Does a fish a day keep the doctor away?

The rôle of omega-3 fatty acids in psychiatry

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Thursday, 20 December, 12

Good morning, everyone. Thank you for coming.

My topic today is omega-3 fatty acids and the role that they play in mental illness.

Outline

- What are omega-3 fatty acids?
- Why are they important?
- What about omega-6 and omega-9 fatty acids?
- How do they affect our health?
- What is their role in mental health?
- What can I do?

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This is what I hope to cover today. What are omega-3s, what makes them important, how do they affect our physical and our mental health, and what can we as individuals do to make use of this information?

Lipids: Fats & Oils

- Fats
  - solid at room temperature
  - found in animals (eg, beef fat)
- Oils
  - liquid at room temperature
  - found in plants (eg corn oil, safflower oil) & in fish
- Usually occur as triglycerides
  - one glycerol molecule
  - three hydrocarbon chains (fatty acids)

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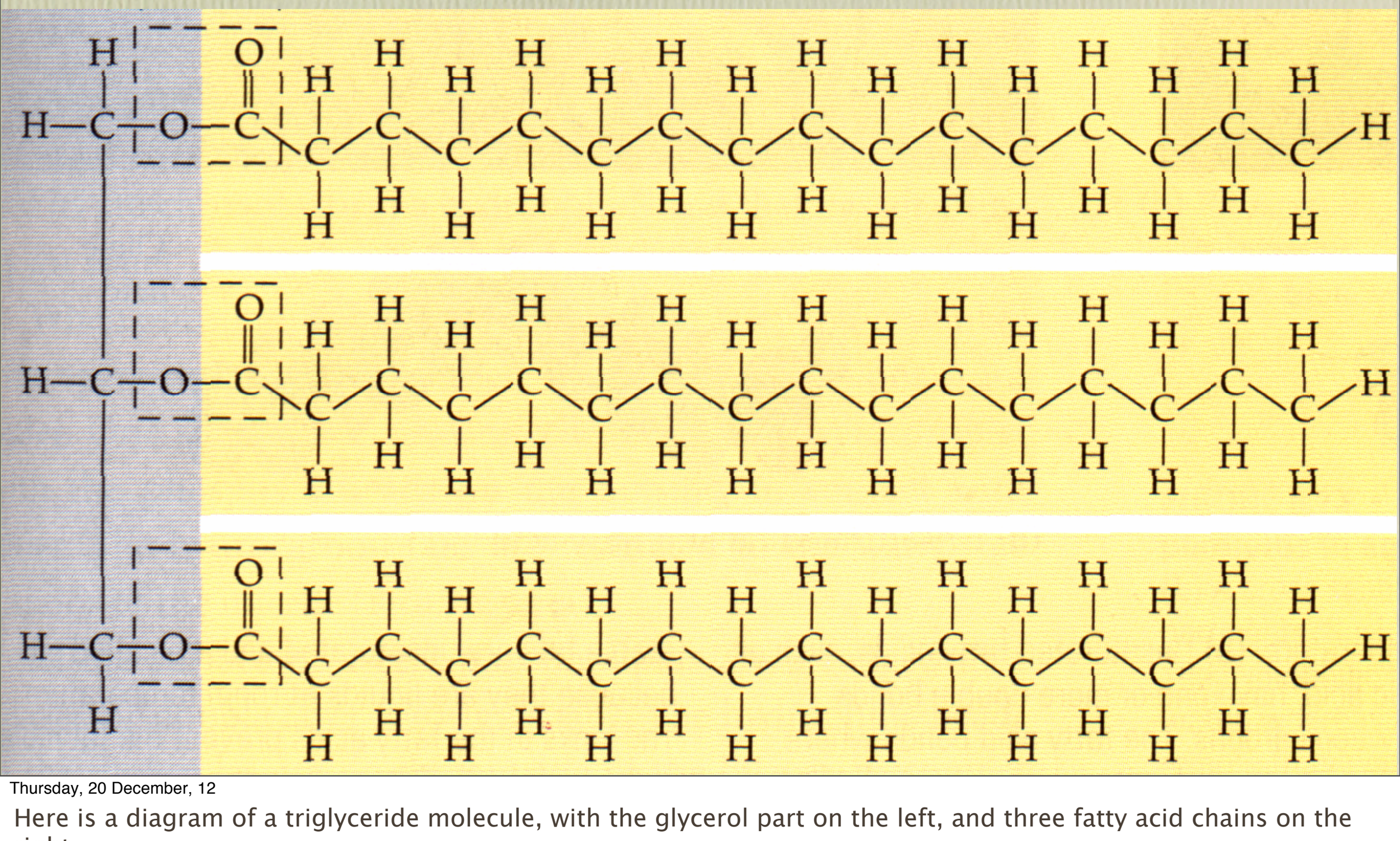
Let's begin by talking about lipids, or more simply, fats and oils.

Fats are solid at room temperature, and come from animals.

Oils are liquid at room temperature, and come from plants and fish.

The most common type of lipid molecule is the triglyceride molecule. This consists of one glycerol molecule with three fatty acid chains attached to it.

A triglyceride molecule



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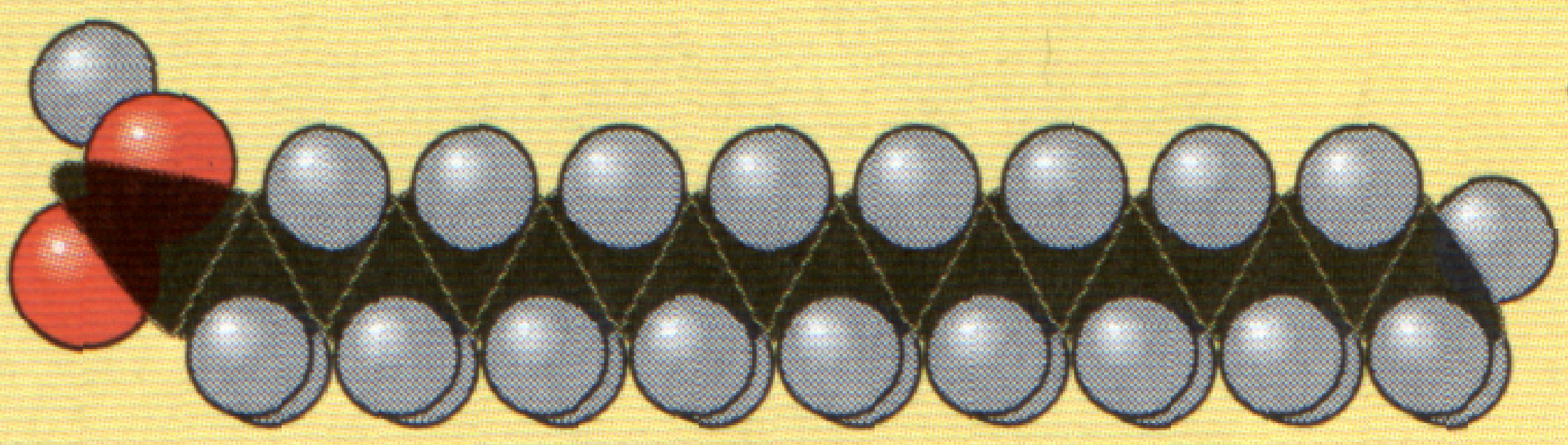
Here is a diagram of a triglyceride molecule, with the glycerol part on the left, and three fatty acid chains on the right.

Saturated fatty acid



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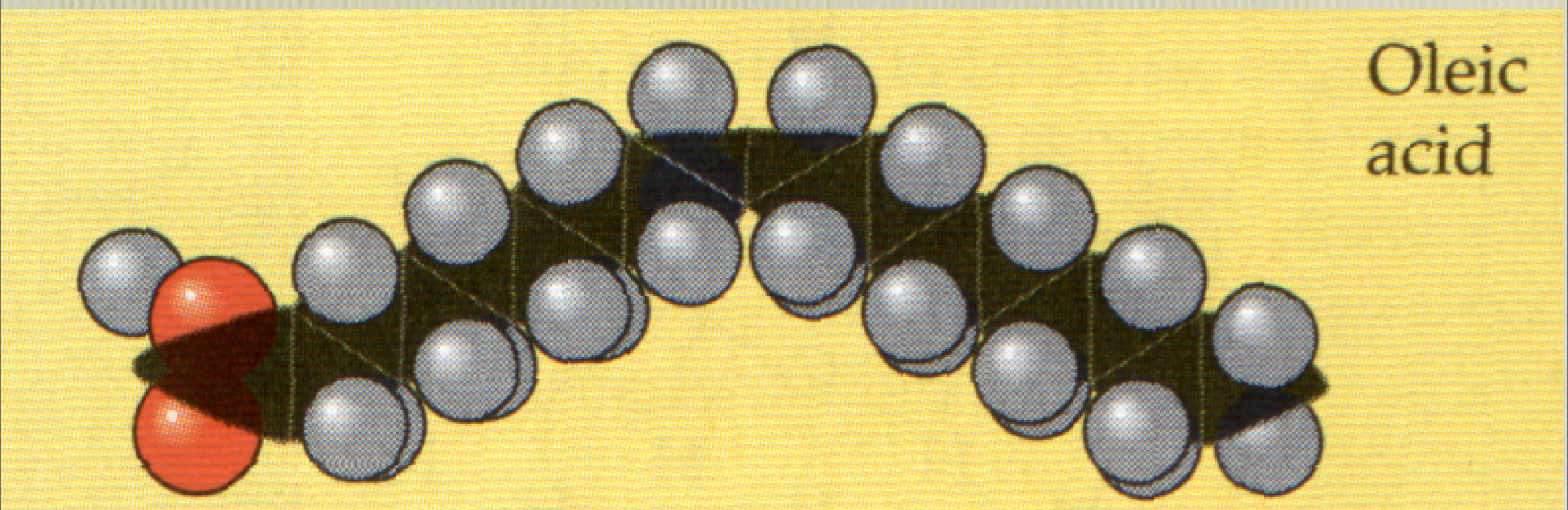
The fatty acids come in two kinds: saturated fatty acids, in which every carbon atom has at least two hydrogens attached to it; in this diagram, the black pieces are carbon, red is oxygen, and the grey balls are hydrogen.

This particular fatty acid has 18 carbons, but any length of hydrocarbon chain is possible.

Unsaturated fatty acid



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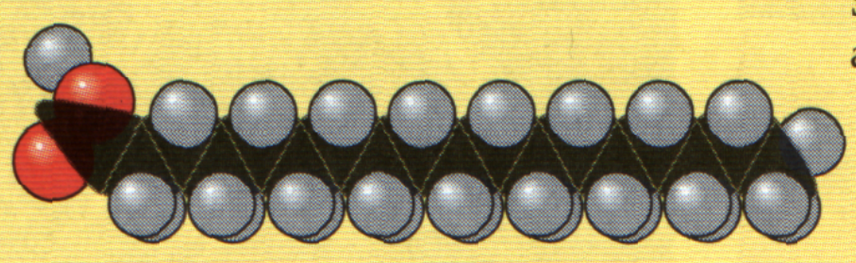
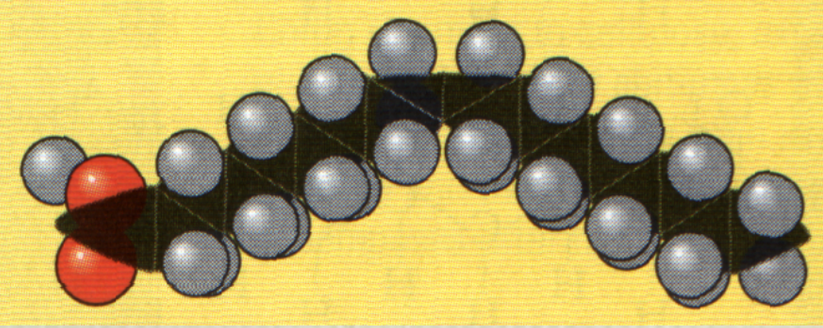
The other kind of fatty acid is unsaturated, in which one or more pairs of adjoining carbon atoms have a double bond between them, meaning that each of these carbon atoms will have only one hydrogen attached. Note that the double bond causes the fatty acid to be kinked.

Saturated vs Unsaturated Fatty Acids



Stearic acid



Oleic acid

Has maximum number of hydrogen atoms possible

Has less than maximum number of hydrogen atoms possible

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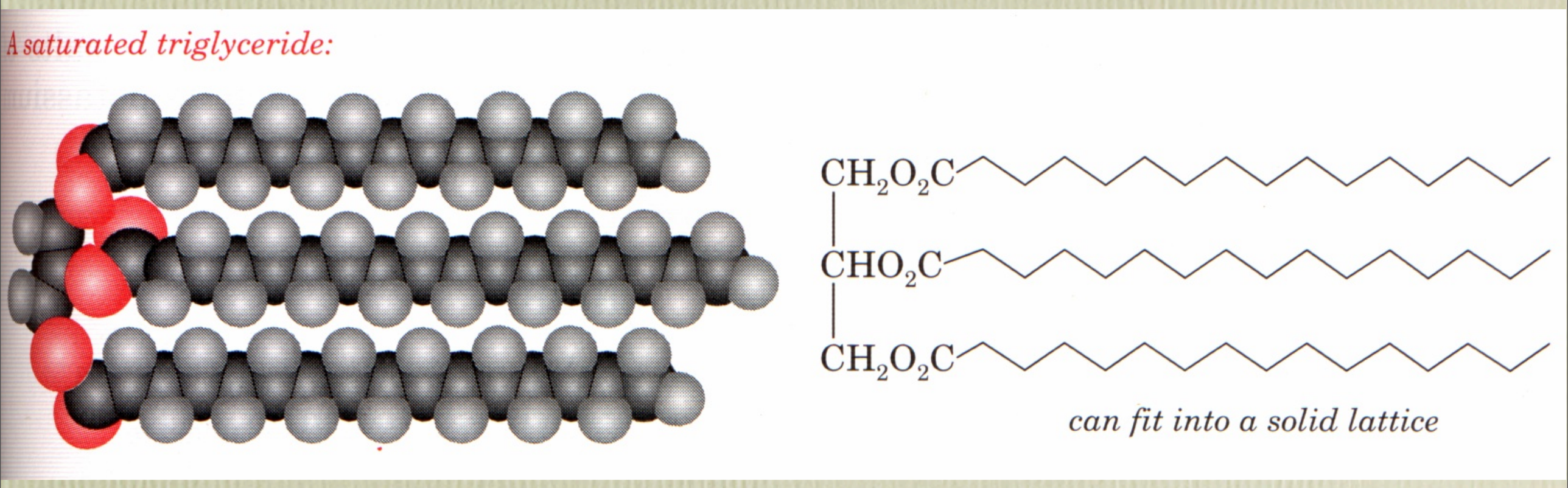
In general, triglycerides that have saturated fatty acids tend to be solid at room temperature, and are thus called fats. With unsaturated fatty acids, you will get lipids that are liquid at room temperature, that is, oils.

Saturated triglyceride



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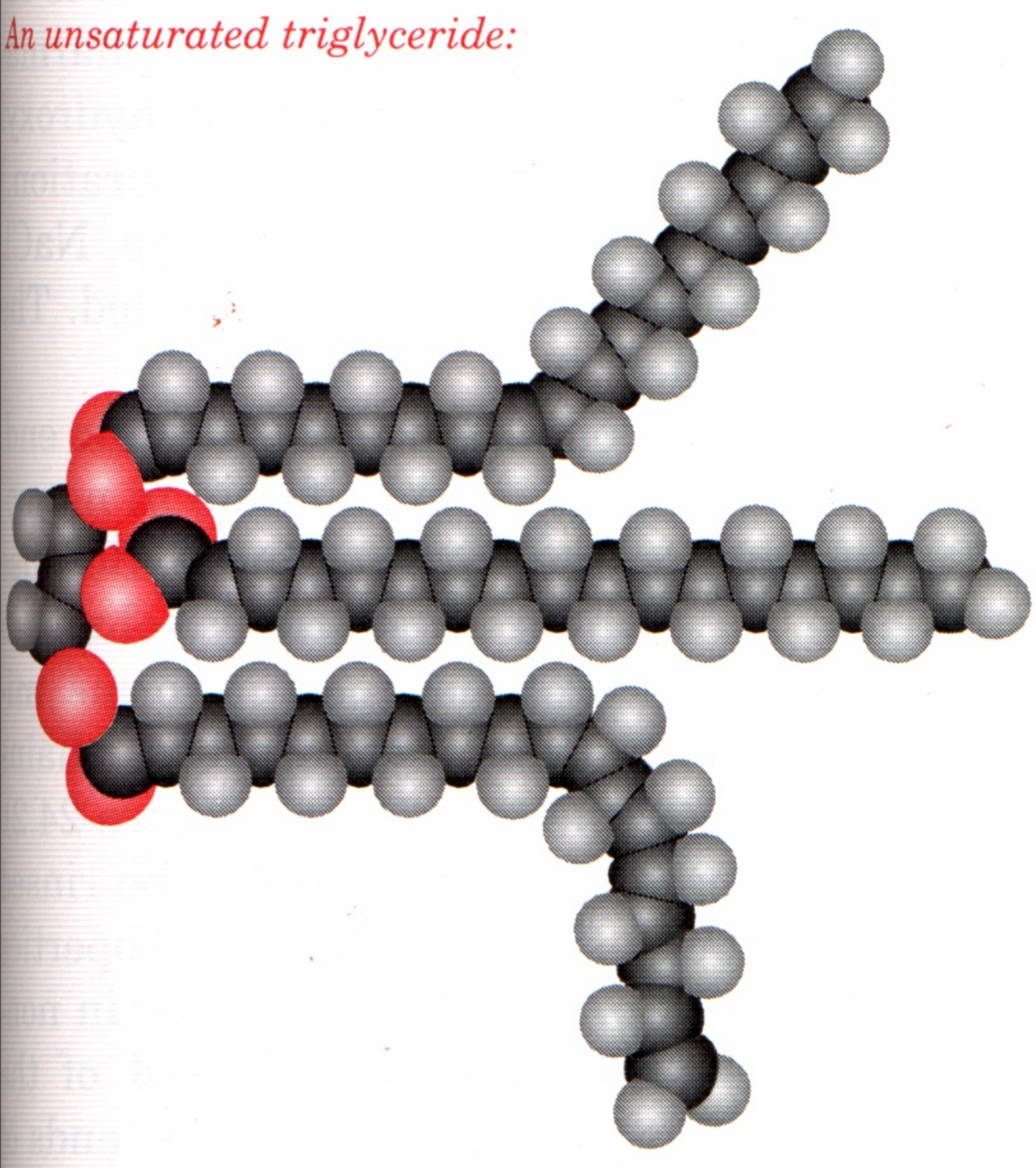
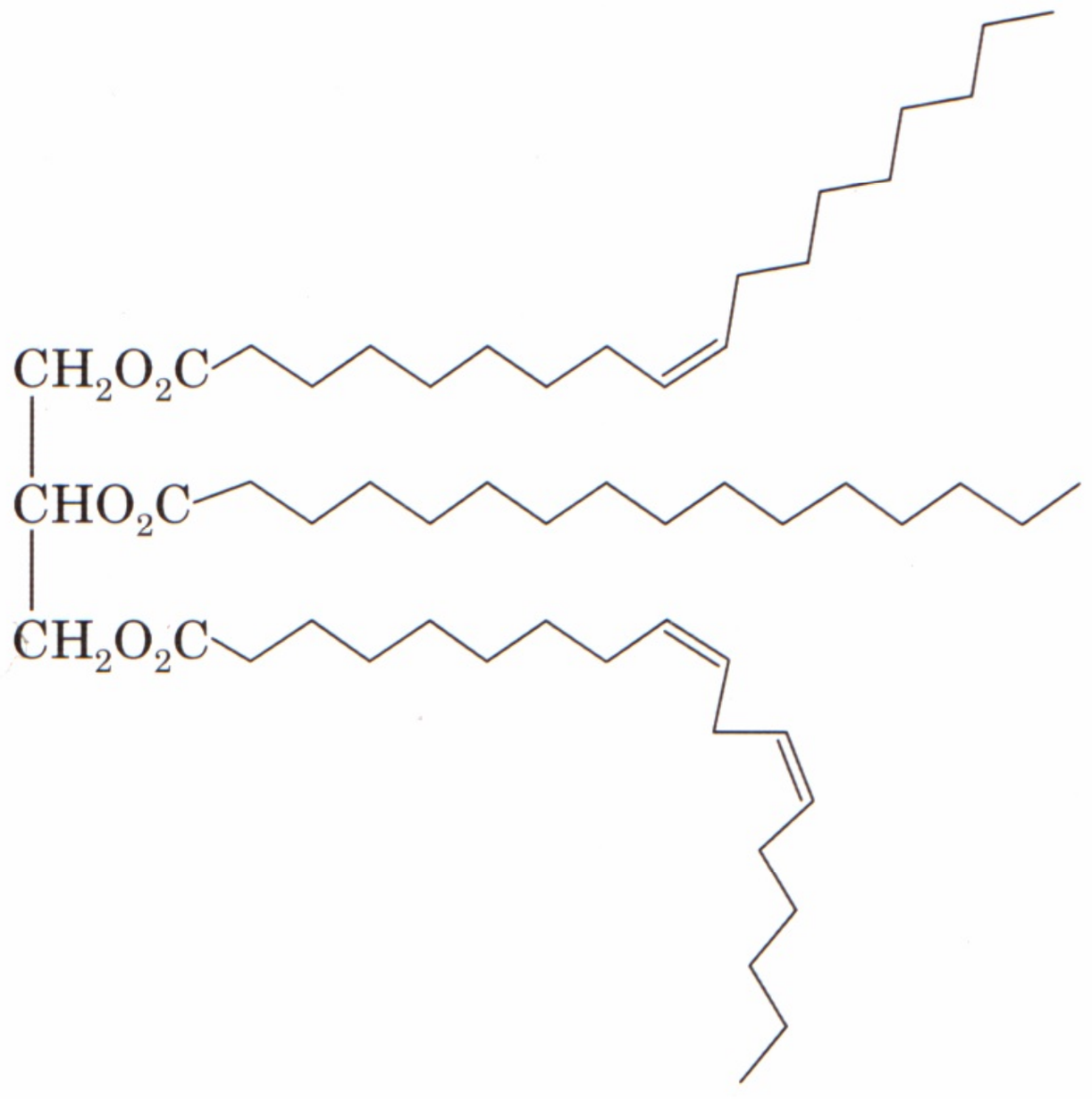
Here is a triglyceride with three saturated fatty acids. As you can see, the straight chains make for a compact molecule. Thus, the individual triglyceride molecules can pack closely together, which helps it to be solid at room temperature.

Unsaturated triglyceride





cannot fit as well into a lattice

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This triglyceride has a monounsaturated fatty acid at the top. Monounsaturated means it has one double bond. The middle fatty acid is saturated, hence straight.

The bottom fatty acid has two double bonds, so it's even more kinked (or is that kinky?) than the fatty acid with one double bond. When a fatty acid has two or more double bonds, it is said to be polyunsaturated.

With this kind of shape, triglyceride molecules with unsaturated fatty acids tend not to pack very closely together, so there is more fluidity.

Fatty acids in humans

- Phospholipids: part of cell membrane structure
- Biological fatty acids usually have an even number of carbons
- PUFAs can be up to 22 carbon atoms long
- LCPUFAs: 20 or 22 carbon atoms long
- Can have up to six double bonds

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Besides being found in the form of triglycerides, animals including humans have fatty acids in the form of phospholipids, which are important structural components of cell membranes. Biological fatty acids almost always have an even number of carbon atoms. Some of the most important fatty acids from the point of view of physiologic functioning are PUFAs, which stands for polyunsaturated fatty acids. In humans and higher mammals, PUFAs are found in chain lengths of up to 22 carbon atoms. The PUFAs with 20 or 22 carbons are sometimes referred to as long chain polyunsaturated fatty acids, LCPUFAs for short.

Saturated Fatty Acids - SFAs

4:0	Butanoic	Butyric	Milk
12:0	Dodecanoic	Lauric	Coconut oil
14:0	Tetradecanoic	Myristic	Coconut, palm oil
16:0	Hexadecanoic	Palmitic	Beef, pork, butter
18:0	Octadecanoic	Stearic	Cocoa butter, beef
20:0	Eicosanoic	Arachidic	Nuts
22:0	Docosanoic	Behenic	Peanut, sunflower oil
24:0	Tetracosanoic	Lignoceric	Peanut oil

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Here is a table with the saturated fatty acids commonly encountered in our diet. The first column shows the designation, where the first number refers to the number of carbon atoms, and the number to the right of the colon indicates the number of double bonds. For saturated fatty acids, this number is, of course, zero.

The second column is the name the organic chemists use, while the third column gives the commonly used name of the fatty acid. The fourth column shows some of the foods containing that fatty acid in appreciable quantities.

Monounsaturated Fatty Acids - MUFAs

14:1	Tetradecenoic	Myristoleic	Beef
16:1 undiff	Hexadecenoic	Palmitoleic	Macadamia nuts, fish, meats
18:1 undiff	Octadecenoic	Oleic	Vegetable oils
20:1	Eicosenoic	Gadoleic	Fish & vegetable oils
22:1 undiff	Docosenoic	Erucic	Mustard oil, fish oil
24:1 c	cis-tetracosenoic	Nervonic	

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This table lists the common monounsaturated fatty acids.

Polyunsaturated Fatty Acids - PUFAs

16:2	Hexadecadienoic		
18:2 n-6	Octadecadienoic	Linoleic	linoleic acid
18:3	Octadecatrienoic	Linolenic	
18:3 n-3 c,c,c		Alpha-linolenic	ALA; αLNA
18:3 n-6 c,c,c		Gamma-linolenic	GLA; γLNA
18:4	Octadecatetraenoic	Parinaric	
20:2 n-6 c,c	Eicosadienoic		

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This is a table for polyunsaturated fatty acids. I would like you to notice, in the first column, the numbers to the right of the colon are now 2 or higher, indicating the number of double bonds as being two or more. In the case of the 18:3 fatty acids, there are several different versions, depending on where the double bonds are located within the chain. Organic chemists count the carbon atoms from the carboxyl end, while the rest of us count from the other end of the chain, called the methyl end.

The first double bond in most species cannot be closer than the third carbon, counting from the methyl end. In the first column, this shows up as n-3, pronounced omega-3. If there is no double bond at the omega-3 position, then the first double bond can be no closer than at the omega-6 position, that is, n-6 in the table. The next possible position for a double bond is the omega-9 position. Thus, the omega number refers to the position of the first double bond in the fatty acid molecule, counting from the methyl end.

The fourth column shows the acronym for some of these fatty acids. I want you to pay particular attention to these. LA, or linoleic acid, is an omega-6 fatty acid found in oils from seeds and grains.

Linolenic acid is the name for the 18:3 fatty acid series. To distinguish the omega-3 and omega-6 varieties, the former is called alpha-linolenic acid, or ALA, and the omega-6 is called gamma-linolenic acid, or GLA.

Polyunsaturated Fatty Acids - PUFAs (2)

20:3	Eicosatrienoic		
20:3 n-3			
20:3 n-6		Homo-gamma-linolenic	
20:4	Eicosatetraenoic		
20:4 n-3			
20:4 n-6		Arachidonic	AA, ARA
20:5 n-3	Eicosapentaenoic	Timnodonic	EPA
22:2	Docosadienoic	Brassic	
22:5 n-3	Docosapentaenoic	Clupanodonic	
22:6 n-3	Docosahexaenoic		DHA

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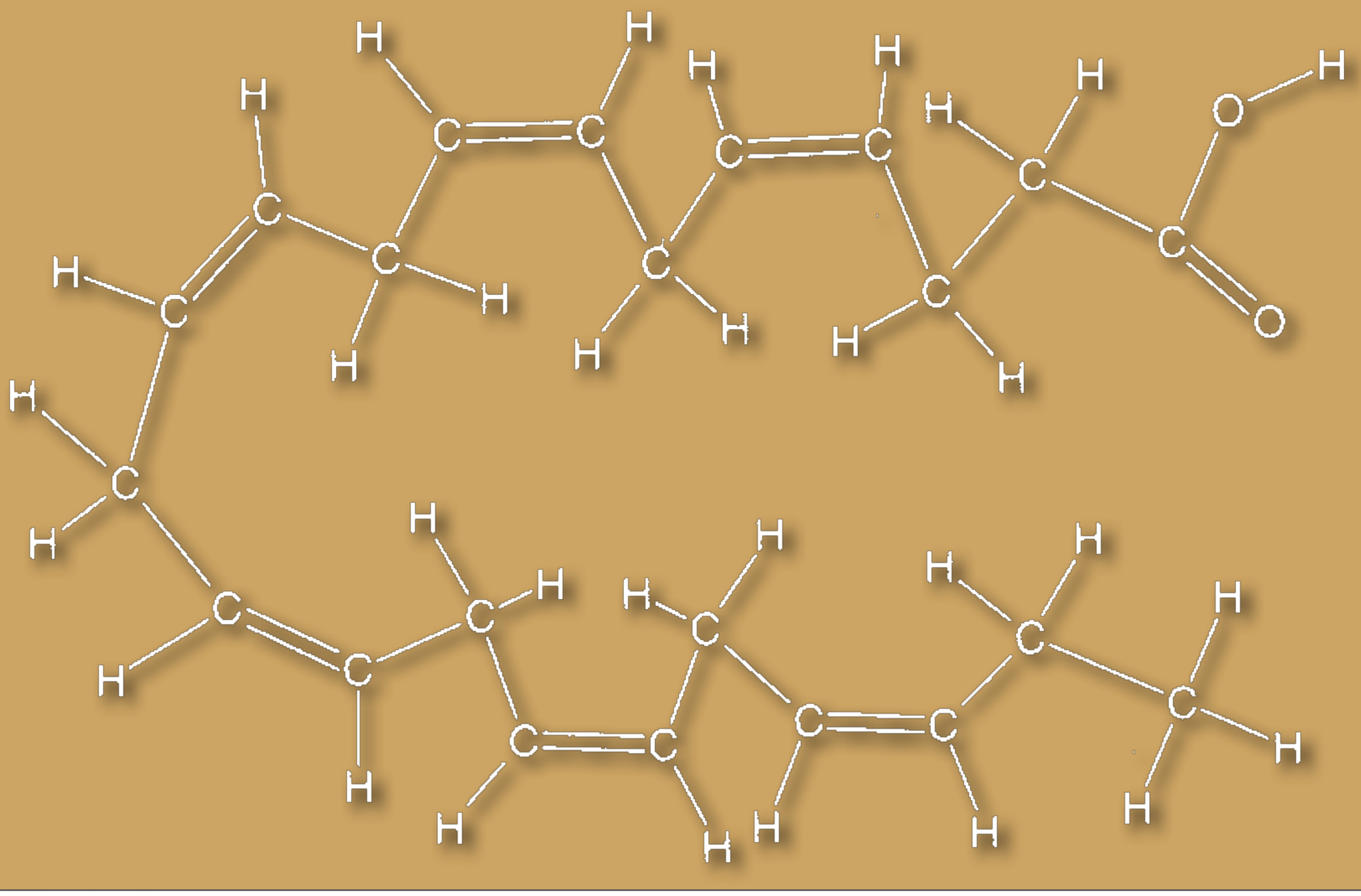
This table lists the rest of the PUFAs that are important in humans. Again, take note of the acronyms: AA, arachidonic acid, is an omega-6; EPA and DHA are omega-3 fatty acids.

Docosahexaenoic Acid, DHA, 22:6 n-3



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This is the chemistry diagram for DHA. This fatty acid, like EPA, is found in cold water fish.

Essential fatty acids

- Many higher mammals cannot synthesize fatty acids with double bonds near the methyl end
- Since these are essential, they must be obtained from the diet
- PUFAs, esp. arachidonic acid, are precursors for prostaglandins, thromboxanes, leukotrienes
- Long-chain PUFAs are important structural components of nervous system cells
- Adult brain: lipids make up 50-60% of dry weight
  - 23% of brain lipids are PUFA; 97% LCPUFA

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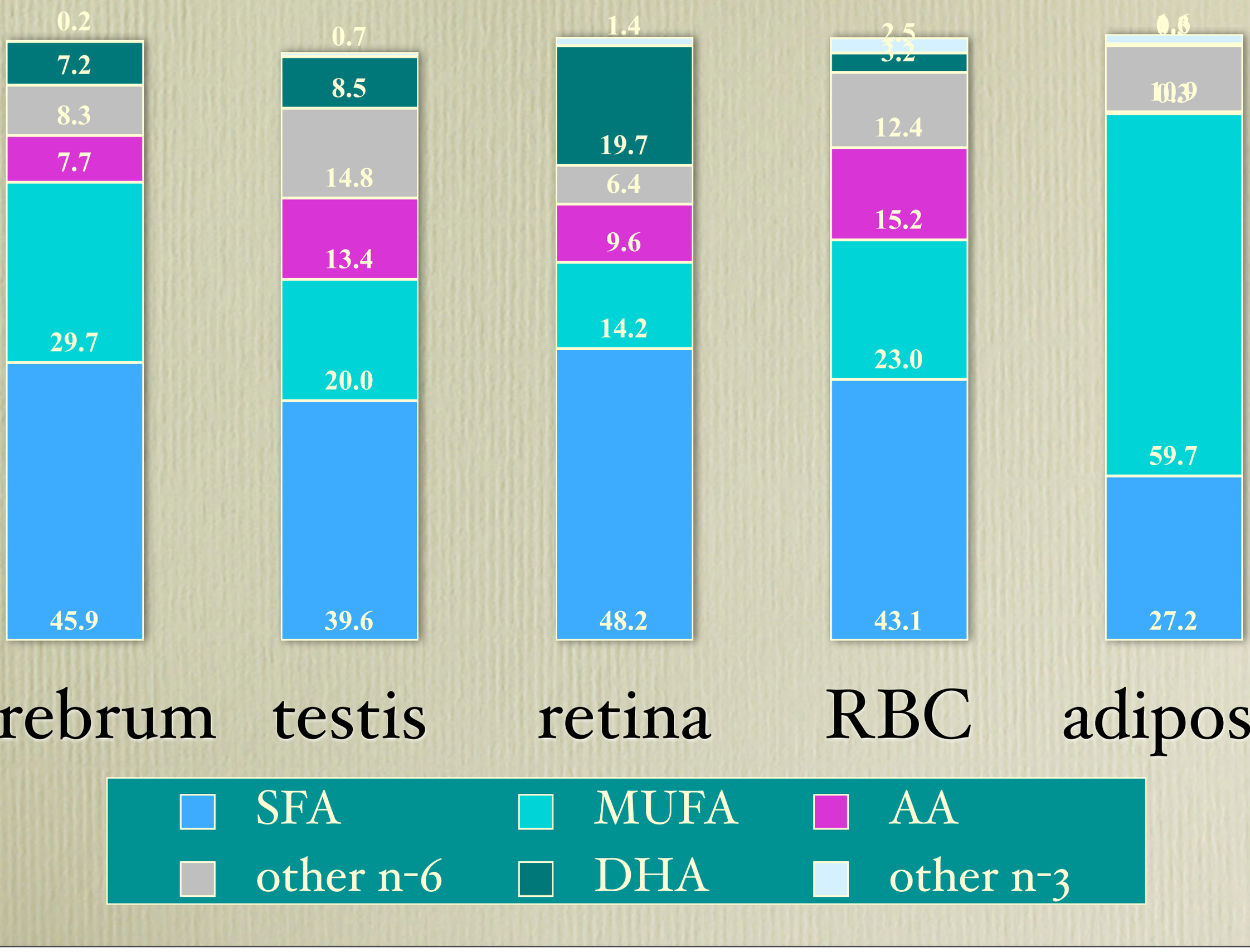
What makes omega-3 and omega-6 important? fatty acids with double bonds in these positions play very important roles in the body. While plants and fish possess the mechanisms to make these fatty acids, higher mammals including humans seem to have lost this ability, and are thus dependent on getting them in our diets. They are therefore called essential fatty acids.

Arachidonic acid is a precursor for all sorts of molecules important in immune system functioning, including prostaglandins, thromboxanes, and leukotrienes.

LCPUFAs, that is, those with 20 or 22 carbons, are important building blocks for the cell membranes of electrically excitable cells. This includes, of course, neurons, but also cardiac cells.

Most of the adult brain is lipid, of which almost a quarter are long chain PUFAs.

Fatty Acid Proportions



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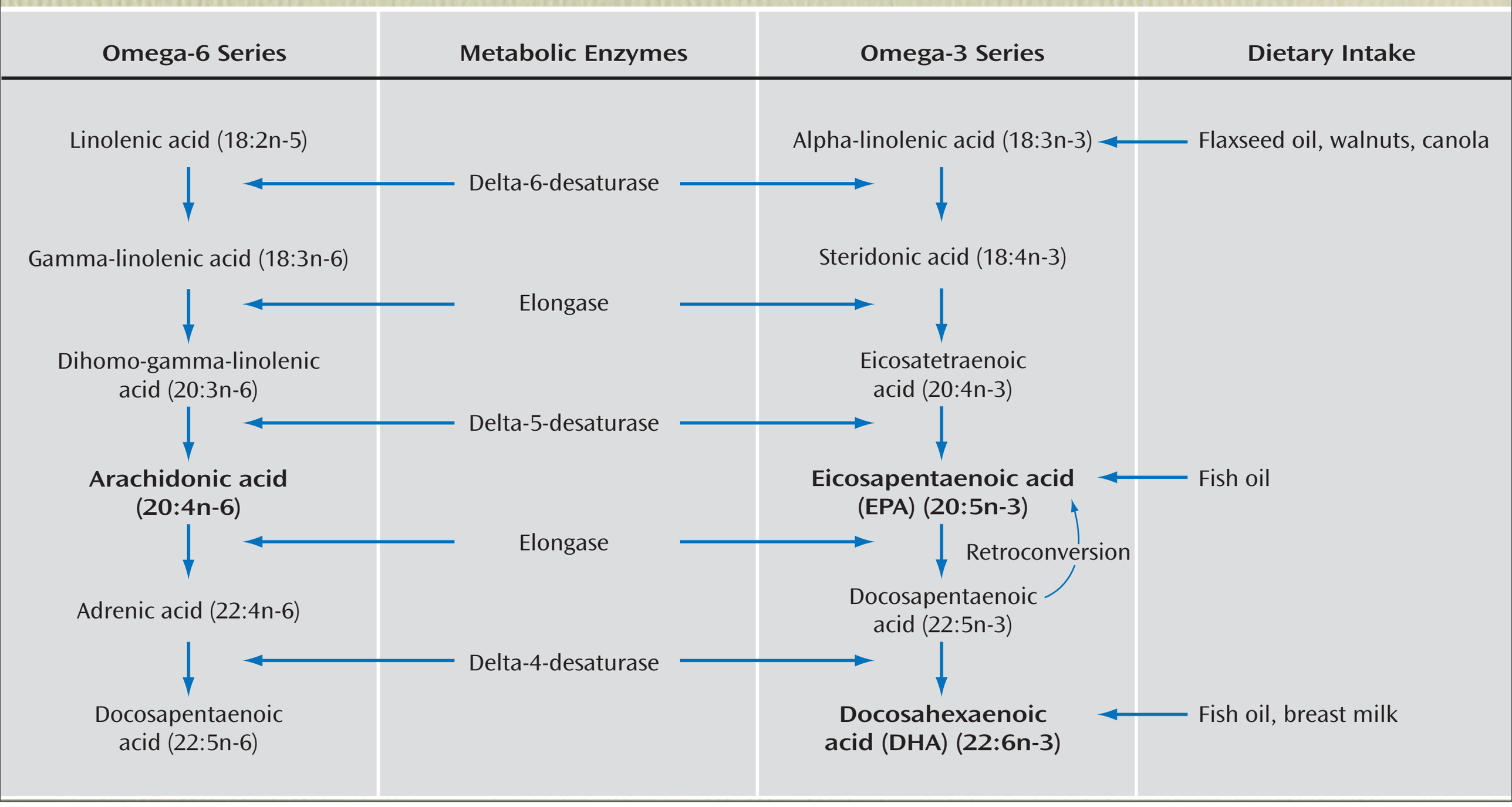
In the adult brain in humans, shown in the left bar, we see that almost half of the fatty acids are saturated, while mono-unsaturated and polyunsaturated each provide about one-quarter. More than a quarter of the polyunsaturates are DHA, which represents about 7% of the total fatty acids, while other omega-3s are almost non-existent.

Compare adipose tissue, which is mostly monounsaturated fat, and has only tiny amounts of omega-3s.

RBCs have considerably less DHA than brain tissue, but have a higher proportion of EPA. The retina has whopping amounts of DHA, 20% of the total fatty acids.



You can get lots of the omega-6 linoleic acid, and some omega-3 alpha-linolenic acid, from a diet with seeds and grains. These 18-carbon PUFAs from plants can be converted inside our cells into LCPUFAs. linoleic acid can be converted to AA, and alpha-linolenic acid can be converted into EPA and DHA.

Both the omega-6 and the omega-3 series use the same set of enzymes to create the long-chain fatty acids from their 18-carbon precursors.

Thus, omega-6s will inhibit the production of long-chain omega-3s, and vice-versa, probably through feedback inhibition of rate-controlling enzymes.

Practically speaking, if your diet had lots of linoleic acid in it, you could make more than enough AA to meet the requirements for cell membranes and immune system elements such as prostaglandins. It is likely that all this AA will feed back to the enzymes to stop them from making more AA. Unfortunately, these turned off enzymes cannot convert alpha-linolenic acid into EPA and DHA.

What this may mean is that if you have lots of linoleic acid in your diet, you may not be able to make EPA and DHA, and you will have to get these two fatty acids directly from your diet. That means from fish.

Omega-3s & omega-6s in diet

- Changes in diet [Tanskanen 2001]
  - Paleolithic diet: ratio ω3:ω6 1:1
  - Western diets in past 100 years: ω3:ω6 1:20 [Simopoulos 2002]
- LA 18:2n-6 & ALA 18:3n-3:
  - not synthesized by mammals
  - Synthesized by plants:
    - LA is stored in grains
    - ALA is stored in leaves
    - ALA also found in flaxseed

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I am bringing up the role of diet in evolution, because there is good evidence that, prior to the agrarian revolution about 10,000 years ago, humankind had become accustomed to a diet where omega-3 fatty acids were obtained from fish, wild game, and plants. In such a diet, the omega-3 to omega-6 ratio was about 1 to 1. This is the diet that we evolved to use optimally for our physical and mental health.

In the past 150 years, omega-3s have been largely replaced by saturated fats from domestic animals, and omega-6s from common vegetable oils and other sources. As a result, our diets have omega-3 to omega-6 ratios which are vastly different, 1:15 or 1:20 in many parts of the world, and up to 1:25 in North America. Grains and seeds are high in linoleic acid, an omega-6 fatty acid. There is alpha-linolenic acid in leaves, but most leaves don't have a lot of oil in them.

An exception is flaxseed, which has lots of alpha-linolenic acid in the seed.

Omega-3s in diet - 2

- DHA & EPA
  - Appreciable quantities only in cold water fish
  - EFAs in meat depend on the animal's diet
- *eg*, beef cattle:
  - Grain fed: ω3:ω6 1:15
  - Grass fed: ω3:ω6 1:2
  - Grass fed, fish oil supplement: 1:0.91
    [Scollan et al 2001]

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So, as consumers of grains and seeds and products made from them, such as vegetable oil, we now get lots of omega-6 fatty acids in our diets.

Not only do we not get much omega-3 in a typical North American diet, the omega-3s we do get are likely to be alpha-linolenic acid, which has to be converted to DHA and EPA before it can be used. It is possible that this conversion is hindered by high levels of omega-6s.

It turns out that free-range cattle, and probably chickens too, have pretty good ratios of omega-3s to omega-6s, certainly compared to grain fed animals. It's possible to improve the ratio even more by including fish oil in the animal's feed.

omega-3 vs omega-6 effects

[Okuyama 1996]

- ω3 suppresses, while ω6 stimulates ischemia/ inflammation which causes free radical injury
- This is thought to be important in aging, carcinogenesis, and atherosclerosis
- Aim for a ω3:ω6 of 1:2 or higher
- Cutting out animal fats worsens ω3:ω6 because of increased LA from vegetable oils

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One way of looking at the omega-3 to omega-6 issue is that omega-6s are like the accelerator in a car, in that omega-6s stimulate inflammation. Omega-3s act like a brake, suppressing immune system activity; that is, reducing inflammation. Just as a car needs both a brake and a gas pedal, we need both omega-3s and omega-6s to function effectively. An imbalance is likely to be unhealthy.

In Japan, there has been a marked shift during the past 50 years in dietary habits. Young people particularly have decreased their intake of fish and vegetables, and increased their consumption of grains. As a result, the dietary omega-3 to omega-6 ratio has decreased. A thought-provoking paper by Okuyama and colleagues presents evidence that the increase in dietary linoleic acid coupled with the decrease in LCPUFAs from fish, may be the cause of the troubling increases in a number of aging-related diseases in Japan, including heart disease, colon cancer, and breast cancer.

They recommend a dietary omega-3 to omega-6 ratio of 1:2 or better, and point out that the decrease in animal fats, espoused by North American nutrition experts for the past 30 years, may actually have a deleterious effect if it results in an increase in linoleic acid from vegetable oils.

Conversion of ALA to DHA or EPA

- most studies of ALA supplementation in men or mixed-gender groups show increased EPA concentrations but unchanged or even decreased DHA concentrations [Burdge 2004]

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Just to make the point again: human beings have only a very limited capacity to make use of the alpha-linolenic acid that we get from flaxseed or from omega-3 eggs or omega-3 milk.

PUFAs and Medical Illness

- Coronary heart disease
- Inflammatory bowel disease
- Macular degeneration
- Neurogenic pain
- Atopy

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I now want to talk a little bit about the role the omega-3 and omega-6 fatty acids play in medical illness.

You will recall that omega-6 fatty acids are precursors for inflammatory substances, and omega-3s play an anti-inflammatory role. Thus, balance is important, because inflammation is associated with most diseases, including cardiovascular disease, certainly the auto-immune disorders, and probably even dementia. There is even the theory that depressive symptoms are caused by inflammation.

Coronary heart disease - 1

- GISSI - Prevenzione trial [Lancet, 1999]
  - 11,324 patients, any age, MI in past 3 months
  - 3.5 year randomized, controlled trial:
    - EPA/DHA (1:2) 850-882 mg/day, vs placebo or vitamin E, or both
  - 30% reduction in cardiovascular deaths (p=0.024)
  - 45% reduction in sudden cardiac death (p=0.01)

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Let's first look at the role of omega-3s in heart health. I 'll focus on one large study and a meta-analysis. This study, published in Lancet in 1999, looked at more than 11,000 patients, mostly men, who had had a recent heart attack, also known as a myocardial infarct. They were randomized into 4 groups, and followed for three and a half years.

Over that time frame, the patients receiving the DHA and EPA had a 30% reduction in deaths due to cardiovascular disease, and a 45% reduction in sudden cardiac death.

Coronary heart disease - 2

- Meta-analysis of randomized controlled trials of omega-3s in patients with coronary heart disease [Bucher et al 2002]

- inclusion criteria: randomized; comparing dietary or supplemental intake of omega-3s with control diet or placebo; reporting MI and mortality; in patients who had either had an MI or CHD diagnosed by angiography; at least 6 months

- 11 trials met criteria: 7951 patients in intervention groups and 7855 in control groups

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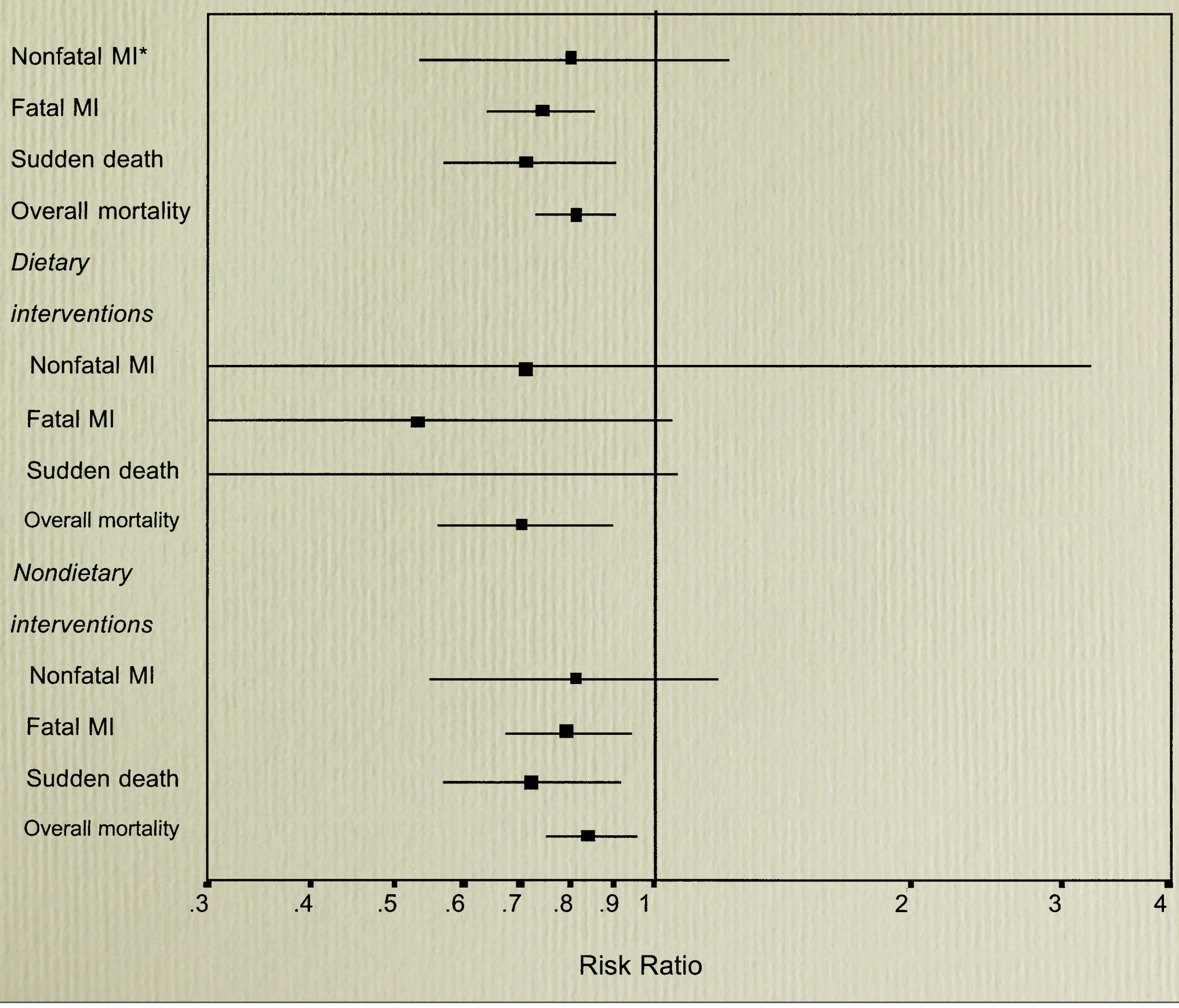
This is a report of a meta-analysis that appeared in the American Journal of Medicine in 2002. They looked at hundreds of articles, and found 11 trials of omega-3s in heart disease that met their criteria. One of these studies was the GISSI-Prevenzione trial that I was just talking about.



When they put together the data for the 11 studies, they found that:

The risk ratio for fatal MI was 0.7 overall. The risk ratio for sudden death was 0.7, and for overall mortality was 0.8.

The risk ratio for nonfatal MI was 0.8, but this result did not reach statistical significance. You can see in the graph that the 95% confidence interval crosses the vertical line for an even risk.

For low-risk patients (for example, under 50 years of age, with minor uncomplicated infarctions, and no comorbid conditions) having mortality of about 2% per year, the number needed to treat is about 250 for 1.5 years to prevent one premature death.

For high-risk patients with mortality of 22% per year, the number needed to treat is about 24.

Inflammatory bowel disease

- Inflammatory bowel disease (IBD), ie Crohn's disease and ulcerative colitis:
  - In reviewing the use of omega-3s in IBD: "taken together, all these studies suggest the effectiveness of these new therapeutic approaches, not only when conventional treatment fails or when it is not possible to treat chronically, but also, in some instances, as first choice." [Belluzzi 2002]

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Inflammatory bowel disease is a serious illness, not to be confused with IBS, or irritable bowel syndrome. There are two types of IBD: Crohn's disease and ulcerative colitis.

This is a quote from the abstract of a recent review on the use of omega-3s to treat IBD:

- "taken together, all these studies suggest the effectiveness of these new therapeutic approaches, not only when conventional treatment fails or when it is not possible to treat chronically, but also, in some instances, as first choice."

Macular Degeneration

[Seddon 2006]

- The leading cause of severe visual impairment and blindness in U.S. elderly
- Being a smoker almost doubles risk (OR 1.9)
- Comparing top quartile of omega-3 fatty acid consumption to bottom quartile:
  - OR 0.23 after controlling for other risk factors, for those with linoleic acid intake below the median
  - No significant association for higher linoleic acid intake

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Macular degeneration is a leading cause of blindness, and affects many of our residents here at Ste. Anne's.

This is a study of male twins who were US WW II veterans. 681 twins were included: 222 had age-related macular degeneration. Food intake and other risk factors were assessed by questionnaire.

The important finding was that being in the top quartile for fish consumption gave a relative risk of less than a quarter for macular degeneration, compared to the bottom quartile for fish consumption.

I think that a very important aspect of this study was controlling for linoleic acid intake. The fact that an association for omega-3 intake and macular degeneration was found only for individuals with low linoleic acid intake, suggests that we will not be able to detect a therapeutic effect in intervention studies with fish oil unless we also control for linoleic acid consumption.

Discogenic pain

- open-label, uncontrolled study in 250 patients seen by a neurosurgeon & found to have nonsurgical neck or back pain [Maroon & Bost 2006]
  - pts were asked to take 1200 mg daily of EPA+DHA as fish oil
  - half of the patients responded to a questionnaire after 75 days (on average) on fish oil

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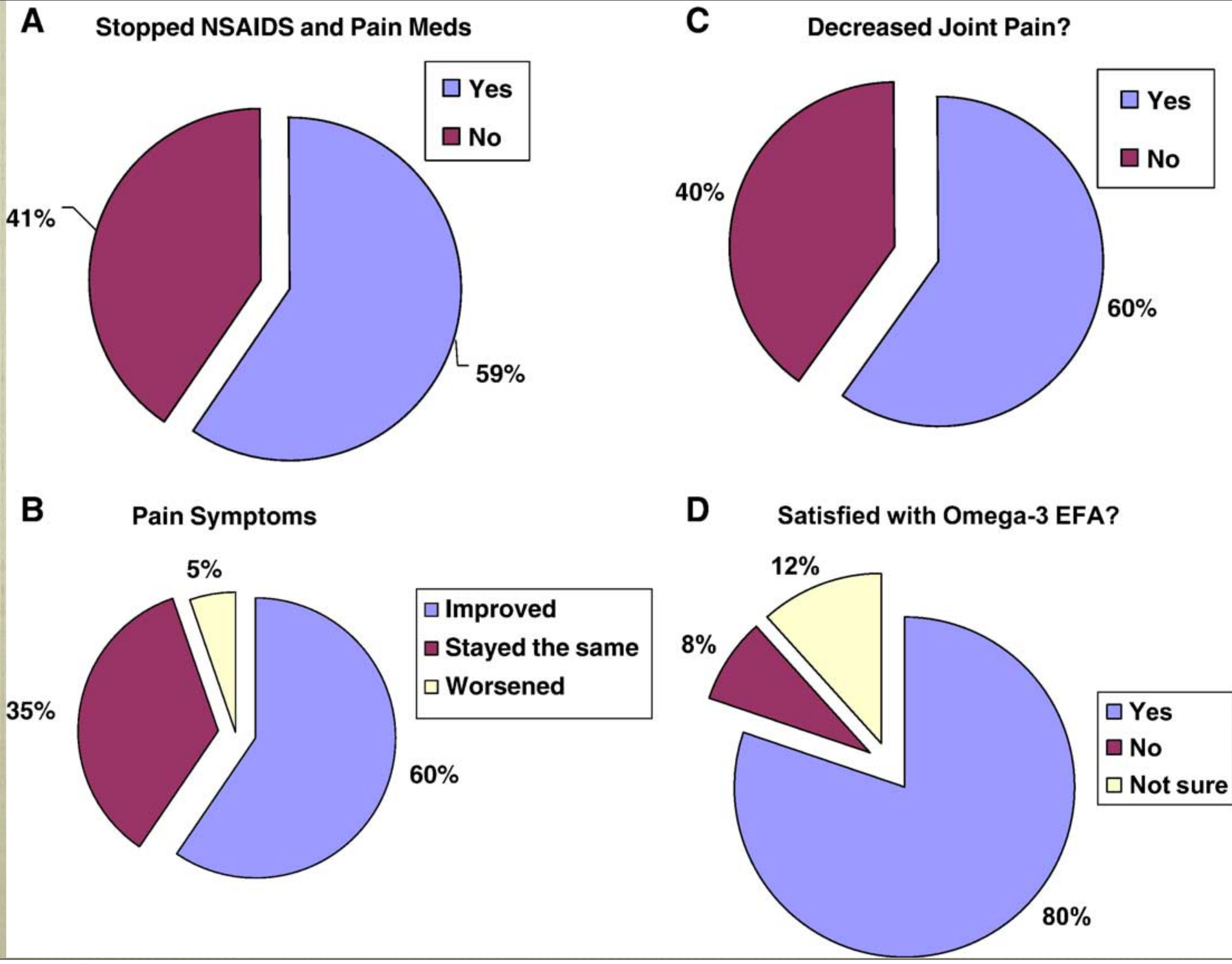
Many patients take non-steroidal anti-inflammatory medications for pain control. This includes aspirin and ibuprofen, as well as a number of prescription-only drugs. All these drugs have side effects including a risk of gastric ulceration. The newer COX-2 inhibitors such as Vioxx have other risks including heart attack and stroke.

What all these NSAIDs have in common is that they inhibit a couple of enzymes called cyclo-oxygenases, which convert arachidonic acid (an omega-6) into prostaglandin H2. Prostaglandin H2 is the precursor for a series of substances that cause inflammation and pain.

But instead of inhibiting the conversion of arachidonic acid, why not competitively inhibit the inflammatory substances with anti-inflammatory substances derived from EPA and DHA? That is the rationale behind this study, where patients with neck or back pain were asked to take fish oil supplements.



These are the results: 59 % of the patients had stopped their NSAIDs and pain medications, 60% reported that their pain symptoms had improved and only 5% that symptoms had worsened, and 80% were satisfied with the omega-3 treatment.

Of course, this kind of study doesn't really prove that fish oil is as good as NSAIDs for controlling pain, but it does suggest that further controlled, randomized, double-blind trials should be carried out.

And I would add: if arachidonic acid is the culprit behind the pain and inflammation, why not suggest to patients to reduce their intake of linoleic acid, which is the precursor to arachidonic acid?

Atopy

- The clustering of eczema (atopic dermatitis), allergic conjunctivitis, allergic rhinitis, and asthma in certain individuals
- increased incidence in last 40 years, believed to be due to increased linoleic acid consumption & less fish [Calder 2003]
- linoleic acid is converted to AA; AA is metabolized to PGE2; PGE2 increases production of IL-4, IL-5, and IL-10, but decreases production of IFN-gamma and IL-2

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The last topic involving medical illness is atopy, which is the name for a condition where several allergic illnesses coexist in a person.

The past 40 years has seen an increase in the incidence of atopy, which is believed by some researchers to be caused by our increased consumption of linoleic acid from vegetable oils, and decreased fish intake.

Linoleic acid is converted to arachidonic acid which then becomes prostaglandin E2. This prostaglandin increases the production of certain inflammatory cytokines that are involved in atopy.

PUFAs and mental illness

- Depression
- Suicide
- Bipolar affective disorder
- Borderline personality disorder
- Cognitive impairment
- Developmental disorder

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All that I've talked about so far is preliminary to the core of today's presentation, the role of omega-3s in psychiatry. I will look at depression, suicide, bipolar disorder, borderline personality disorder, cognitive impairment in the elderly, and childhood developmental disorder.

Depression

- It has been suggested that the sharp rise in depression rates in the 20th century is fueled by increased consumption of vegetable oils [Smith 1991; Hibbeln & Salem 1995]

- Patients with unipolar and bipolar depressions have high levels of inflammatory eicosanoids derived from AA [Lieb et al 1983]

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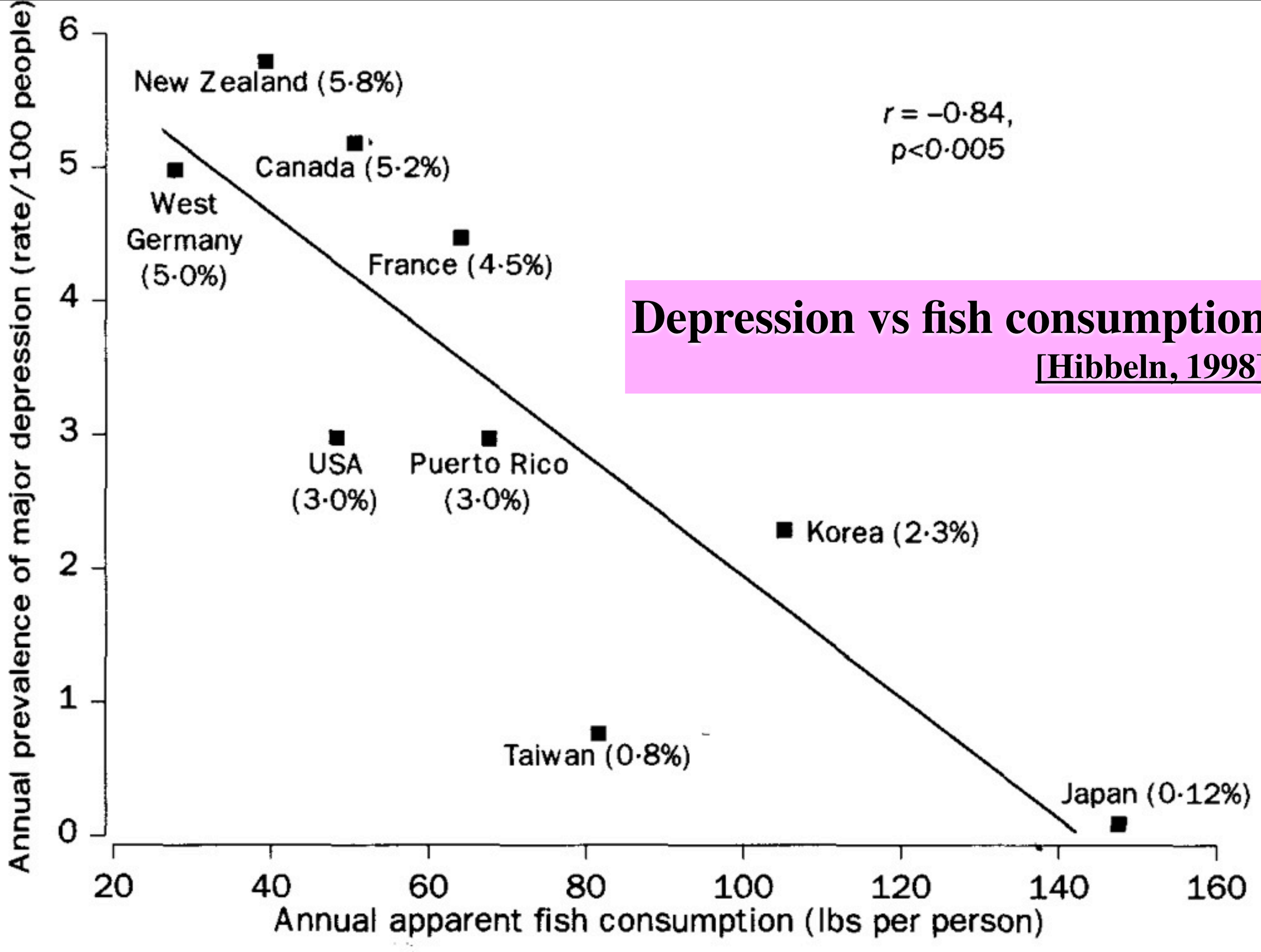
As for atopy, some researchers believe that the increased incidence of depression in past decades has been brought about by increased consumption of vegetable oils containing linoleic acid.

In support of this argument, depressed patients have been found to have high levels of inflammatory substances derived from arachidonic acid which is itself a product of linoleic acid.



Depression vs fish consumption

[Hibbeln, 1998]

Thursday, 20 December, 12

Another factor is fish consumption.

Annual prevalence of depression shows nearly a 60-fold variation across countries. The pattern is similar to that for coronary artery disease mortality, which suggests that there are similar factors at work, such as diet.

This paper used major depression prevalence figures reported by Myrna Weissman and her colleagues. The prevalences were obtained using rigorous methodology, including structured clinical interviews.

Apparent fish consumption was calculated as:

Fish catch + imports - exports

More fish consumption is strongly associated with less depression.

The correlation coefficient was very high, 0.84, with a probability of less than .005 that this finding was due to chance.

Fish consumption & depression

[Tanskanen et al, 2001]

- Questionnaire study: 3004 Finnish adults; 1767 responded (59%)
  - Fish consumption by food frequency questionnaire
    - Frequent fish consumer: twice or more weekly
  - Depression: Beck Depression Inventory ≥ 10
  - Depression and suicidal ideation significantly lower among frequent fish consumers, after controlling for:
    - sex, age, marital status, education, employment status, work ability, area of living, financial status, general health, smoking, alcohol intake, coffee drinking, and physical activity

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As was found for heart disease, frequent fish consumers have lower rates of depression than infrequent consumers, as shown in this study of fish consumption in Finnish adults.

Trial of omega-3s in depression - 1

- 4-week, placebo-controlled, randomized, double-blind trial of 20 patients (17 women, 3 men) [Nemets et al 2002]
- ethyl-EPA 1 g twice daily, or matching placebo
- added to their ongoing antidepressant therapy

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But of course there is little point in finding that people who eat lots of fish have less depression, if you cannot demonstrate using the gold standard of intervention research, a randomized, controlled, double-blinded trial, that the fish ingredient will actually make a difference.

Here is one such study, only in 20 patients, unfortunately.

TABLE 1. Effects of the Ethyl Ester of Eicosapentaenoic Acid (E-EPA) or Placebo for Treatment of Depressive Episodes in 20 Patients Receiving Maintenance Antidepressant Medication

Patient	Age (years)	Sex	Treatment	Hamilton Depression Rating Scale Score: Baseline	Week 1	Week 2	Week 3	Week 4	Number of Years Since First Treatment	Number of Previous Episodes
All patients taking placebo										
Mean	52.1			22.3	21.7	20.1	19.7	20.0	8.0	1.9
SD	10.2			2.8	4.6	7.8	8.5	8.8	6.5	1.3
All patients taking E-EPA										
Mean	54.2			24.0	23.8	16.6	13.7	11.6	7.6	2.1
SD	13.9			2.9	3.0	4.4	4.2	6.2	7.6	2.6

In spite of the small size of the study, the results were impressive enough to be published in the American Journal of Psychiatry in 2002.

Ethyl-EPA was significantly different from placebo at weeks 2, 3, and 4.

The Hamilton depression scale score dropped 12.4 for the patients receiving ethyl-EPA, but only 1.6 for those receiving placebo.

Six of 10 patients getting the omega-3 had a 50% decrease in the Hamilton score, compared to only 1 patient in 10 getting placebo.

Trial of omega-3s in depression - 2

- 8-week, randomized placebo-controlled double-blind trial [Su et al 2003]

- 28 depressed outpatients 18-60 years old

- high-dose omega-3 (2200 mg EPA, 1100 mg DHA twice daily; total 6.6 g/day) added to their regular antidepressant treatment

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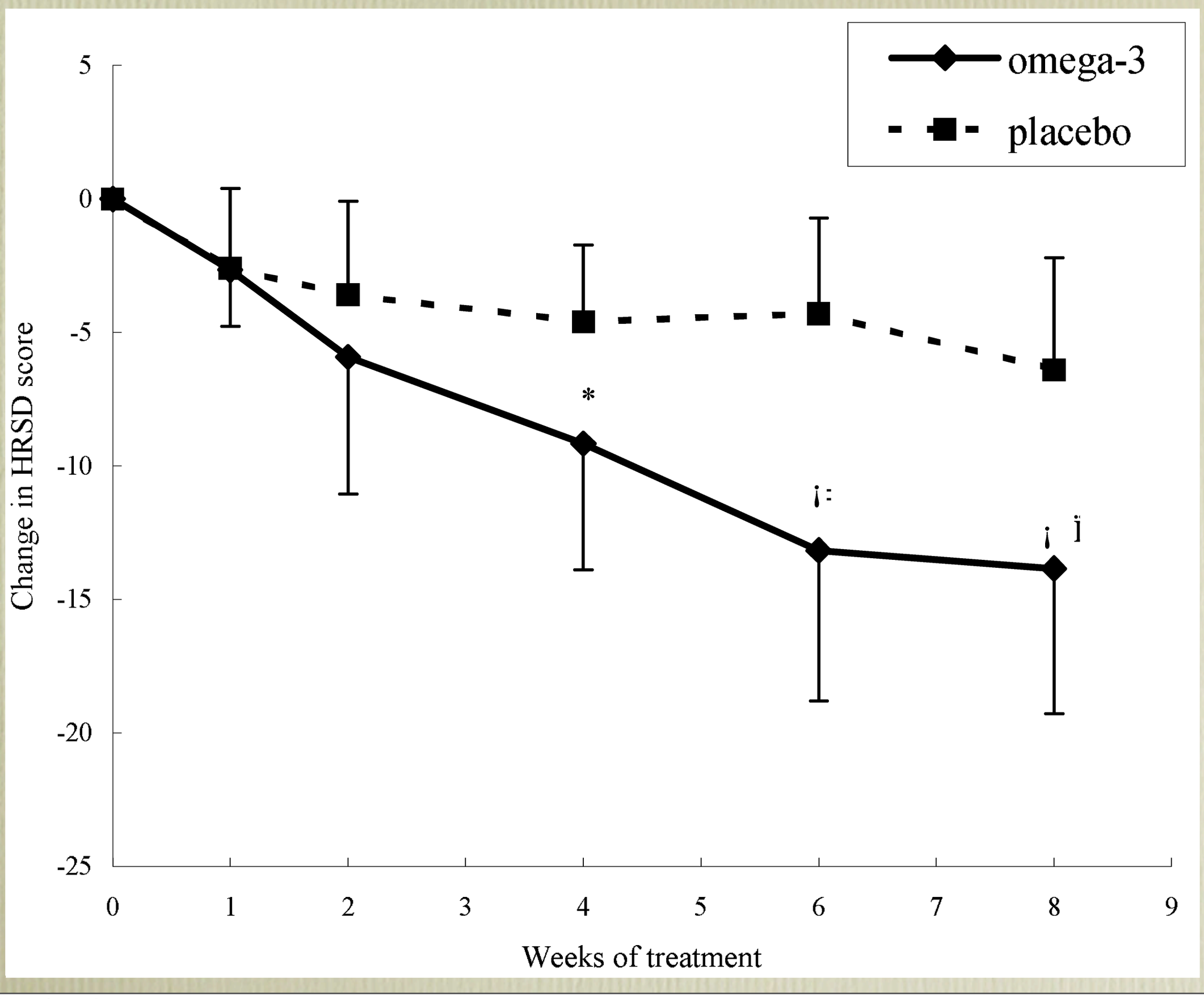
Another study was carried out over 8 weeks, using much higher doses of omega-3s, again added to the ongoing antidepressant medication.



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This graph shows the decrease in Hamilton Rating Scale for Depression scores over the 8 weeks. Differences between placebo and omega-3 treatment were statistically significant at weeks 4, 6, and 8. The rate of reduction in scores was also significantly different.

Postpartum depression

- 8 week, dose finding study [Freeman et al 2006]
- 16 women with postpartum depression
- random assignment to dosage group
- ratio of EPA:DHA 1.5:1
- three dosage groups: 0.5, 1.4, or 2.8 g
- placebo capsules used to maintain blinding as to group

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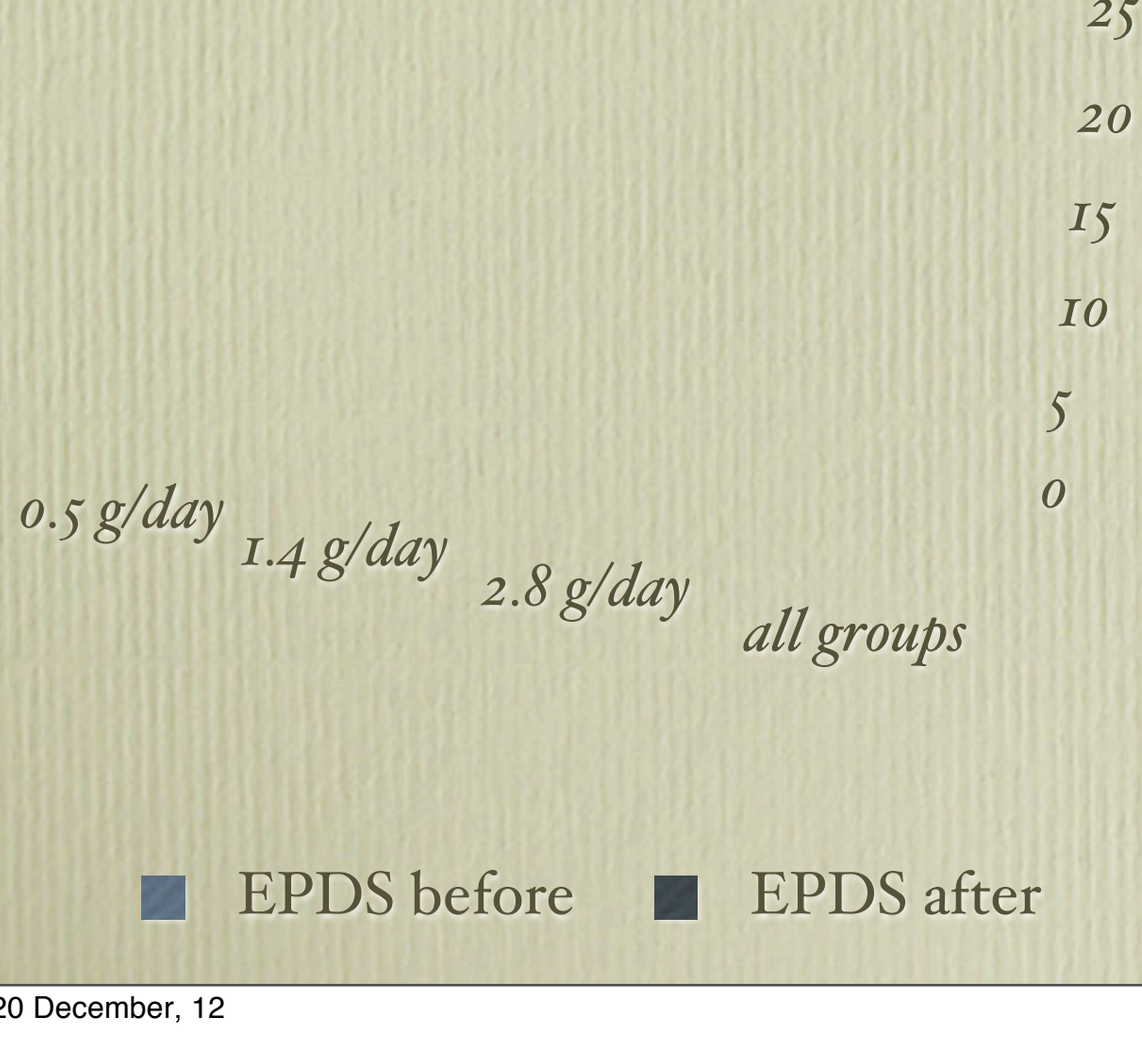
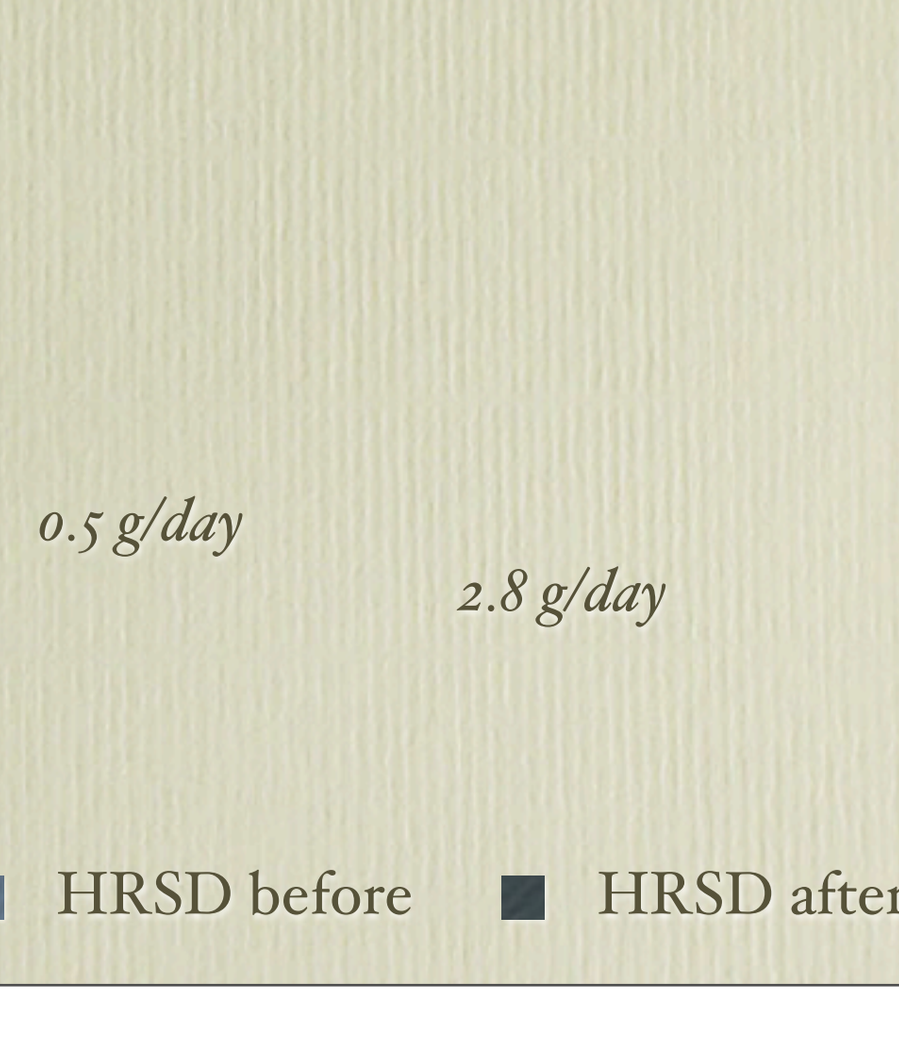
Postpartum depression is thought to be particularly likely to be linked to low omega-3 levels. This is because during fetal development, the fetus obtains its requirements for DHA which are necessary for its brain and retina, from its mother. If the mother is not getting enough DHA or EPA in her diet, then the fetus will suck the DHA it needs out of the mother's brain! One estimate is that the mother's brain can shrink by up to 5% with this process.

This study was published earlier this year in the prestigious journal Acta Psychiatrica Scandinavica. Again, very few subjects, and there was no control group, but the results were still impressive.

Dosage group	Subjects per group	Mean pretreatment EPDS score	Mean Post-treatment EPDS score	Mean Pretreatment HRSD score	Mean Post-treatment HRSD score
0.5 g/day	6	18.5	8.5	18.0	9.3
1.4 g/day	3	15.3	5.0	19.0	7.0
2.8 g/day	7	19.0	11.9	20.3	11.9
All groups	16	18.1	9.3	19.1	10.0





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The table at the top comes from the article; the graphs were generated by my presentation software. For all three dose levels, there were significant reductions in both the Edinburgh Postnatal Depression Scale and the Hamilton Rating Scale for Depression, over the 8 weeks of the study.

Suicide

- case-control study of suicide attempters in China [Huan et al 2004]
- 100 suicide attempt cases admitted to 3 hospitals in Dalian, China
- controls were patients injured by accidents, matched to cases for age, gender, and smoking status
- gas chromatography used to obtain fatty acid composition

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Not all depressed people are suicidal, and not all suicidal people are depressed, so it's worthwhile to consider suicide as a topic separate from depression.

This is a study done in China, looking at 100 individuals who had been admitted to hospital after attempting suicide. They were matched by age, gender, and smoking status to 100 controls who had been admitted for injuries due to accidents. Cases were compared to controls for fatty acid composition. The study was published in 2004 in the journal Biological Psychiatry.

Table 2. Fatty Acid Levels in the Total Phospholipid Fraction of Red Blood Cells

Fatty Acid	Percentage of Total Fatty Acids: Suicide ($n = 100$)	Percentage of Total Fatty Acids: Control ($n = 100$)	p Values
n-3 unsaturated			
18:3 n-3	1.8 ± 1.1	1.8 ± 1.1	.98
20:5 n-3 (EPA)	.74 ± .52	1.06 ± .62	<.0001
22:5 n-3	1.5 ± .5	1.7 ± .5	.004
22:6 n-3 (DHA)	4.4 ± 1.6	5.3 ± 1.7	.0003
Subtotal	8.5 ± 2.4	9.9 ± 2.9	.0002
n-6 unsaturated			
18:2 n-6	13.1 ± 2.3	12.1 ± 1.9	.10
20:3 n-6	1.5 ± .6	1.4 ± .6	.29
20:4 n-6(AA)	11.2 ± 2.1	11.3 ± 2.3	.82
22:4 n-6	2.2 ± .7	2.1 ± .7	.20
22:5 n-6	.49 ± .29	.51 ± .33	.56
Subtotal	28.4 ± 3.7	27.8 ± 3.8	.25
n-6/n-3	3.6 ± 1.1	3.0 ± 0.9	<.0001

This table shows that there were significant differences in the EPA, DPA, and DHA concentrations between suicide attempters and controls.

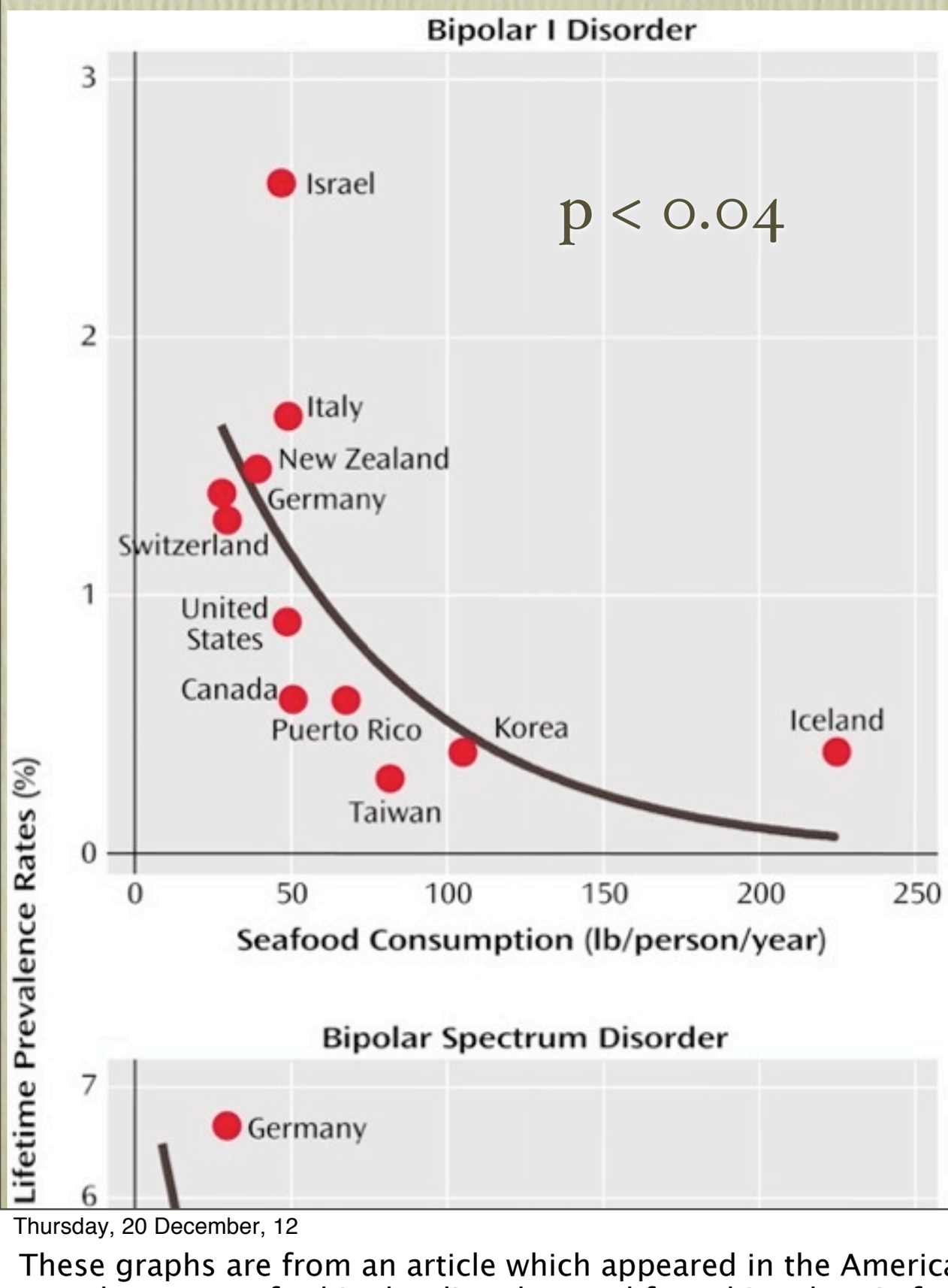
Comparing the highest and the lowest quartiles of EPA concentration for all 200 subjects, the odds ratio for suicide attempt was 0.12 for the highest quartile. In other words, the 50 individuals with the lowest EPA levels were 8 times more likely to have made a suicide attempt than the 50 people with the highest EPA levels.

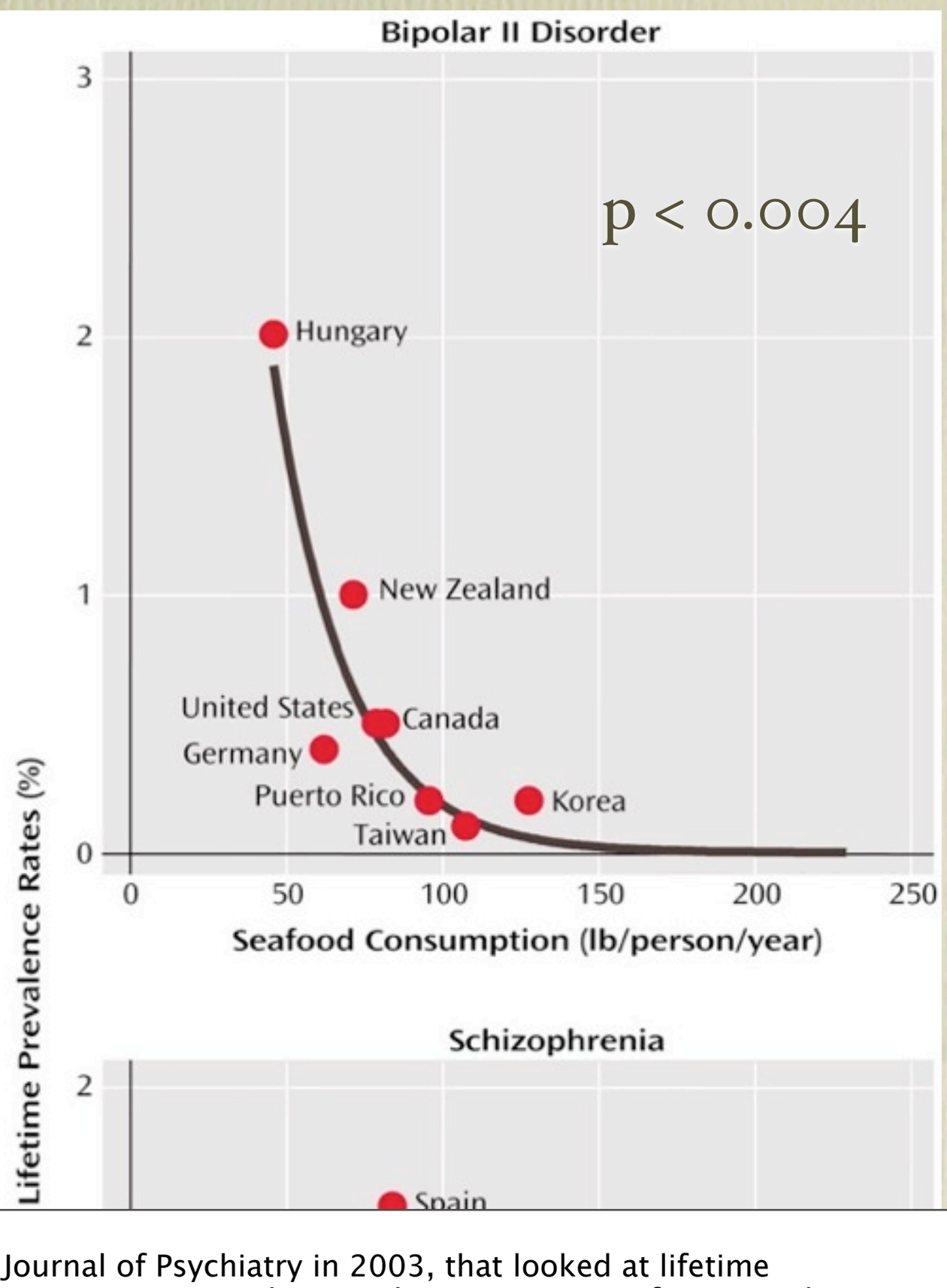
Bipolar Affective Disorder

Thursday, 20 December, 12

Now, let's look a bipolar affective disorder, or what used to be called manic-depressive illness.

[Noaghiul & Hibbeln 2003]





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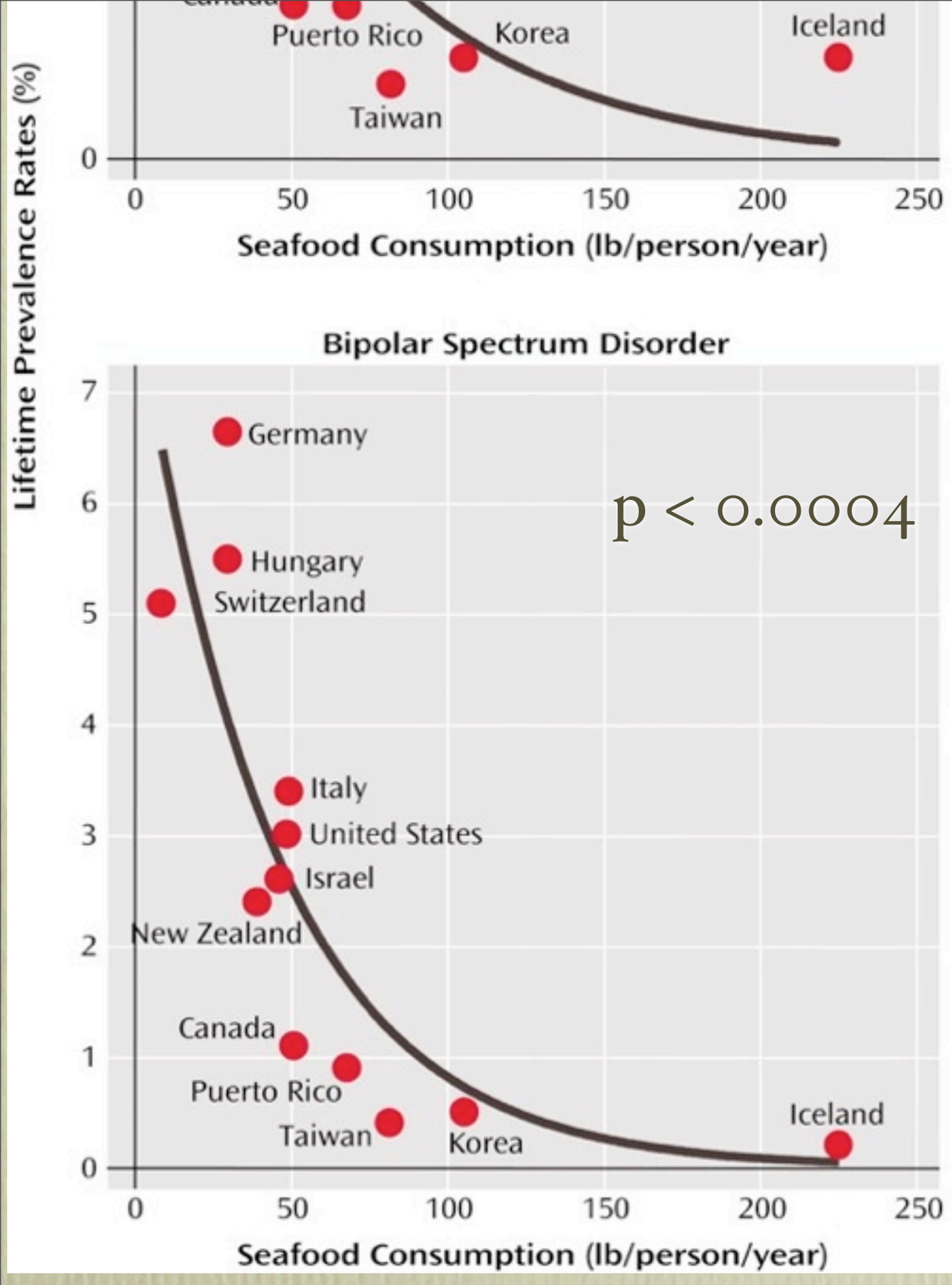
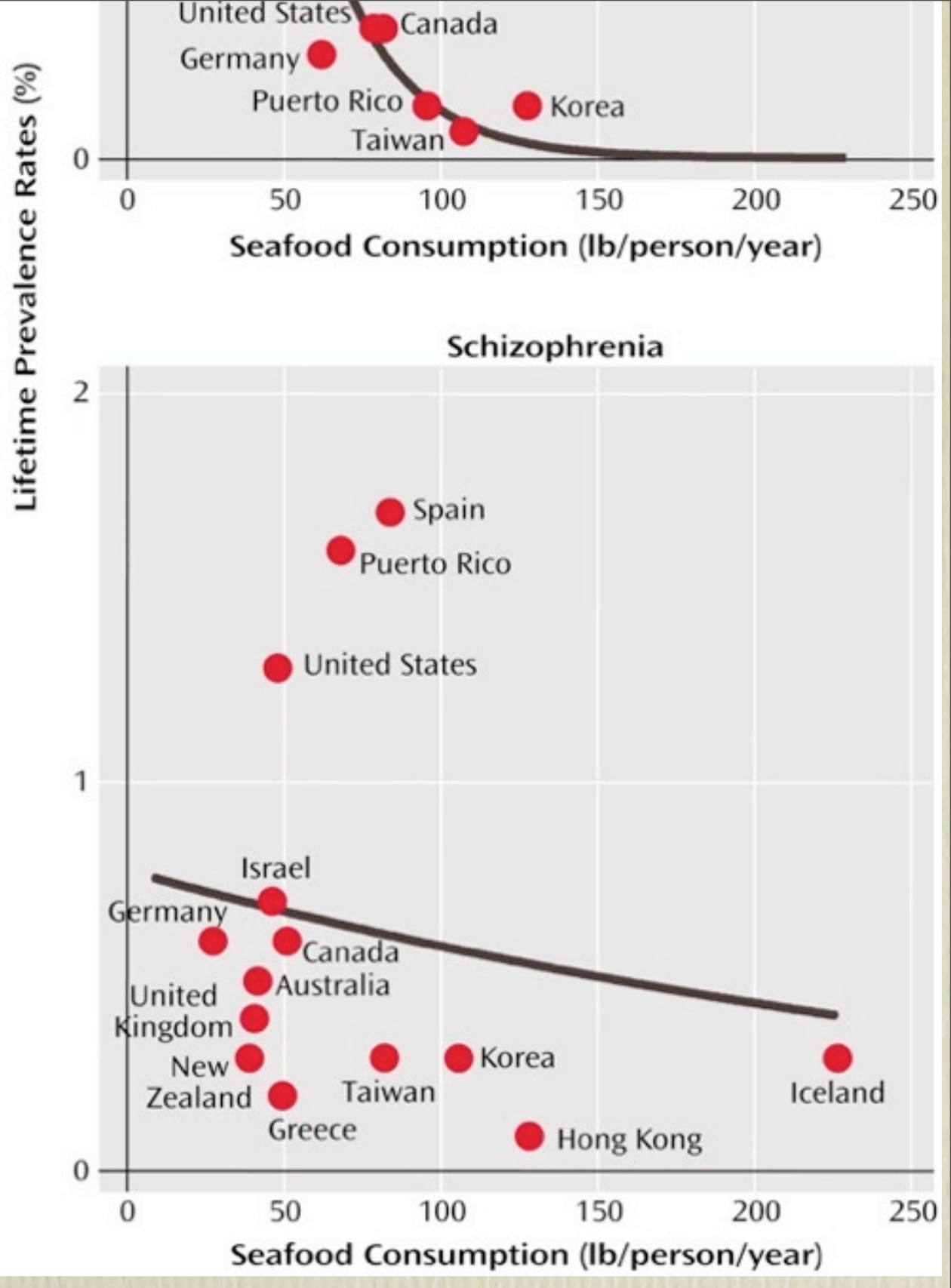
These graphs are from an article which appeared in the American Journal of Psychiatry in 2003, that looked at lifetime prevalence rates for bipolar disorders and for schizophrenia for various countries. The prevalence rates came from population-based epidemiologic studies, with large sample sizes, using structured diagnostic interviews. These prevalence figures were then compared to seafood consumption for these countries. The best fit was obtained with simple exponential decay regression. I've added the p values to each chart.





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The data for bipolar spectrum disorder show the highest correlation.

There were no correlations found for schizophrenia and seafood consumption.

Bipolar disorder [Stoll et al 1999]

- Double-blind, randomized, placebo-controlled trial
- 30 patients, 4 months
- Rx: 14 caps/day of 440 mg EPA, 240 mg DHA (total 9.6 g/day ω3)
- Placebo: olive oil
- Outcome measure: time to exit in trial because of emergence or change of mood symptoms sufficient to warrant a change of treatment
- 3 patients developed side effects (loose stools): dosage reduced to 5 caps/day
- 44 patients enrolled; only 30 analysed as trial was stopped prematurely (production cessation of ω3 caps)

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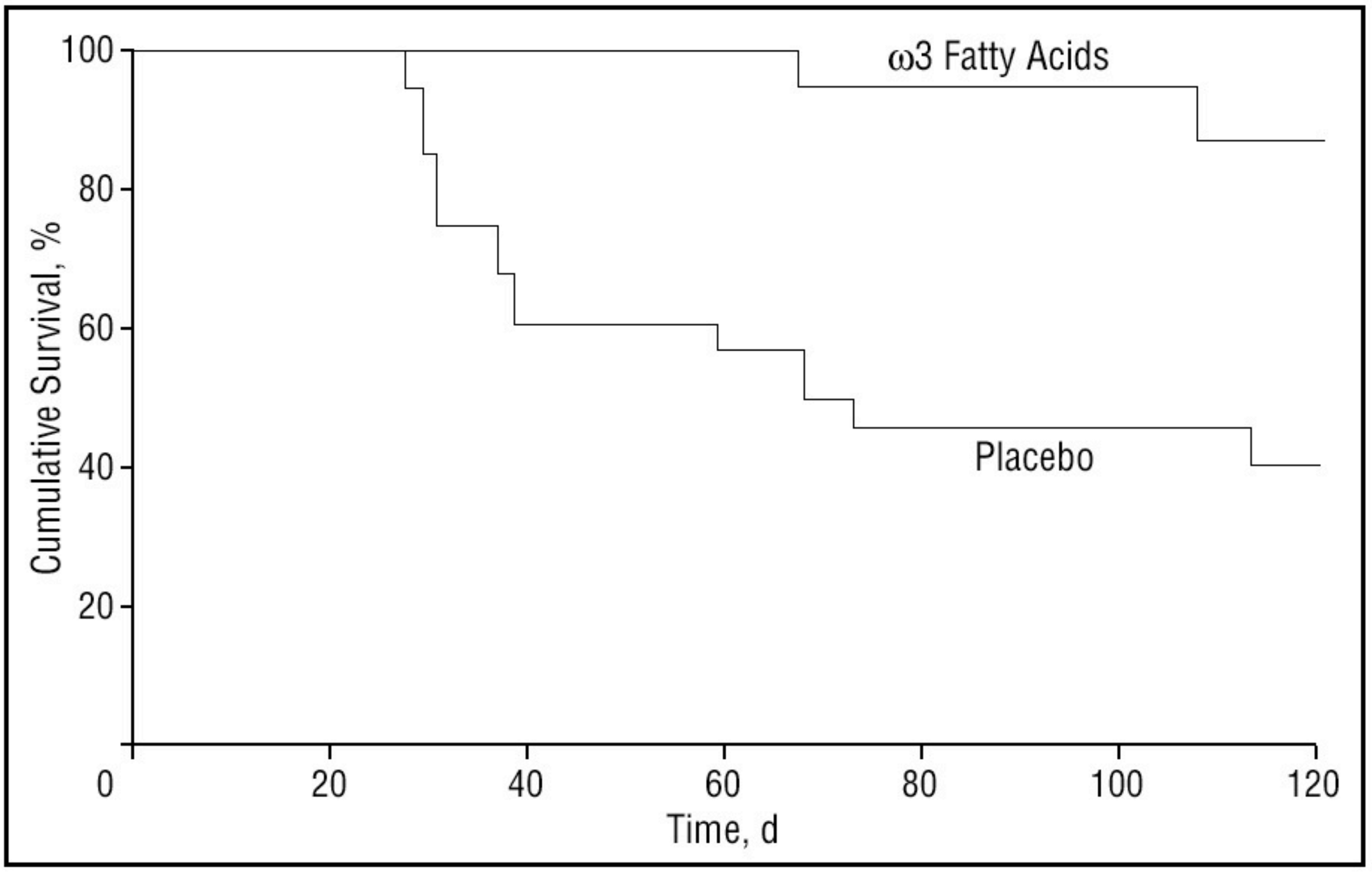
This is a study which I found particularly relevant. It was a double-blind, placebo-controlled, randomized trial, in other words, the gold standard in research methodology, comparing high levels of omega-3 supplementation with placebo, in patients with bipolar affective disorder. It appeared in the Archives of General Psychiatry in 1999.

Patients had to have had a manic or hypomanic episode during the 12 months before the study. 40% of the patients were rapid-cycling.

All except 4 of the patients were on medication for their bipolar disorder. All were outpatients. What was measured was how long it took for patients to develop symptoms sufficiently severe to require changes in medication.

The trial was initially intended to study 44 patients, but because the manufacturer stopped making the omega-3 supplement, the trial had to be terminated early.

ω3 survival analysis



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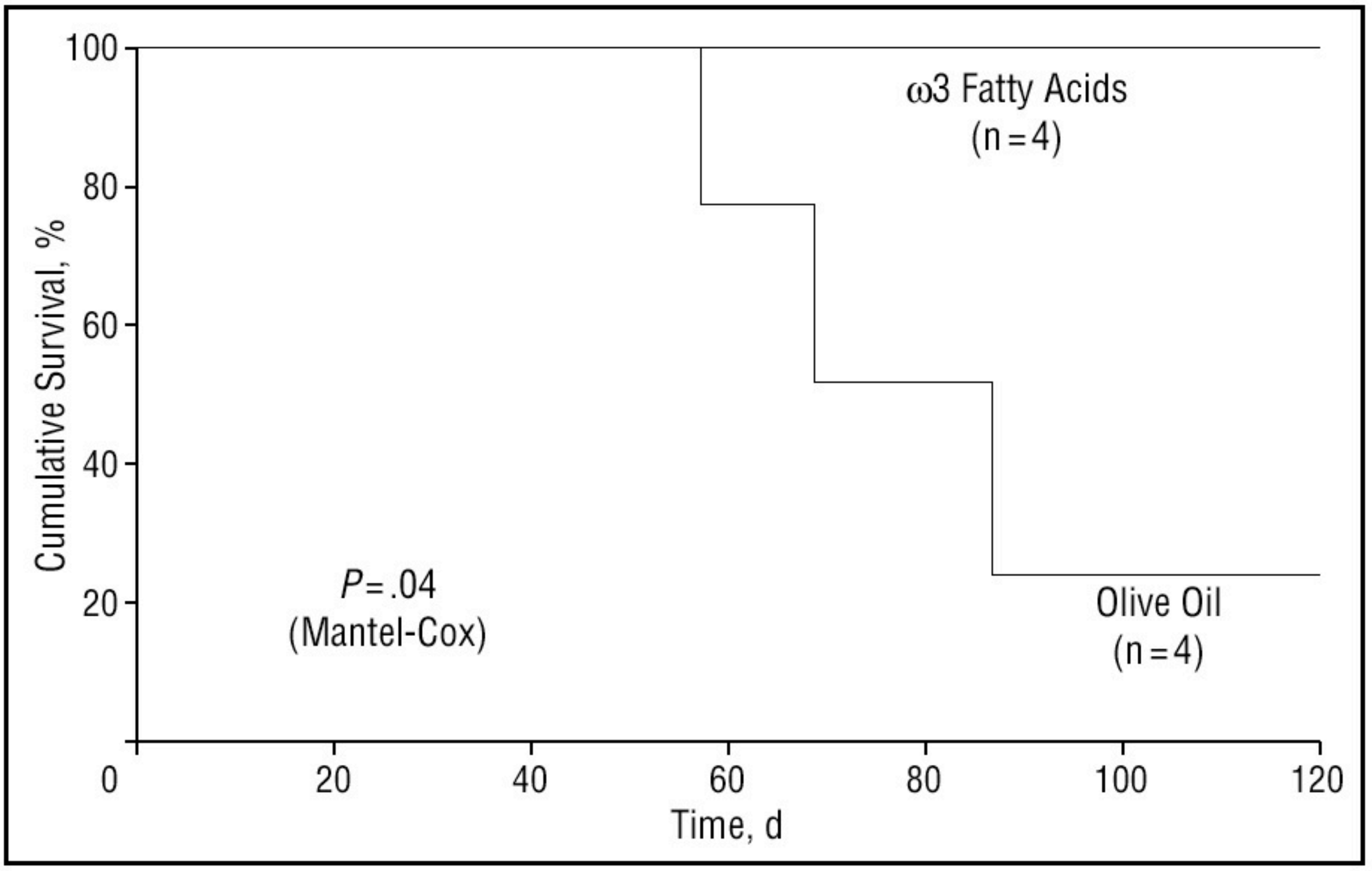
For the 30 patients as a whole, you can see that after 4 months, about 60% of the placebo patients had to have medication changes because of symptoms, versus only about 14% of the omega-3 group.

ω3 monotherapy survival analysis



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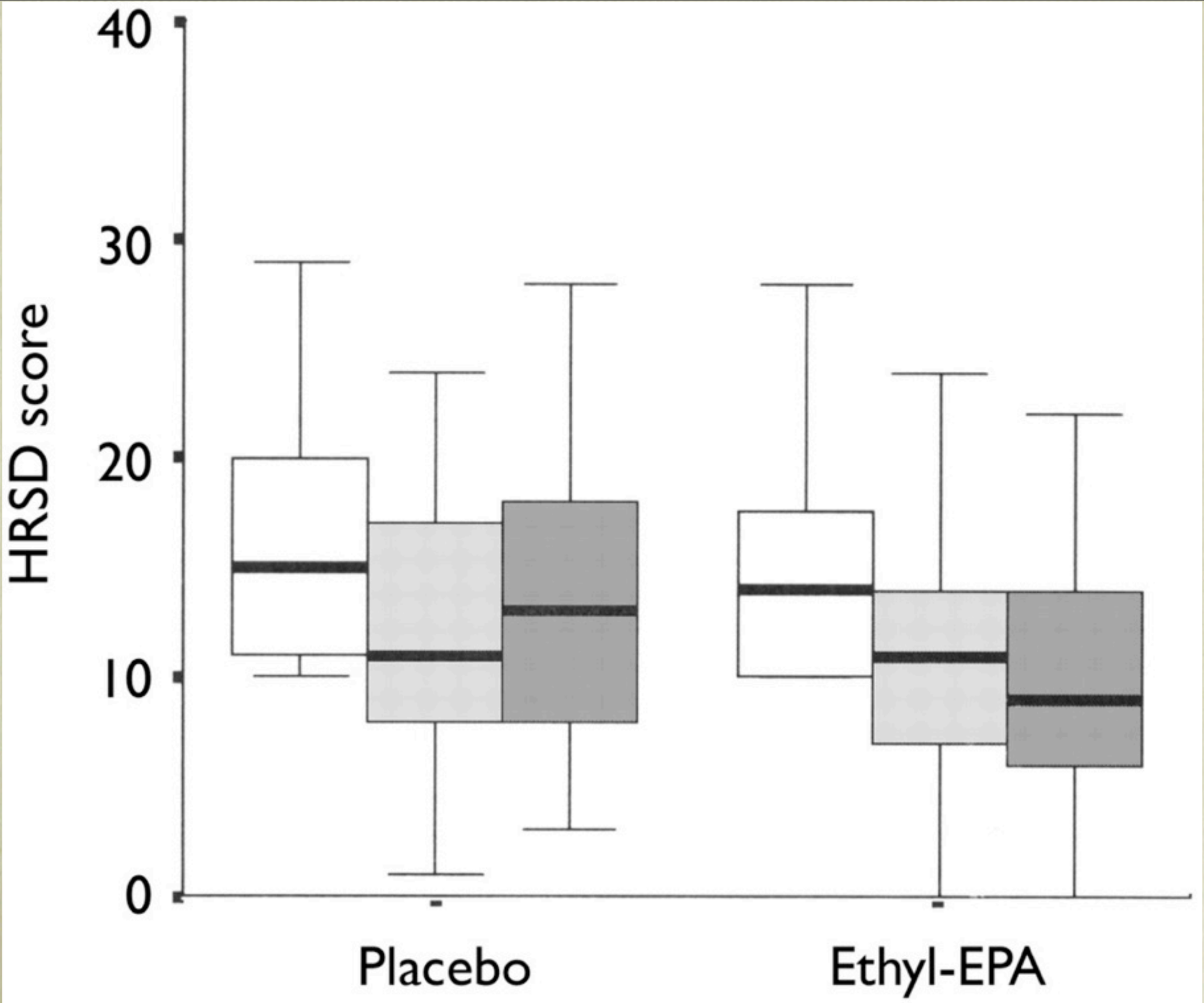
For the 8 patients not taking any other mood-stabilizing treatment, the results were even more impressive. None of the omega-3 patients decompensated, but 3 out of 4 placebo patients became symptomatic.

Bipolar disorder - 2 [Frangou 2006]

- Double-blind randomized placebo-controlled study
- 75 patients with bipolar depression, twelve weeks
- Rx: 1 g/day or 2 g/day of ethyl-EPA

Thursday, 20 December, 12

This is a more recent study, published just last January in the British Journal of Psychiatry, a journal with high standards. It involved 75 patients with bipolar depression, randomized to one of two doses of ethyl-EPA or to placebo, and followed for 12 weeks.



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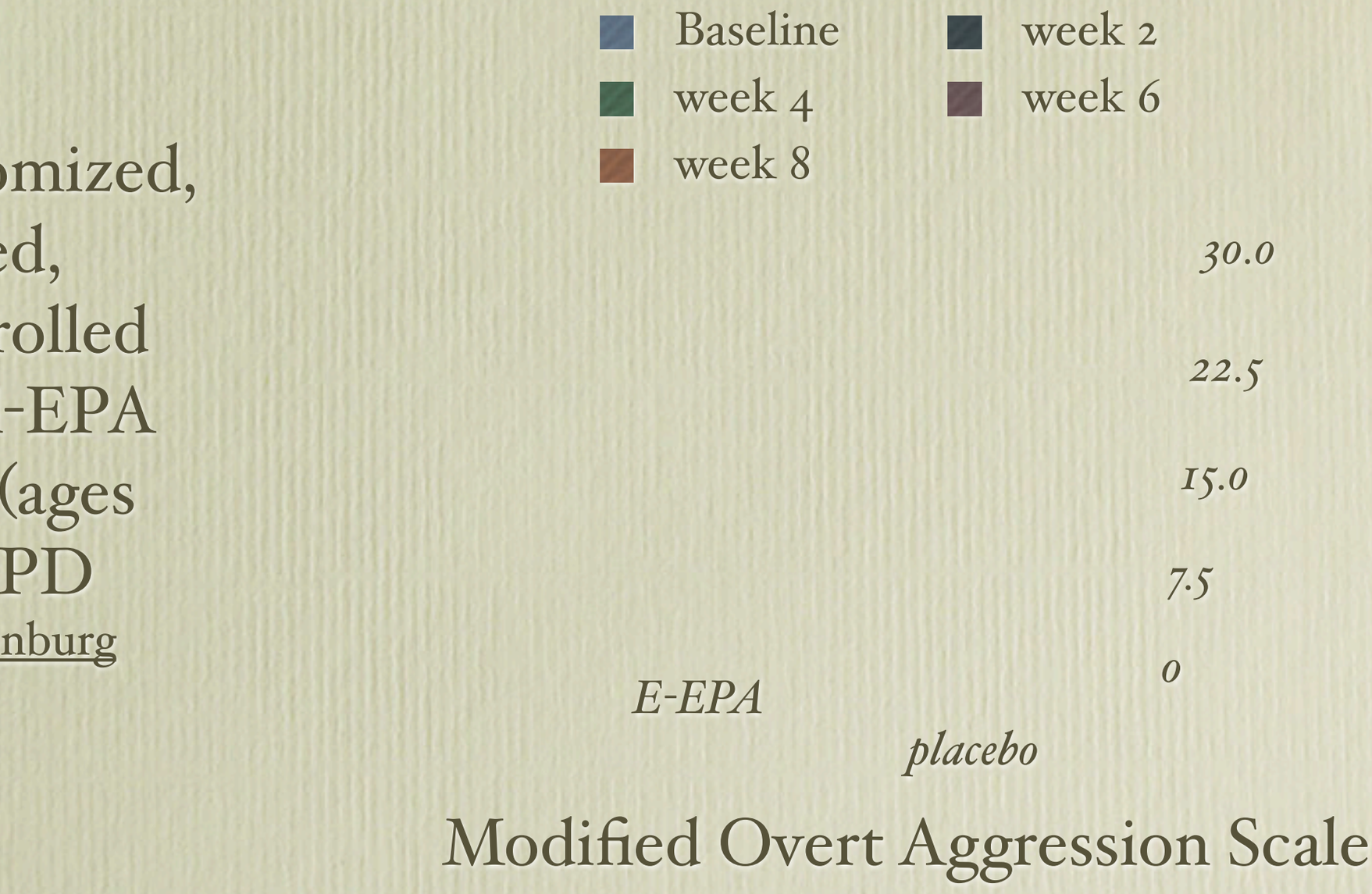
There was significant improvement with active treatment compared to placebo in Hamilton Rating Scale for Depression (HRSD) scores. White bars are baseline, light gray at 4 weeks, dark gray at 12 weeks.

Borderline Personality Disorder

- 8 week, randomized, double-blinded, placebo-controlled study of ethyl-EPA in 30 women (ages 18-40) with BPD [Zanarini & Frankenburg 2003]



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This article, which appeared in the American Journal of Psychiatry in 2003, described an 8 week study where 1 gram per day of ethyl-EPA was added to the treatment of 20 women with borderline personality disorder, while 10 women received placebo.

The between groups difference in aggression scores and in depression severity was statistically significant at $P<0.0001$. However, you can see that, even though the patients were randomized to either treatment or placebo, the baseline scores were not the same for aggression.

Cognitive impairment

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Now let's look at the role of omega-3s in preventing cognitive decline in the elderly.

- In a cohort of 342 men 69-89 years, MMSE scores and diet were looked at [Kalmijn et al 1997]:
  - High linoleic acid intakes associated with cognitive impairment
  - High fish consumption inversely associated with cognitive impairment

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Here is a cohort study which looked at cognitive function and diet in a group of elderly males. This study is important because it found that higher consumption of linoleic acid was associated with more cognitive impairment. Linoleic acid, once again, is the 18-carbon omega-6 fatty acid found in vegetable oils, which we North Americans are consuming in such prodigious amounts.

- Personnes Agées QUID, U. de Bordeaux [Larrieu et al 2004]:
  - 1460 people over 65 yrs, followed 8 yrs
  - Fish 1x/week: relative risk (RR) 0.66, compared to rare/never fish eaters
  - moderate drinkers had about half the risk of developing dementia over 8 years, compared to non-drinkers

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This is an epidemiologic study carried out in southwestern France, involving 2950 initially non-demented subjects over 65 years of age. A subsample of 1460 people was studied to look for a relationship between fish consumption and risk of developing dementia during the 8 years of the study.

Those who ate fish once a week had only two thirds the risk of developing dementia, compared to those who ate fish rarely or not at all.

Many of us who enjoy a glass of wine with dinner were happy with the finding that moderate drinkers had only half the risk of becoming demented compared to non-drinkers.

- The Cochrane Dementia and Cognitive Improvement Group looked for randomized, placebo-controlled, double-blinded trials of omega-3 fatty acids for the prevention of dementia, but were unable to find any (Oct 2005)

- Two such studies are expected to report in 2008 [Lim et al 2006]

Unfortunately, so far there are no high-quality intervention studies of omega-3 supplementation for the prevention of dementia, although at least two are underway and are expected to publish findings in 2008.

- Another review looked at 497 studies and identified 5 which met their inclusion criteria
  - “In four studies that assessed the effects of omega-3 fatty acids on incidence and treatment of dementia, a trend in favour of omega-3 fatty acids (fish and total omega-3 consumption) toward reducing risk of dementia and improving cognitive function was reported.” [Issa et al 2006]

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While the strength of the Cochrane reviews is their rigorous approach, that doesn’t take away from the value of other reviews with less strict standards.

These reviewers identified 5 intervention studies that met their criteria. Taken together, they concluded that there was a trend for omega-3 supplementation to be beneficial.

Developmental disorder

- evidence that fatty acid imbalance contributes to several common and overlapping childhood neurodevelopmental disorders:
  - attention-deficit/hyperactivity disorder (ADHD)
  - dyslexia (specific reading difficulties)
  - dyspraxia (developmental coordination disorder - DCD)
  - autistic spectrum disorders

Thursday, 20 December, 12

Now let's turn briefly to childhood development. I will look at only one recent study in this field, although there are quite a number. There is lots of epidemiologic evidence, once again, that fatty acid imbalance appears to play an important role in disrupting normal childhood neurological and psychological development.

Developmental coordination disorder - DCD

- affects ~5% of school-aged children
- core deficits in motor function
- difficulties in learning, behaviour, & psychosocial adjustment that persist into adulthood

Thursday, 20 December, 12

The study we will look at was specifically concerned with a condition called developmental coordination disorder, or DCD for short. DCD affects about 5% of schoolchildren, and manifests with both motor and neuropsychiatric dysfunctions.

- randomized, double-blinded, placebo-controlled trial of EFA supplementation in 78 boys & 39 girls, age range 70-147 months (5.8-12.3 years) [Richardson & Montgomery 2005]

- treatment: 6 caps of 80% fish oil, 20% evening primrose oil (558 mg EPA, 174 mg DHA, 60 mg GLA)

- after 3 months, placebo group was crossed over to active treatment for another 3 months

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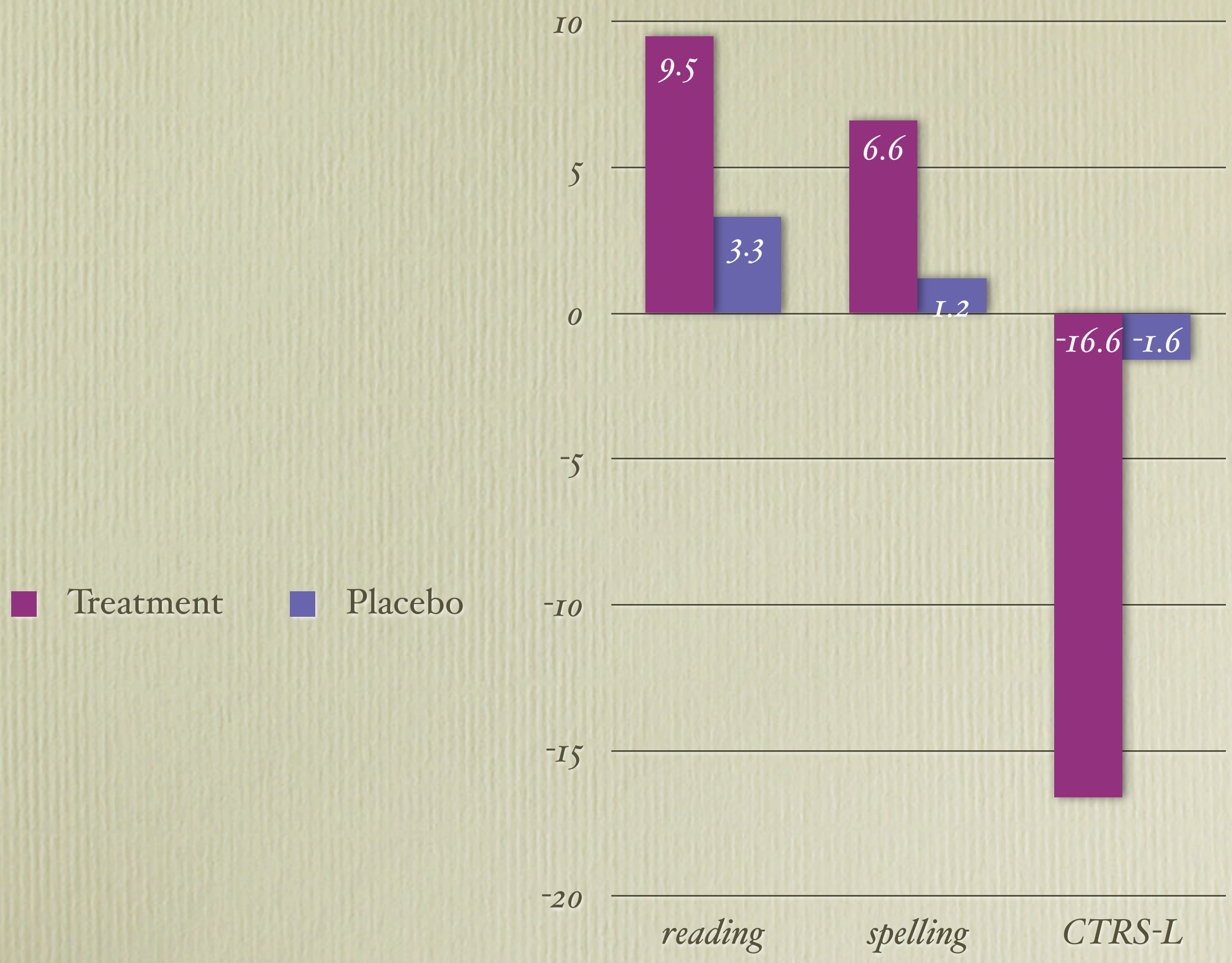
The study involved 117 children from about 6 to 12 years of age. Two-thirds were boys. The active treatment was a mix of mostly omega-3 along with some omega-6 fatty acids.

The placebo group got olive oil capsules.

Although the total study duration was 6 months, I will only report results from the first 3 months, when active treatment was being compared to placebo.



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Here are the results.

There was no difference between treatment and placebo groups in terms of changes in motor skills.

Reading skills improved by an average of 9.5 months for the treatment group during the 3-month phase, but only 3.3 months for the placebo group. The difference for spelling skills was more pronounced, 6.6 months vs 1.2 months.

The CTRS-L stands for the Conners' Teacher Rating Scales, Long Version, which is a standardized assessment for ADHD symptoms. Mean scores decreased by 16.6 for the treatment group, vs 1.6 for the placebo group.

I've given you a biased distillation of some of the research out there, biased in favour of omega-3s. But there is research which I haven't mentioned, randomized controlled trials of omega-3s which did not show a significant benefit.

Very little of the research being done actually controls for omega-6 intake. I think this is a real problem. You recall the study on macular degeneration. There was no association between omega-3s and this condition, for individuals with higher levels of linoleic acid intake.

My guess is that we would be more likely to show a benefit for omega-3 supplementation in preventing or treating illness if part of the intervention included reducing linoleic acid intake.

What should I do?

- Increase long-chain omega-3s DHA & EPA
    - Eat more fish or take fish oil supplements
- Decrease omega-6 intake (linoleic acid)
    - Use less vegetable oil

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So what can we, as individuals, do?

First, eat more fish or take fish oil supplements.

Second, cut back on our intake of vegetable oil. This is the tricky part, so I'll deal with it first.

	LA	saturated fat	monounsaturated fat
Sunflower oil, high oleic	3.6	9.7	83.6
Olive oil	9.8	13.8	73.0
Flaxseed oil*	12.7	9.4	20.2
Canola oil	20.3	7.1	58.9
Soybean oil	51.3	14.4	23.3
Sunflower oil, 65% linoleic	65.7	10.3	19.5
Safflower oil	74.6	6.2	14.4

*ALA in flaxseed oil: 53.3 g/100 g

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When shopping, read the labels, and avoid products such as baked goods made with vegetable oil, especially the ones with loads of linoleic acid, such as safflower oil.

Sunflower oil is more problematic: it shows up twice in this table, which is based on the U.S. Department of Agriculture nutrient database. The uppermost entry has very little linoleic acid, while the high-linoleic acid sunflower oil has almost as much as safflower oil.

For salads, olive oil may be your best bet.

Flaxseed oil is quite low in linoleic acid, and very high in alpha-linolenic acid, a short-chain omega-3. While unsuitable for cooking, flaxseed oil can certainly be used with salads, and ground flaxseed finds many other uses as a food supplement.

Cooking fats

	LA	saturated fat	monounsaturated fat
Butter, unsalted	2.2	51.4	21.0
Bacon drippings	9.4	32.0	41.4
Lard	10.2	39.2	45.1
Shortening	25.2	25.0	42.5
Margarine, tub	26.5	13.0	36.1

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For frying or baking, it makes sense to avoid shortening altogether, as it is high in trans fats, which used to be labelled as partially hydrogenated vegetable oils. Trans fats are most definitely bad for your cholesterol and your heart!

You can buy margarine nowadays that has no trans fats in it, but margarines in general are high in linoleic acid, so I would suggest to avoid them also.

For frying and baking, butter is still the ingredient of choice for many professional chefs. Concerns about butter and its contribution to heart disease need to be taken seriously. However, a recent prospective study suggests that the risk of the so-called “Western” diet containing lots of meat and dairy products applies only to overweight and obese individuals.

ω3s: dietary recommendations

[Holub 2002]

- Health Canada, 1990:
  - Recommended omega-3 intake: 1.0 g daily for males over 75; 1.8 g daily for males 16-18 years
- NIH workshop 1999:
  - Combined avg EPA & DHA intake of 650 mg/day for healthy adults
  - Obtained with fatty fish 2-3x/wk
  - Based on data from MRFIT study, showing decreased CHD & total mortality with intakes up to 665 mg/day

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For omega-3 intake, we have recommendations by a couple of government organizations.

Way back in 1990, Health Canada issued its recommendations for omega-3 intake, ranging from 1 to 1.8 grams per day, depending on age and gender. It's interesting that we never hear about this.

For heart health, several organizations have weighed in with their recommendations. For example, the National Institutes of Health in Washington suggests around 600 mg per day of EPA and DHA combined. You can get this by eating fatty fish two or three times per week.

American Heart Association Recommendations 2006

[Lichtenstein et al 2006]

Fish Oil Supplements

Fish intake has been associated with decreased risk of CVD.[83,84] On the basis of the available data, the AHA recommends that patients without documented CHD eat a variety of fish, preferably oily fish, at least twice a week.[42] Patients with documented CHD are advised to consume ≈1 g of EPA+DHA per day, preferably from oily fish, although EPA+DHA supplements could be considered in consultation with their physician. For individuals with hypertriglyceride-mia, 2 to 4 g of EPA+DHA per day, provided as capsules under a physician's care, are recommended.[42]

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This is from a paper that appeared in the July 2006 issue of "Circulation", the journal of the American Heart Association. The article has as its title: "Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee."

For individuals with documented coronary heart disease, the AHA recommends about 1 gram of EPA+DHA per day. This is the amount you would get from eating about 4 ounces of farm rainbow trout every day. Alternatively, you could take 3 fish oil capsules daily to meet this recommendation. This is likely the preferred route, as we'll see in a bit.

EPA + DHA, g/100g

Fish Oils	
Menhaden oil	21.8
Salmon oil	21.2
Sardine oil	20.8
Cod liver oil	17.9
Herring oil	10.5
Omega-3 eggs	0.17

Mackerel, Atlantic	
raw	2.30
cooked	1.20
Herring, Atlantic	
raw	1.57
cooked	2.02
pickled	1.39
kippered	2.15

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This slide shows the gram content of omega-3 LCPUFAs DHA and EPA in various fish oils, as well as fish. These numbers are from the US Department of Agriculture nutrient database.

I've included the values for pickled and kippered herring.

Also for comparison, the DHA + EPA content for omega-3 eggs is given. This figure comes from the website of Burnbrae Farms. The alpha-linolenic acid content is even lower, only 61 mg, or 0.061 g, per 100 g of egg.

EPA + DHA, g/100g

Salmon, Atlantic	
Wild, raw	1.44
Wild, cooked	1.84
Farmed, raw	1.91
Farmed, cooked	2.15
Sockeye, canned	1.15
Lox	0.45
Rainbow Trout	
Wild, raw	0.59
Wild, cooked	0.99
Farmed, raw	0.93
Farmed, cooked	1.15
Sardines	
Atlantic, canned in oil	0.98
Pacific, canned in tomato sauce	1.60

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On this slide, note that lox may be tasty, but it's not very good in terms of preserving the omega-3 content of salmon. I was pleasantly surprised to learn that farmed salmon and farmed trout are better sources than their wild counterparts. This is entirely the opposite of what occurs with meat, where range-fed animals have a better omega-3 to omega-6 ratio than grain-fed.

EPA + DHA, g/100g

Tuna, bluefin		**Tuna, light**	
raw	1.07	Canned in oil	0.13
cooked	1.50	Canned in water	0.27
Tuna, skipjack		**Tuna, white**	
raw	2.15	Canned in water	0.86
cooked	1.15	**Halibut**	
Tuna, yellowfin		Raw	0.36
raw	0.22	Cooked	0.47
cooked	0.28		

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The USDA data has some anomalies which I can't explain. For example, cooking blue-fin tuna improves the omega-3 content, but reduces it for skipjack tuna.

Fish oil vs fatty fish

[Melanson 2005]

Selected Environmental Toxin Content of 5 Preparations of Fish Oil

Brand Name	Polychlorinated Biphenyls, ppb	Organochlorine, ppb
CVS	None detected	None detected
Kirkland	None detected	None detected
Natrol	None detected	None detected
Omega Brite	None detected	None detected
Sundown	None detected	None detected

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But of course, fish contains mercury, PCBs, pesticide residues, and other stuff that's not good for us. Pregnant women and children in particular are advised to avoid certain fish and limit their consumption of other fish because of concerns about mercury.

Fortunately, fish oil may be a safer way to obtain DHA and EPA.

These researchers performed analyses of several brands of fish oil supplements commercially available in the U.S., and found that the level of PCBs and organochlorines were below what they could detect.

Fatty fish vs fish oil

[Foran 2003]

Mercury Content of 5 Preparations of Fish Oil

Fish Oil Brand Name	Mercury Level, μg/L
CVS	10
Kirkland	<6
Nordic Ultimate	<6
Omega Brite	12
Sundown	<6

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The same group also looked at mercury content of fish oil.

Large carnivorous fish that are high in the food chain, such as swordfish or shark, have the highest tissue concentration of mercury (1 microgram/gram) whereas tuna, trout, pike, and bass have intermediate concentrations (0.1–0.5 microgram/gram).

Commercial fish oils are usually made from small fish, low down in the food chain, and thus already low in mercury. The type of processing also reduces contaminants.

Fish vs fish oil

	2 cans of tuna per week	2 fish oil capsules per day
DHA+EPA	0.92 g	4.2 g
mercury	68 mcg	0.17 mcg

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I've done the calculations for you here. Compared to eating two cans of light tuna per week, taking 2 fish oil capsules daily would give you 4.6 times more DHA+EPA, but only one quarter of 1 percent as much mercury.

		*HC/CFIA STANDARDS: **2.0ppm**	*HC/CFIA STANDARDS: **20ppt**	*HC/CFIA STANDARDS: **0.5ppm**		
Product:	**TOTAL mg**	**PCBs**	**Dioxins**	**Mercury**	**DISTILLATION**	**AXYS ANALYTICAL PCB LAB TESTS**
HERBAL SELECT: Salmon Oil	1000	< 0.09ppm	max 1.5ppt	< 0.1ppm	steam	not tested
HEALTH BALANCE: Salmon Oil (Costco Wholesale's brand)	1000	< 0.09ppm	< 1.5ppt	< 0.1ppm	steam	not tested
LIFE: Omega 3:6:9 (Shoppers Drug Mart brand)	1200	< 0.09ppm	< 1.5ppt	< 0.01ppm	molecular	not tested
HOLISTA: Premium Fish Oil	1000	0.09ppm	1.5ppt	0.1ppm	steam	not tested
JAMIESON: Omega Protect Salmon Oil	1000	< 0.09ppm	max 1.5ppt	< 0.1ppm	steam and molecular	not tested
TRULY PREMIUM ALL NATURAL: Salmon Oil	1000	max 1ppm	0.58ppt	< 0.005ppm	molecular	not tested
REXALL NATURALS: Salmon Oil (Pharma Plus brand)	1000	max 1ppm	0.58ppt	< 0.005ppm	molecular	not tested
SWISS HERBAL: Salmon Oil	1000	< ppb	< 1.5ppt	0.005ppm	molecular	not tested
CLEARWATER	1000	1ppt	.387ppt	< 10ppb	molecular	not tested
WEBBER NATURALS: Cardio Support Super Concentrate	1000	0.09ppm	2ppt	0.1ppm	molecular	not tested
WEBBER NATURALS: Salmon & Fish Oils	1000	0.09ppm	1.5ppt	0.1ppm	steam	not tested
ORGANIKA: Wild Pacific Salmon Oil (Nutrition House Extra)	1000	< 0.030ppm	not detectable	< 0.05ppm	steam and molecular	not tested
NATURAL FACTORS RX: Wild Sockeye Salmon Oil	1000	1ppm	1ppt	1ppm	steam	**0.06ppm
LIFE: Salmon Oil (Shoppers Drug Mart brand)	1000	< 0.09ppm	< 1.5ppt	< 0.01	molecular	**0.04ppm

* Health Canada and Canadian Food Inspection Agency standards.
**NOTE: AXYS' pcb tests found LOWER trace amounts than even the trace amounts listed on the Certificates of Analysis

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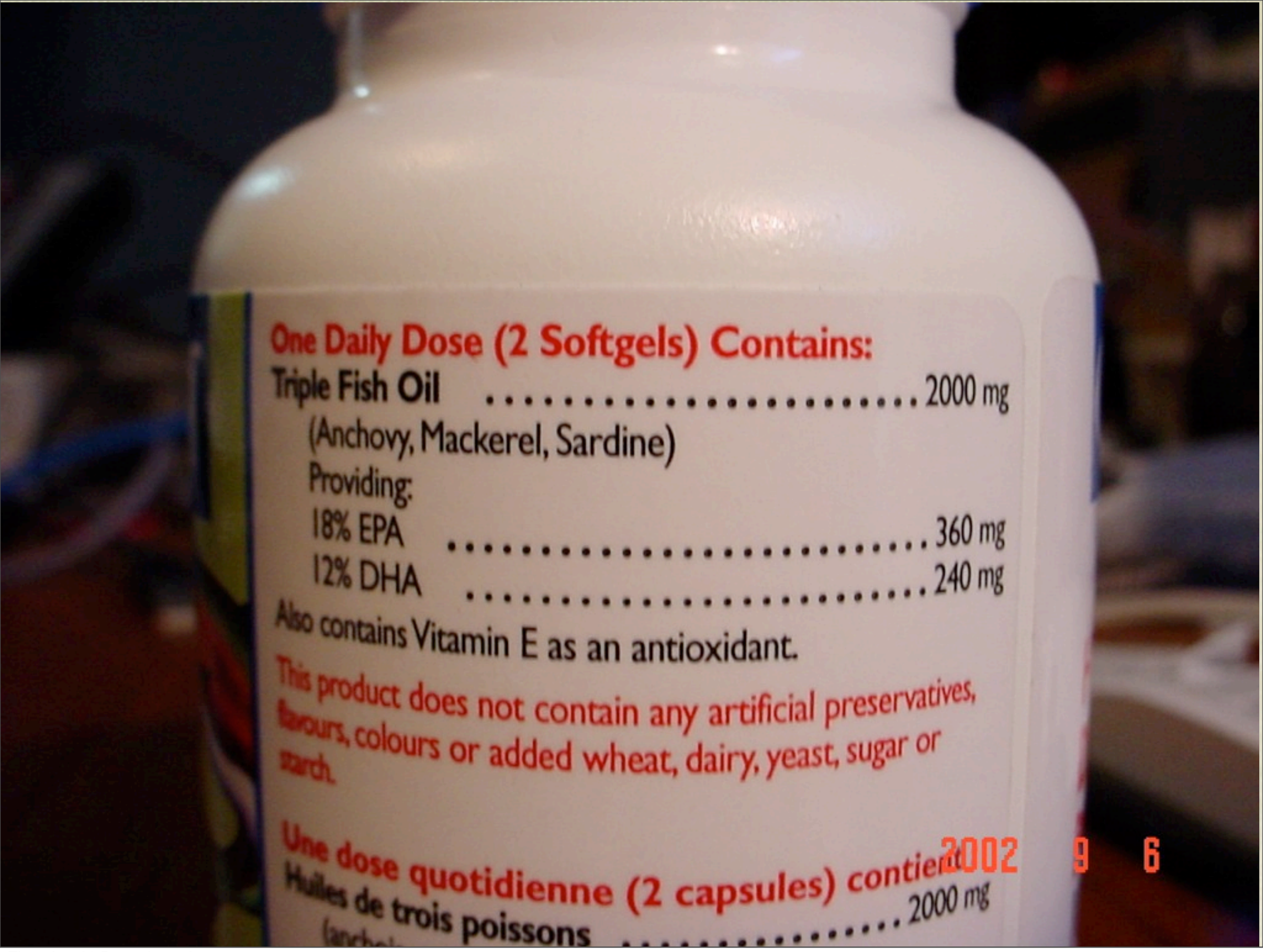
This table comes from the CTV network web site. It contains data from a series of tests that CTV had ordered for a number of different fish oils available in Canada. This slide is very hard to read, but it demonstrates that the levels of PCBs, dioxins, and mercury are all quite low, although the range of mercury levels varies considerably from one product to another.

So if you don’t eat fatty fish every day, what should you do?

I’ve been recommending to my patients to take fish oil supplements, for example, two or three capsules per day of 1000 mg each.



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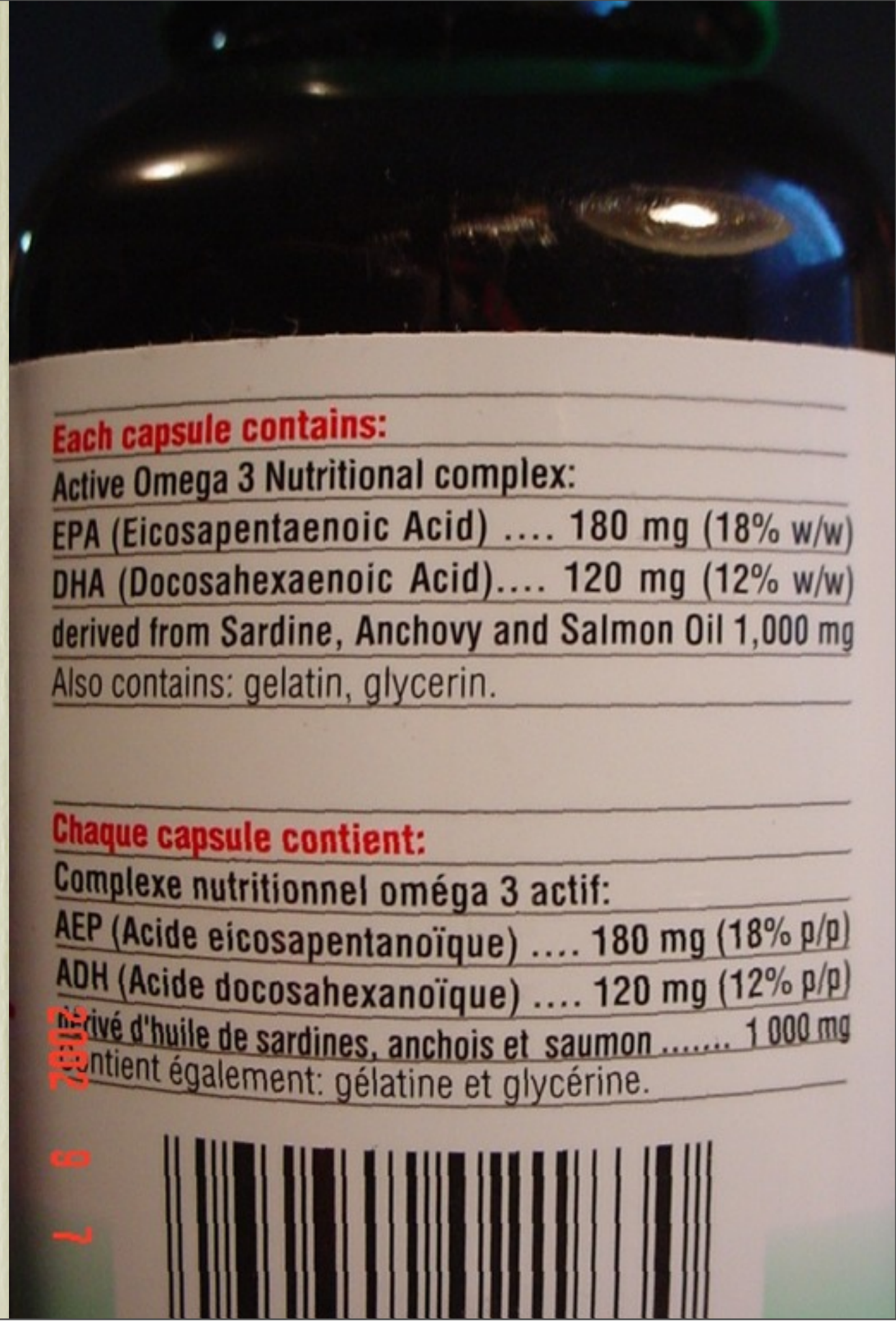
Two capsules a day of this product would yield a total of 600 mg of omega-3s.

But check the label. I've come across preparations which either don't tell you the amounts of DHA and EPA at all, or have concentrations only one-third of what's in this product.

How the product is made is also important, but the manufacturers don't tell you about this. These highly unsaturated fatty acids oxidize very easily. This produces a rancid, fishy smell and taste. To prevent this, the oil should be extracted from the fish at low temperatures, and processing into capsules is ideally done in a nitrogen atmosphere to avoid contact with oxygen.

I've had people tell me that some preparations they've tried caused them to burp a lot, leaving an unpleasant fishy taste in their mouths.



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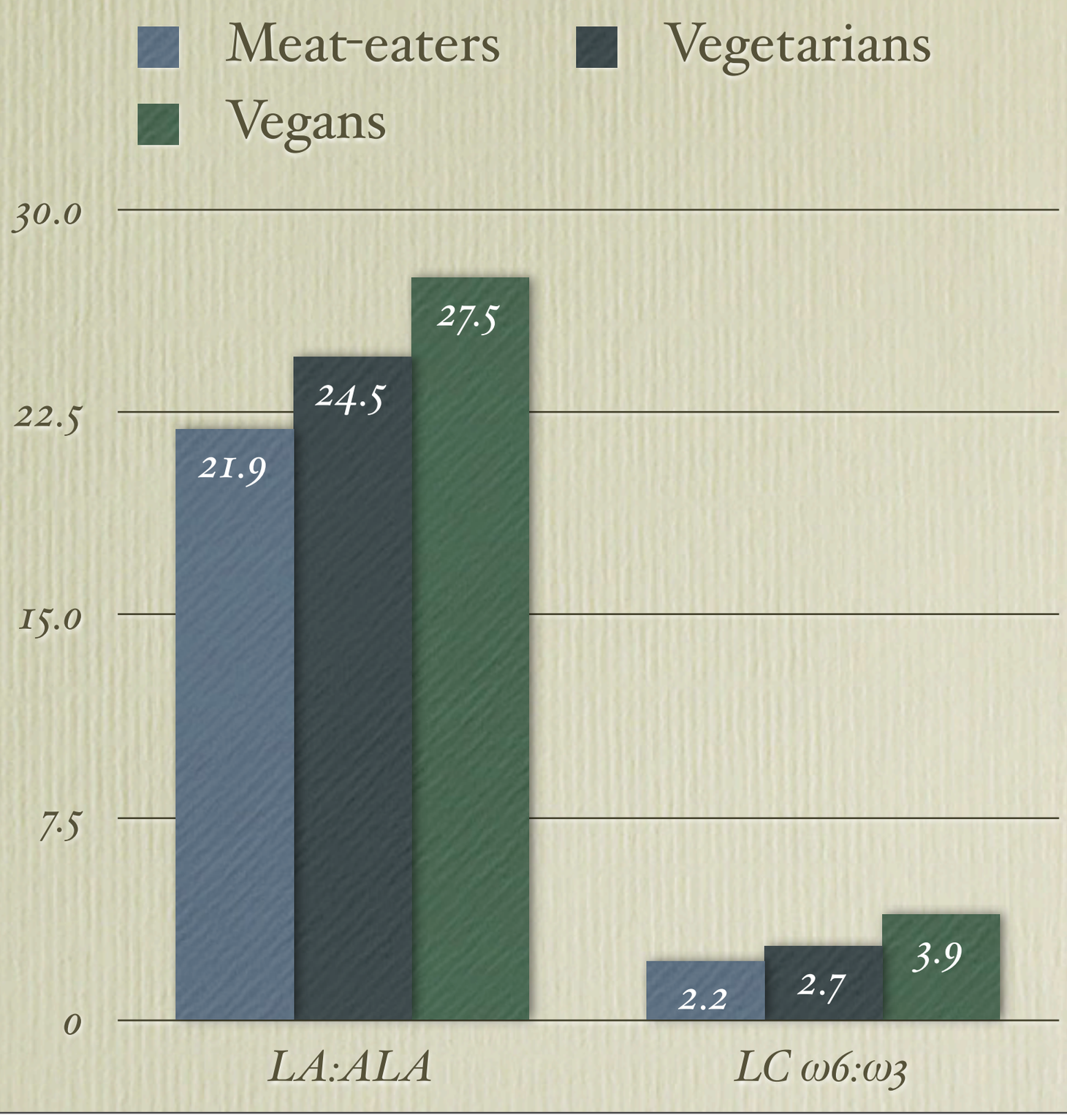
So far, I've not heard many complaints about this product. I use it myself.

Vegetarians

- cross-sectional study of 659 U.K. men: questionnaire re diet, smoking, etc.; lab for fatty acids [Rosell et al 2005]
- 196 meat-eaters, 231 vegetarians, 232 vegans
- LC ω6: AA+GLA
- LC ω3: EPA+DPA +DHA



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There are many people these days who avoid meat, sometimes for ethical reasons, but often for their health. If they also avoid fish, and won't take fish oil capsules, that may pose a problem.

Here is a study which looked at fatty acid profiles in a sample of British men: meat-eaters, vegetarians, and vegans.

The graph shows that the ratio of linoleic to alpha-linolenic acid gets worse as you eat fewer animal products. Even worse, though, is the ratio of the long-chain omega-6 to omega-3 fatty acids, where vegans have almost double the ratio of meat-eaters. This suggests that vegans are at higher risk of inflammatory diseases.

What about omega-9?

- We can make omega-9 fatty acids ourselves, therefore these are not considered essential fatty acids.
- We get plenty of omega-9 fatty acids in vegetable oil, eg olive oil is 71% oleic acid, canola oil 56%.

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What about omega-9? Many people buy commercial preparations with labels such as omega 3-6-9, reasoning that if omega-3 is good, omega 3-6-9 has to be better, right?

Not so. I've already pointed out that we need to reduce omega-6 consumption, that we get lots in our North American diets. Why pay good money for something we already get lots of?

This slide gives the low-down on omega 9.

Summary

- Decrease omega-6 and increase omega-3 consumption to improve medical and mental health
  - reduce vegetable oil consumption
  - increase fatty fish or fish oil consumption

I think I've covered everything I have time for. Thank you very much! You've been a great audience!