals	Anti atherosclerotic effect [35].
In non human primates	Enhances left ventricular diastolic function [41,42].

&20:5n-3(EPA) of 250-500g /day reduces the risk of cardiac mortality by ~35% [46].

As a fatty fish meal could contain widely varying amounts of Omega-3 fatty acid, it would be difficult to recommend a specific number of fish meals, although the physicians' health study showed, with regard to strokes, that subjects who had an intake of five fish meals a week fared better than those with an intake of a single fish meal per week (47). Thus, although the AHA recommends 1g /day of fish oil (20:5n-3+22:6n-3) for subjects suffering from ischemic heart disease even smaller amounts may be beneficial. Consumption not less than 250g per day has been suggested for healthy individuals.

A Cochrane meta analysis on the effect of Omega-3 fatty acids on mortality, combined cardiovascular events or cancer has been published, which concluded that there was no clear benefit of Omega-3 PUFA on any of these end points. It has however been pointed out that the null result seems to have occurred due to the DART-2 data which were against any benefit derived from fish oil consumption. Once the DART-2 data is excluded, the Cochrane analysis shows benefit. Similar findings have been reported by a recent meta analysis by Aung *et al* [48].

It is accepted that if fish oils are contaminated by methyl mercury or organic compounds, the benefits of the fish oil would be mitigated or reversed. Hence nutritionists do warn against excess consumption.



## Conclusions

The results of this study suggest that consuming > 250g of fish per week give a protective Omega-3 indices in approximately one third of individuals. However marked individual variability suggests that assay of the Omega-3 index would be appropriate for better defining the risk zone of an individual.

## Addenda - Case reports

### Intervention with supplement of flax seed oil or marine omega-3 oil

17 of the 45 study subjects had commenced on dietary supplements with commercial preparations of flax seed oil or fish oil in capsule form, on being informed of the value of the omega-3 index in cardiovascular protection by the administrators of the FFQs at the final review. The change in the omega-3 indices in subjects who had consistently consumed a specific branded supplement of either flax seed oil or fish oil for 3 months are presented here.

#### Supplementation in Category- I

Three subjects who were pure vegetarians had commenced supplementation with a flax seed oil capsule preparation providing 1.5g/day of flax seed oil and had been on the supplement for 3 months or more. On the basis that 70% of flax seed oil would be

$\alpha$  LNA, these subjects would have had their dietary intake fortified by approximately 1g/day of  $\alpha$  LNA.

All 3 subjects had low omega-3 indices at baseline which showed a non-significant increase with flax seed oil supplementation. (Table 6). However the omega-3 indices did not achieve the low risk zone value. None of the subjects in Category I had consumed fish oil supplements.

#### Supplementation in Category- II

7 subjects whose fish consumption was < 250g fish/week had commenced on flax seed oil supplementation consuming 1.5g/day, continuously for 3 months.

Three subjects who had omega-3 indices in the intermediate risk zone at baseline demonstrated a rise in their omega-3 indices into the low risk zone. However the response to flax seed oil supplementation was diverse (figure 3). No confounding factors could be identified which could account for the difference in response seen in individual patients. The cohort as a whole showed a statistically non-significant increase in the omega-3 index. (Table 7, figure 3)

Yet another 7 patients in Category II had commenced supplementation with fish oil capsules providing 600mg/day of EPA and DHA, continuously for 3 months. 6 subjects demonstrated an increase in their omega-3 indices to the low risk zone. The cohort as a whole demonstrated a statistically significant rise in the omega-3 index with fish oil supplementation. (Table 8)

The estimated consumption of  $\alpha$  LNA in the western countries is 0.6-1.7g/d for males and 0.5-1.4g/d for females.

The percentage of  $\alpha$  LNA that is converted into the longer chain FA is controversial.





**Table 6** – Omega-3 index values in vegetarian group, pre and post flax seed oil supplementation

	Mean	N	Std deviation	Std Error of Mean
Pair 1				
Pre Omega-3 index	3.7300	3	.86608	.50003
Post Omega-3 index	4.4500	3	.45000	.25981

	Paired differences					t	df	Sig(2 tailed)
	Mean	Std deviation	Std Error of mean	95% confidence interval of the difference				
				Lower	Upper			
Pair 1 Pre Omega3 index – Post Omega-3 index	-7.200	.41725	.24090	-1.75651	.31651	-2.989	2	.096

**Table 7-** Omega-3 index values in inadequate fish intake group, pre and post flax seed oil supplementation

	Mean	N	Std deviation	Std Error of Mean
Pair 1				
Pre Omega-3 index	7.7329	7	1.4423	.54515
Post Omega-3 index	8.7071	7	1.00970	.38163

	Paired differences					t	df	Sig(2 tailed)
	Mean	Std deviation	Std Error of mean	95% confidence interval of the difference				
				Lower	Upper			
Pair 1 Pre Omega3 index – Post Omega-3 index	-9.7429	1.78874	.67608	-2.62860	.68002	-1.441	6	.200



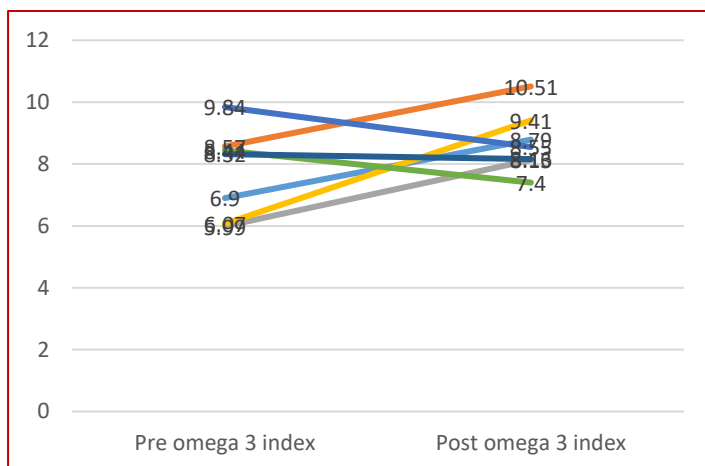
**Table 8-** Omega-3 index values in inadequate fish intake group, pre and post marine Omega-3 oil supplementation

	Mean	N	Std deviation	Std Error of Mean
Pair 1				
Pre Omega-3 index	6.1943	7	1.36739	.51683
Post Omega-3 index	10.0786	7	2.12248	.80222

	Paired differences					t	df	Sig (2 tailed)
	Mean	Std deviation	Std Error of mean	95% confidence interval of the difference				
				Lower	Upper			
Pair 1 Pre Omega3 index – Post Omega-3 index	-3.88429	1.76940	.66877	-5.52070	-2.24787	-5.808	9	.001

**Figure 3-**Category II : supplementation with flax seed oil

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Subject 7
Pre supplemental Omega-3 index	6.9	8.57	5.99	6.07	9.84	8.44	8.32
Post supplemental Omega-3 index	8.79	10.51	8.13	9.41	8.55	7.4	8.16

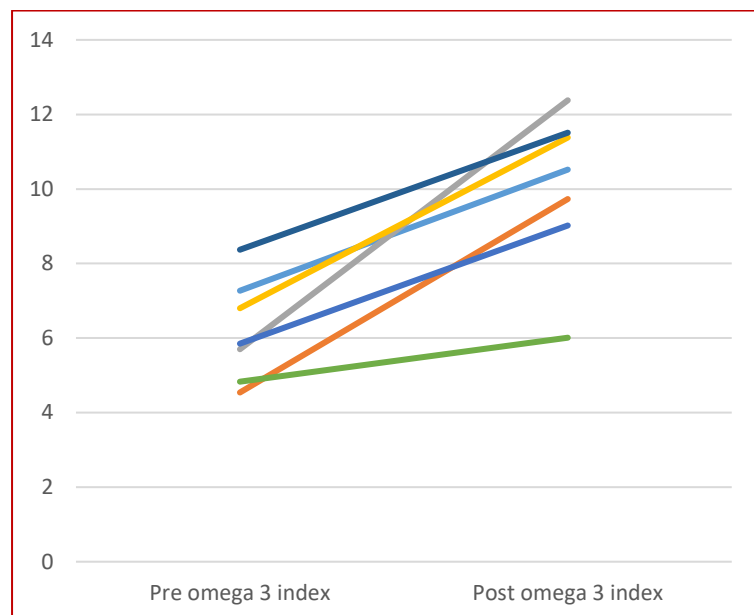




**Figure 4-** Category II -Supplementation with marine Omega-3 fish oil

**Research**

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Subject 7
Pre supplemented Omega-3 index	7.27	4.54	5.7	6.8	5.85	4.83	8.37
Post supplemented Omega-3 index	10.52	9.73	12.38	11.38	9.02	6.01	11.51



**Table 9:** Estimates of Omega-3FA/ALA content in foods

	Serving Size	Omega-3 content (g)	ALA content (g)
<b>Fats Oil <sup>(50)</sup></b>			
Coconut oil	5ml	t	t
Palm oil	nc		
Soya oil	5ml	0	0.31
Canola oil	5ml	0	0.42
Wheat germ oil	nc		
Flaxseed oil	nc		
Olive oil	nc		
Margarine fortified with Omega-3	nc		
<b>Seed (nuts, beans, grains)</b>			
Flax seed	nc		
Soya beans	175ml (3/4cup)	0	0.76
Soya products	nc		
Peas	175ml (3/4cup)	0	0.11
Almonds	nc		
Pea nuts	144g	0	2.18
Cashew nuts			
Walnuts	nc		
Wild rise	nc		
Eggs	02 eggs	0.07	0.06 – 0.28
Beef (pasture raised )	nc		
Organ meats	nc		



Milk & milk products ( fortified with Omega-3)	nc		
<b>Fish<sup>(18)</sup></b>			
Dark meat	6-8 oz	1.51	0
Canned tuna	6-8 oz	0.42	0
Other fish	6-8 oz	0.48	0
Shrimp, lobster,	6-8 oz	0.32	0
Fish roe	nc		
Spinach <sup>(50)</sup>	100g, wet weight	0	.089
Lettuce	100g, wet weight	0	.026
Red Lettuce	100g, wet weight	.012	.031
Mustered Leaves	100g, wet weight	.032	.048
Purslane	100g, wet weight	.001	.405

On the assumption that approximately 5% of  $\alpha$  LNA is converted to EPA it is possible to calculate that 1g of  $\alpha$  LNA will generate 0.05g of EPA. The basic assumption that 5% of  $\alpha$  LNA is converted to EPA is not accepted by all workers, some of whom suggest that only 0.2% of dietary  $\alpha$  LNA is converted to EPA. A value of 2% for the conversion seems reasonable. Hence in the present study, it could be calculated that the subjects ingesting flax seed oil capsules had an added omega-3 intake of 21mg and which is considerably lower than the recommended intake.

Of the 3 subjects in Category I who consumed flax seed oil supplements, 2 were females. Of the 7 subjects in Category II who consumed flax seed oil supplements, three were females. It is reported that conversion of  $\alpha$  LNA into longer chain derivation in humans is greater in women compared to men. However no significant difference in the omega-3 index was seen in our subjects.

All subjects consuming fish oil supplements demonstrated a significant rise in the omega-3 indices. The subjects selected for study were on steady-state supplementation with 600mg/d of omega-3 fish oil.

When stroke patients were placed on fish oil supplementation providing 1.2g/d of total omega-3 fatty acid it was found that EPA increased from 1.29±0.91% to 1.63±0.72% and that DHA increased from 3.90±1.12% to 5.29±1.71%. Thus there is probably a wide individual variability in blood omega-3 levels related to dietary intake. All patients consuming supplementations of fish oil probably show a trend towards an increase in the omega-3 index which was seen even in the small number of subjects in the present study.

## Conclusion

Marine Omega-3 oil supplementation has greater efficacy in improving the omega-3 index than flax seed oil supplementation.

**Limitation of the study:** - The relatively small number of study subjects in our series raises the necessity for a larger trial.

**Acknowledgement:** The assay of Omega-3 index was arranged by Seven Seas Limited, Hull, England.



## References

1. Sinclair, H.M., *The Diet of Canadian Indians and Eskimos*. Proceedings of the Nutrition Society, 2007. **12**(1): p. 69-82.
2. Bang, H.O., J. Dyerberg, and N. Hjoorne, *The composition of food consumed by Greenland Eskimos*. Acta Med Scand, 1976. **200**(1-2): p. 69-73.
3. Kromhout, D., E.B. Bosschieter, and C. de Lezenne Coulander, *The inverse relation between fish consumption and 20-year mortality from coronary heart disease*. N Engl J Med, 1985. **312**(19): p. 1205-9.
4. Lemaitre, R.N., et al., *n-3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study*. Am J Clin Nutr, 2003. **77**(2): p. 319-25.
5. Iso, H., et al., *Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I*. Circulation, 2006. **113**(2): p. 195-202.
6. Siscovick, D.S., et al., *Dietary intake and cell membrane levels of long-chain n-3 polyunsaturated fatty acids and the risk of primary cardiac arrest*. JAMA, 1995. **274**(17): p. 1363-7.
7. Keli, S.O., E.J. Feskens, and D. Kromhout, *Fish consumption and risk of stroke. The Zutphen Study*. Stroke, 1994. **25**(2): p. 328-32.
8. Gillum, R.F., M.E. Mussolino, and J.H. Madans, *The relationship between fish consumption and stroke incidence. The NHANES I Epidemiologic Follow-up Study (National Health and Nutrition Examination Survey)*. Arch Intern Med, 1996. **156**(5): p. 537-42.
9. von Schacky, C., *The role of omega-3 fatty acids in cardiovascular disease*. Curr Atheroscler Rep, 2003. **5**(2): p. 139-45.
10. Harris, W.S., et al., *Towards establishing dietary reference intakes for eicosapentaenoic and docosahexaenoic acids*. J Nutr, 2009. **139**(4): p. 804s-19s.
11. Mozaffarian, D., et al., *Effect of fish oil on heart rate in humans: a meta-analysis of randomized controlled trials*. Circulation, 2005. **112**(13): p. 1945-52.
12. Mozaffarian, D., et al., *Dietary fish and n-3 fatty acid intake and cardiac electrocardiographic parameters in humans*. J Am Coll Cardiol, 2006. **48**(3): p. 478-84.
13. Mozaffarian, D., et al., *Fish intake and risk of incident atrial fibrillation*. Circulation, 2004. **110**(4): p. 368-73.
14. Carlson, S.E., et al., *Visual-acuity development in healthy preterm infants: effect of marine-oil supplementation*. Am J Clin Nutr, 1993. **58**(1): p. 35-42.
15. Neuringer, M., G.J. Anderson, and W.E. Connor, *The essentiality of n-3 fatty acids for the development and function of the retina and brain*. Annu Rev Nutr, 1988. **8**: p. 517-41.
16. Leitzmann, M.F., et al., *Dietary intake of n-3 and n-6 fatty acids and the risk of prostate cancer*. Am J Clin Nutr, 2004. **80**(1): p. 204-16.
17. Angerer, P., et al., *Effect of dietary supplementation with omega-3 fatty acids on progression of atherosclerosis in carotid arteries*. Cardiovasc Res, 2002. **54**(1): p. 183-90.
18. Iso, H., et al., *Intake of fish and omega-3 fatty acids and risk of stroke in women*. JAMA, 2001. **285**(3): p. 304-12.
19. von Schacky, C. and W.S. Harris, *Cardiovascular benefits of omega-3 fatty acids*. Cardiovasc Res, 2007. **73**(2): p. 310-5.
20. Harris, W.S., et al., *Omega-3 fatty acids in cardiac biopsies from heart transplantation patients: correlation with erythrocytes and response to supplementation*. Circulation, 2004. **110**(12): p. 1645-9.
21. Harris, W.S., *The omega-3 index as a risk factor for coronary heart disease*. Am J Clin Nutr, 2008. **87**(6): p. 1997s-2002s.
22. Priori, S.G., et al., *Update of the guidelines on sudden cardiac death of the European Society of Cardiology*. Eur Heart J, 2003. **24**(1): p. 13-5.
23. Harris, W.S., *Extending the cardiovascular benefits of omega-3 Fatty acids*. Curr Atheroscler Rep, 2005. **7**(5): p. 375-80.
24. Harris, W.S. and C. Von Schacky, *The Omega-3 Index: a new risk factor for death from coronary heart disease?* Prev Med, 2004. **39**(1): p. 212-20.
25. Raper, N.R., F.J. Cronin, and J. Exler, *Omega-3 fatty acid content of the US food supply*. J Am Coll Nutr, 1992. **11**(3): p. 304-8.
26. von Schacky, C., *Omega-3 fatty acids and cardiovascular disease*. Curr Opin Clin Nutr Metab Care, 2007. **10**(2): p. 129-35.
27. Dyerberg, J., H.O. Bang, and N. Hjoorne, *Fatty acid composition of the plasma lipids in Greenland Eskimos*. Am J Clin Nutr, 1975. **28**(9): p. 958-66.
28. Geleijnse, J.M., et al., *Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials*. J Hypertens, 2002. **20**(8): p. 1493-9.
29. Chin, J.P., et al., *Marine oils dose-dependently inhibit vasoconstriction of forearm resistance vessels in humans*. Hypertension, 1993. **21**(1): p. 22-8.
30. Kenny, D., et al., *Effect of omega-3 fatty acids on the vascular response to angiotensin in normotensive men*. Am J Cardiol, 1992. **70**(15): p. 1347-52.
31. James, M.J., R.A. Gibson, and L.G. Cleland, *Dietary polyunsaturated fatty acids and inflammatory mediator production*. Am J Clin Nutr, 2000. **71**(1 Suppl): p. 343S-8S.
32. Grimsgaard, S., et al., *Effects of highly purified eicosapentaenoic acid and docosahexaenoic*



- acid on hemodynamics in humans. *Am J Clin Nutr*, 1998. **68**(1): p. 52-9.
33. Kang, J.X. and A. Leaf, *Prevention of fatal cardiac arrhythmias by polyunsaturated fatty acids*. *Am J Clin Nutr*, 2000. **71**(1 Suppl): p. 202S-7S.
34. Thies, F., et al., *Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomised controlled trial*. *Lancet*, 2003. **361**(9356): p. 477-85.
35. von Schacky, C., *Prophylaxis of atherosclerosis with marine omega-3 fatty acids. A comprehensive strategy*. *Ann Intern Med*, 1987. **107**(6): p. 890-9.
36. von Schacky, C., *A review of omega-3 ethyl esters for cardiovascular prevention and treatment of increased blood triglyceride levels*. *Vasc Health Risk Manag*, 2006. **2**(3): p. 251-62.
37. Dyerberg, J. and H.O. Bang, *Haemostatic function and platelet polyunsaturated fatty acids in Eskimos*. *Lancet*, 1979. **2**(8140): p. 433-5.
38. Demaison, L., et al., *Effect of dietary polyunsaturated fatty acids on contractile function of hearts isolated from sedentary and trained rats*. *Reprod Nutr Dev*, 2000. **40**(2): p. 113-25.
39. Pepe, S. and P.L. McLennan, *Cardiac membrane fatty acid composition modulates myocardial oxygen consumption and postischemic recovery of contractile function*. *Circulation*, 2002. **105**(19): p. 2303-8.
40. von Au, D., et al., *Influence of a diet rich in fish oil on blood pressure, body weight and cardiac hypertrophy in spontaneously hypertensive rats*. *Eur J Appl Physiol Occup Physiol*, 1988. **58**(1-2): p. 97-9.
41. Charnock, J.S., P.L. McLennan, and M.Y. Abeywardena, *Dietary modulation of lipid metabolism and mechanical performance of the heart*. *Mol Cell Biochem*, 1992. **116**(1-2): p. 19-25.
42. McLennan, P.L., et al., *Dietary fat modulation of left ventricular ejection fraction in the marmoset due to enhanced filling*. *Cardiovasc Res*, 1992. **26**(9): p. 871-7.
43. *Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico*. *Lancet*, 1999. **354**(9177): p. 447-55.
44. Marchioli, R., et al., *Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione*. *Circulation*, 2002. **105**(16): p. 1897-903.
45. Burr, M.L., et al., *Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART)*. *Lancet*, 1989. **2**(8666): p. 757-61.
46. Baigent, C., et al., *Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins*. *Lancet*, 2005. **366**(9493): p. 1267-78.
47. Morris, M.C., et al., *Fish consumption and cardiovascular disease in the physicians' health study: a prospective study*. *Am J Epidemiol*, 1995. **142**(2): p. 166-75.
48. Aung, T., et al., *Associations of Omega-3 Fatty Acid Supplement Use With Cardiovascular Disease Risks: Meta-analysis of 10 Trials Involving 77917 Individuals*. *JAMA Cardiol*, 2018. **3**(3): p. 225-234.
49. Burdge, G.C. and P.C. Calder, *Dietary alpha-linolenic acid and health-related outcomes: a metabolic perspective*. *Nutr Res Rev*, 2006. **19**(1): p. 26-52.
50. Wickramanayake, T.W., *Food and Nutrition*. 3rd ed. 1996: Trumpet Publisher.