Nutrition and the Modern Mind

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Every person with a brain deserves good nutrition!

Nutritional medicine as mainstream in psychiatry

Jerome Sarris, Alan C Logan, Tasnime N Akbaraly, G Paul Amminger, Vicent Balanzá-Martínez, Marlene P Freeman, Joseph Hibbeln, Yutaka Matsuoka, David Mischoulon, Tetsuya Mizoue, Akiko Nanri, Daisuke Nishi, Drew Ramsey, Julia J Rucklidge, Almudena Sanchez-Villegas, Andrew Scholey, Kuan-Pin Su, Felice N Jacka, on behalf of The International Society for Nutritional Psychiatry Research

Lancet Psychiatry, 2015

- The emerging and compelling evidence for nutrition as a crucial factor in the high prevalence and incidence of mental disorders suggests **that diet is as important to psychiatry as it is to cardiology, endocrinology, and gastroenterology**.

- Evidence is steadily growing for the relation between dietary quality (and potential nutritional deficiencies) and mental health, and for the select use of nutrient-based supplements to address deficiencies, or as monotherapies or augmentation therapies.

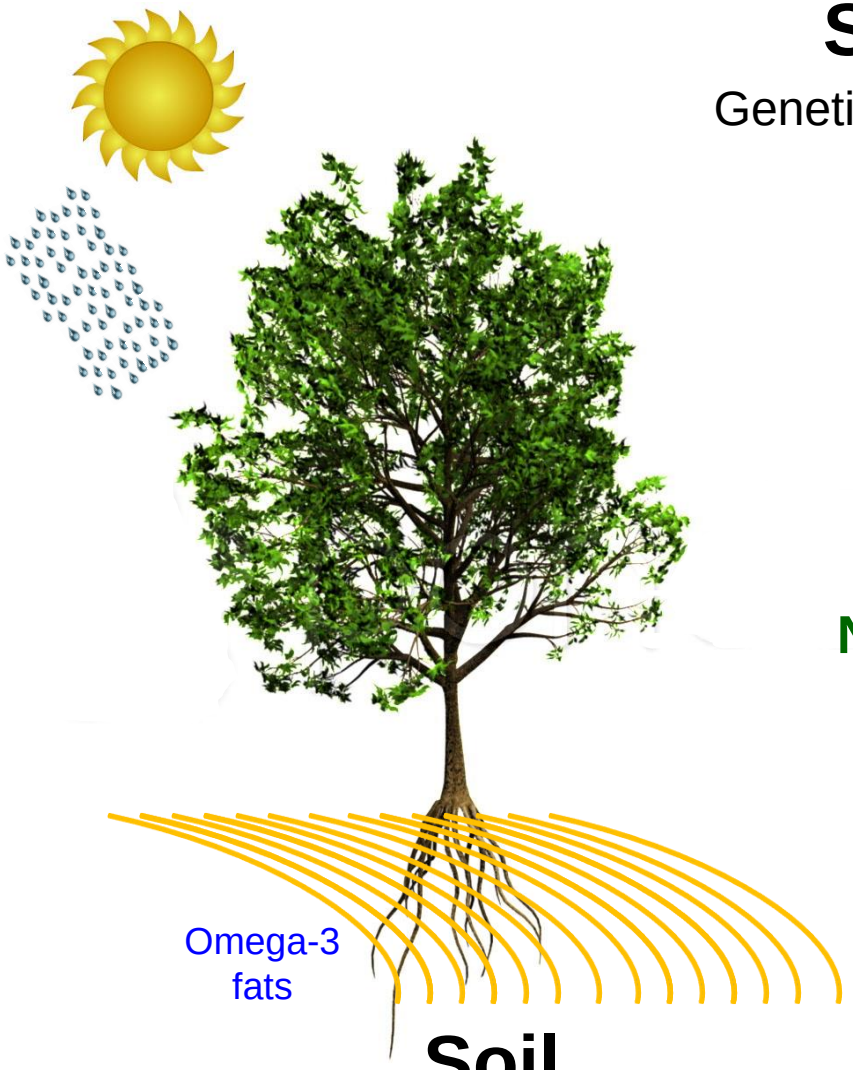
- **The members of the International Society for Nutritional Psychiatry Research advocate recognition of diet and nutrition as central determinants of both physical and mental health.**

Family love and social learning

Family chaos and social strife

Seed

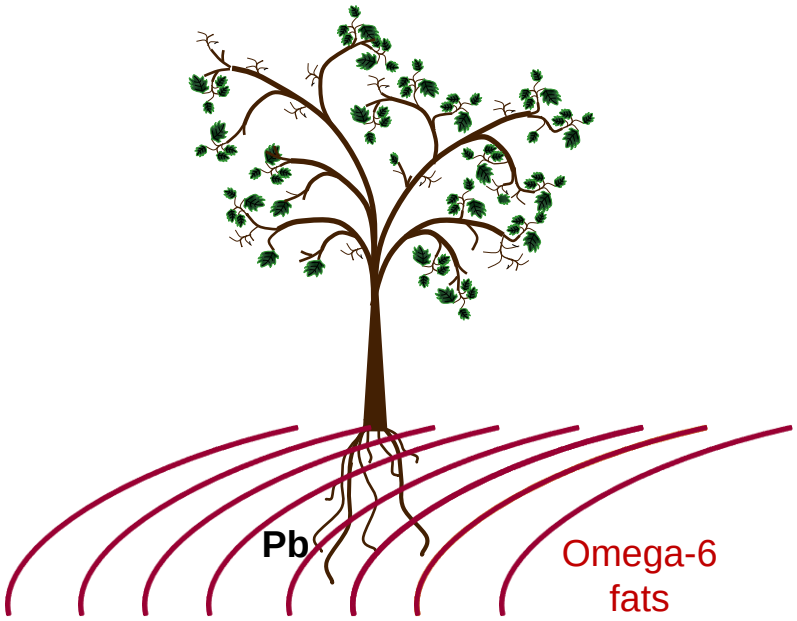
Genetic Inheritance



Soil

Essential Brain Nutrients

Neuron

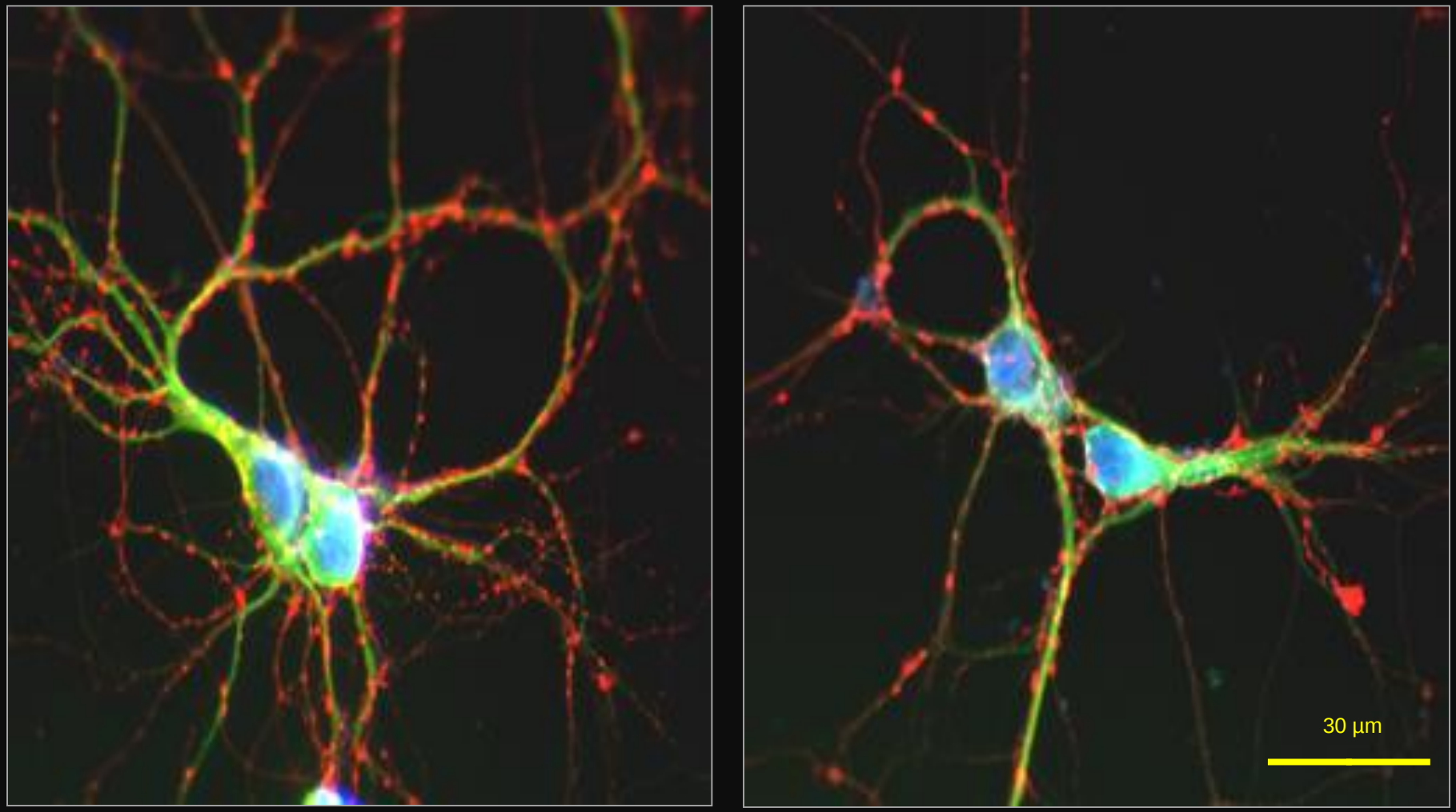


Poor Soil

Deficient in Nutrients

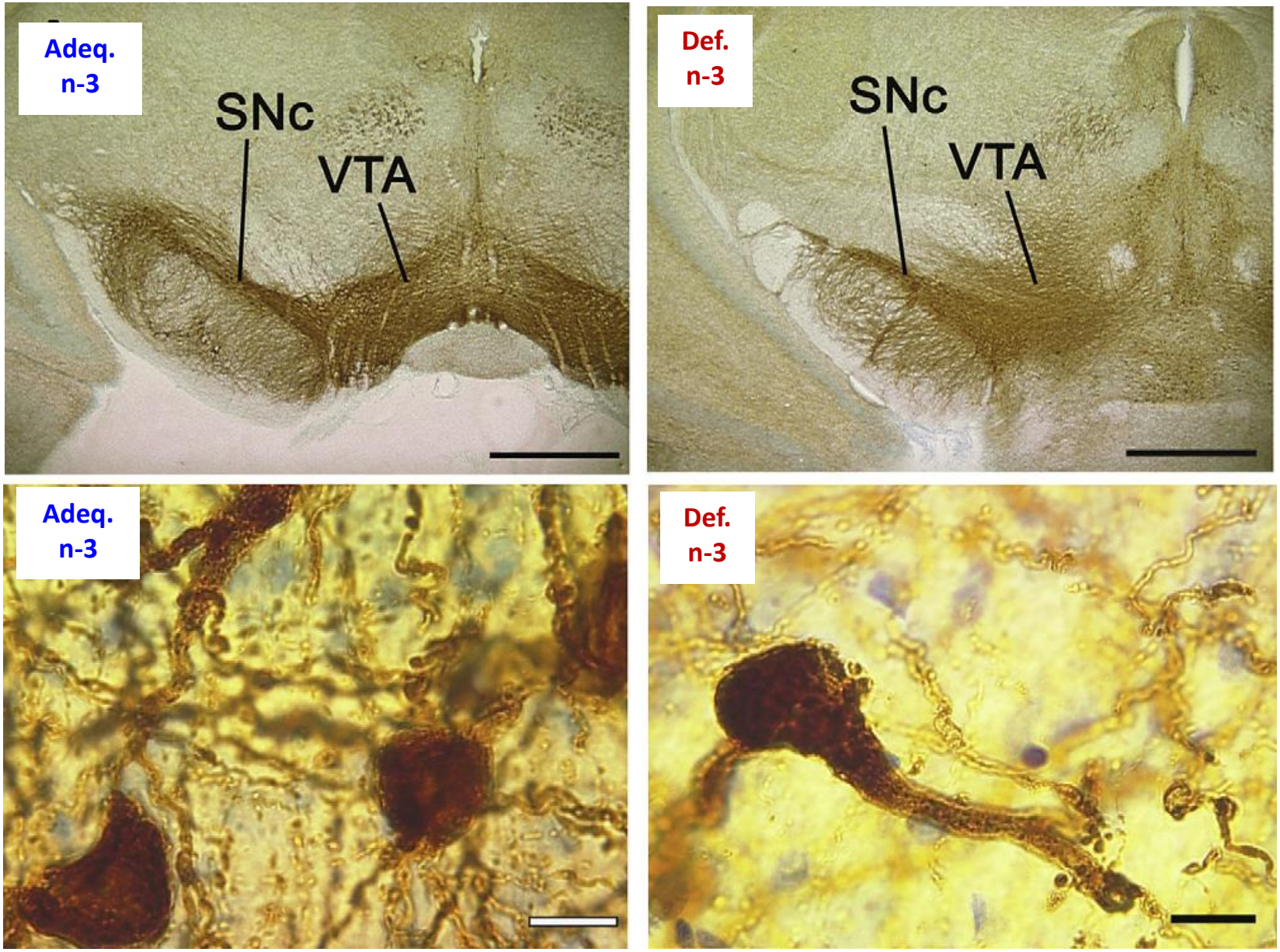
Adequate DHA (22:6n-3)

Deficient (22:5 n-6)



Cao et al. *J. Neurochem.* 2009

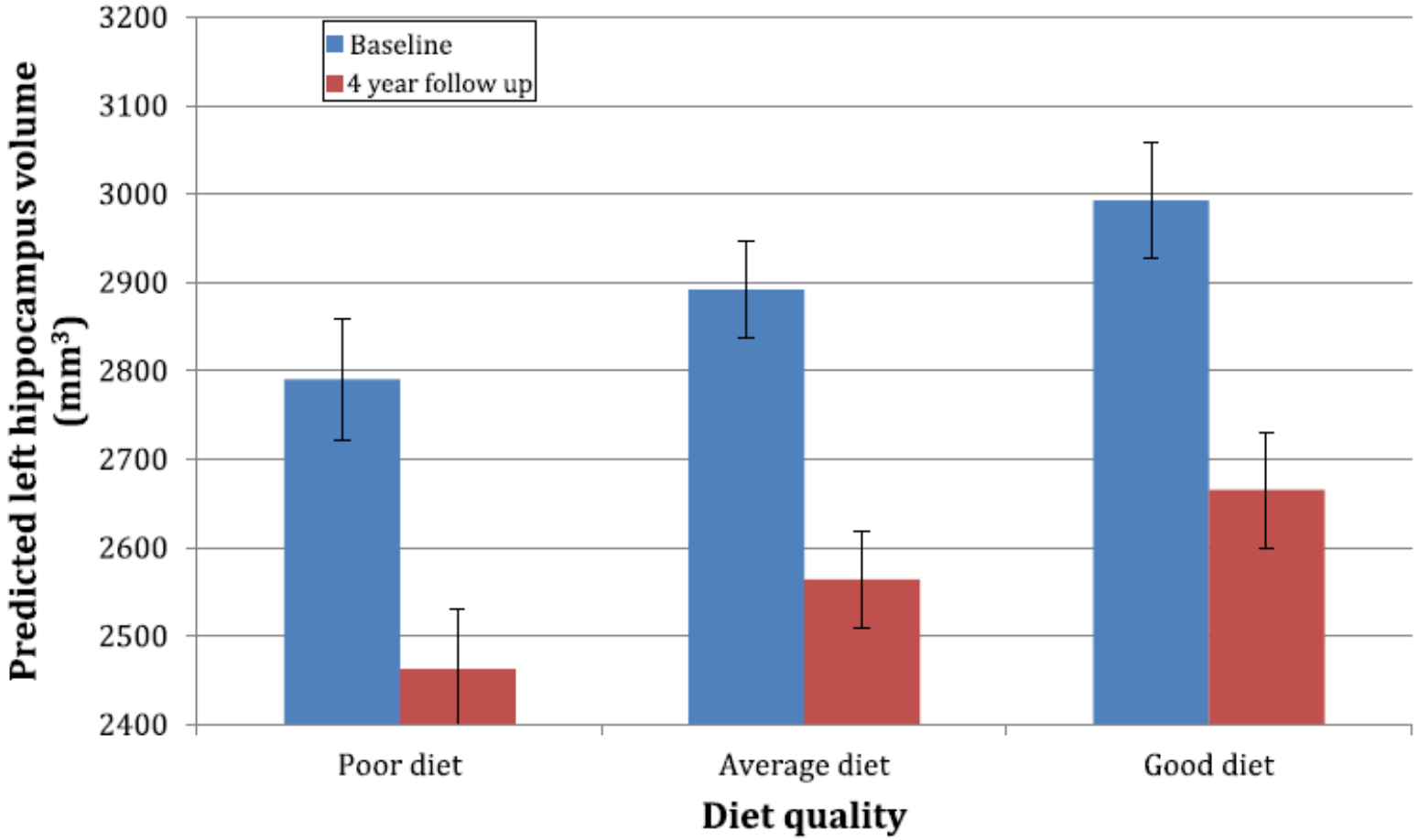
n-3 HUFA deficient diets cause 50% loss of dopaminergic neurons



Tyrosine hydroxylase staining

Ahmad, Levant et al Neurosci Let (2008) 438 303–307

“Poor” diets are associated with smaller brain volumes



“Good” diet: fresh vegetables, salad, fruit and grilled fish
“Poor” diet: roast meat, sausages, hamburgers, steak, chips, crisps and soft drinks

Jacka et al. BMC Medicine (2015) 13:215

Essential Fats: Metabolism and Dietary Sources

Omega-6

18:2n-6 linoleic acid,
LA

Soy bean oil
Safflower oil
Corn oil

- Competition -

D6 desat
D5 desat
D6 desat
FADS 1-2

20:4n-6, arachidonic acid
AA

Meat,
Organs

22:5n-6 DPA n-6

Omega-3

18:3n-3 alfa-linolenic acid,
ALA

Flax
~ Canola
Leaf plants

20:5n-3,eicosapentaenoic acid,
EPA

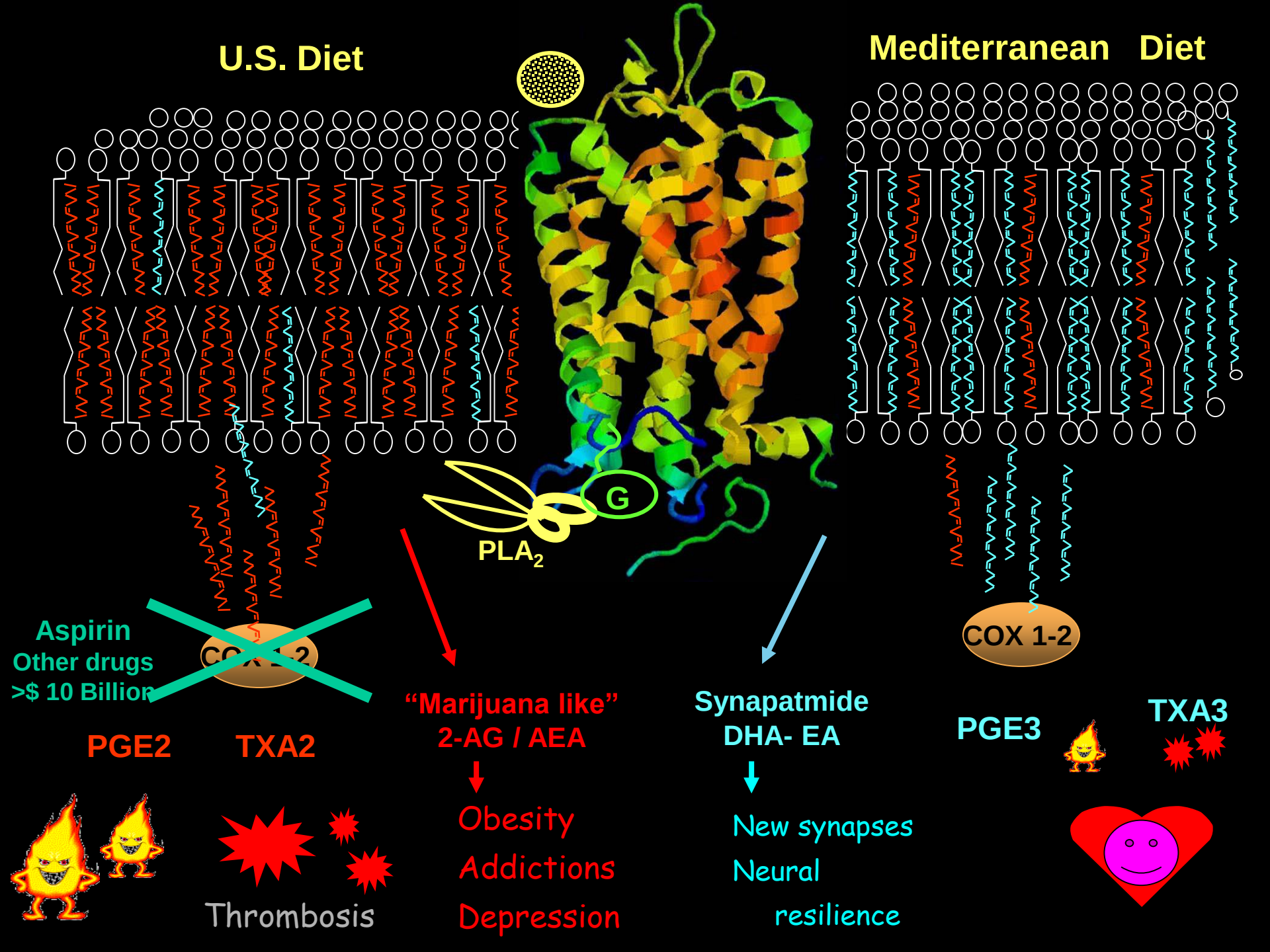
Seafood
Breast milk
(DHA)

22:6n-3, docosahexaenoic acid,
DHA
(brain, retina, testis)

Bioactive lipid mediators

2-series Prostanoids	3-series Prostanoids
4-series Leukotrienes	5-series Leukotrienes
Hepoxilins	Resolvins
Lipoxins	Maresins
HETEs	Protectins
EETs	n-3 monoepoxides
AEA (anandamide)	DHA-EA (synaptamide)
2-AG	2-DHG

immune - metabolic - developmental responses


U.S. Diet
Mediterranean Diet
G
PLA2
Aspirin
Other drugs
>$ 10 Billion
COX 1-2
COX 1-2
PGE2
TXA2
Thrombosis
"Marijuana like"
2-AG / AEA
Obesity
Addictions
Depression
Synapatmide
DHA- EA
New synapses
Neural
resilience
PGE3
TXA3

Omega-3
Plants/Leaves/Insects

Traditional Farming & Poultry Raising Utilized a More Varied, Natural & Wild-Type Diet - Rich in Omega-3

Omega-6
Plants/Seeds

In the Last Century, Industrialized Farming of Soy and Corn Has Changed Chicken to Be High in n-6 and Low in n-3

FOODS

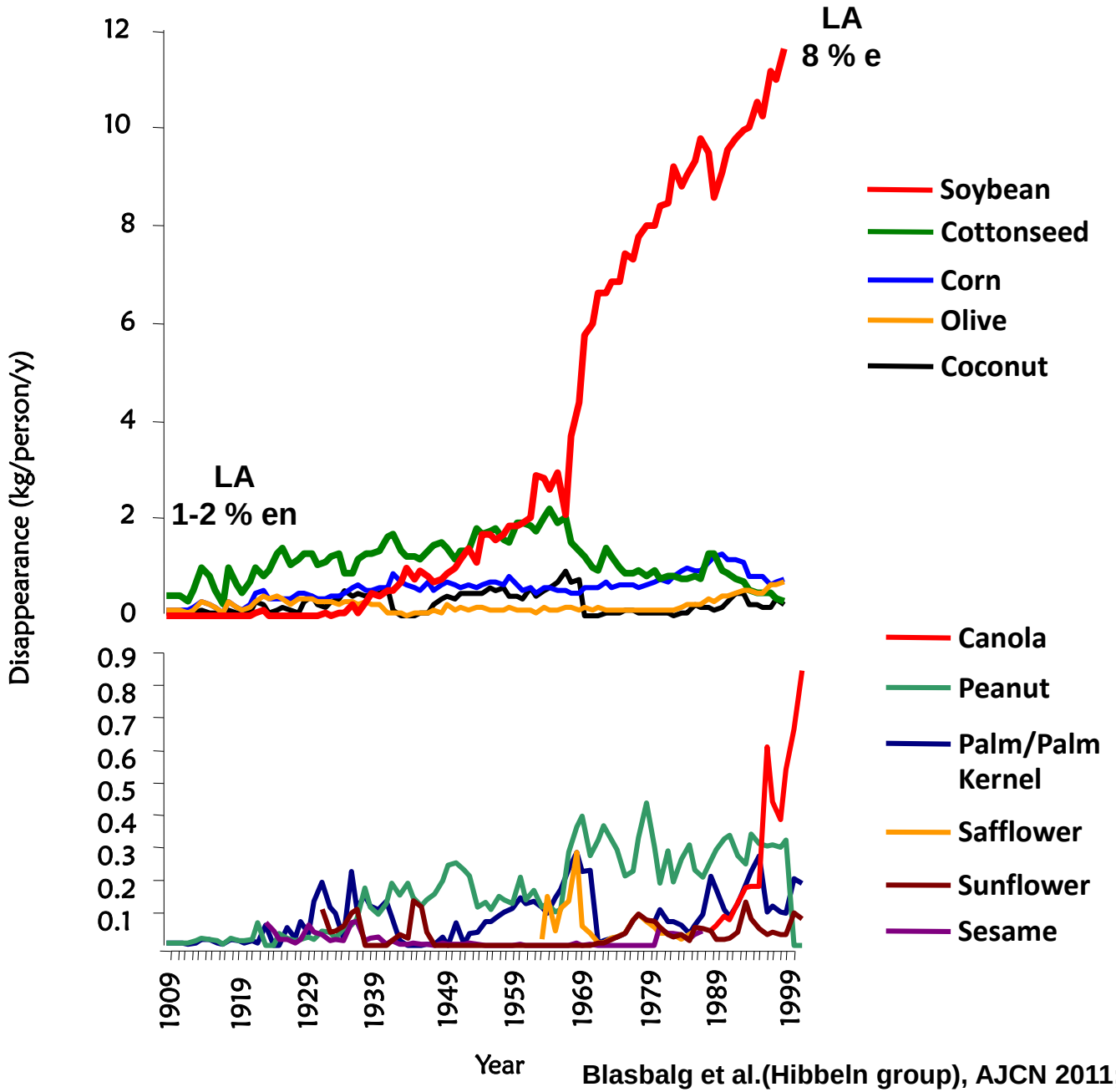
- Grass Fed Lamb
- Farm Beef
- n-3 Chicken
- n-6 Chicken
- Wild Fish
- Farm Fish
- Olive Oil
- Soy Oil

Reduced Inflammation & Disease Risk

Strong Inflammation & Disease Risk

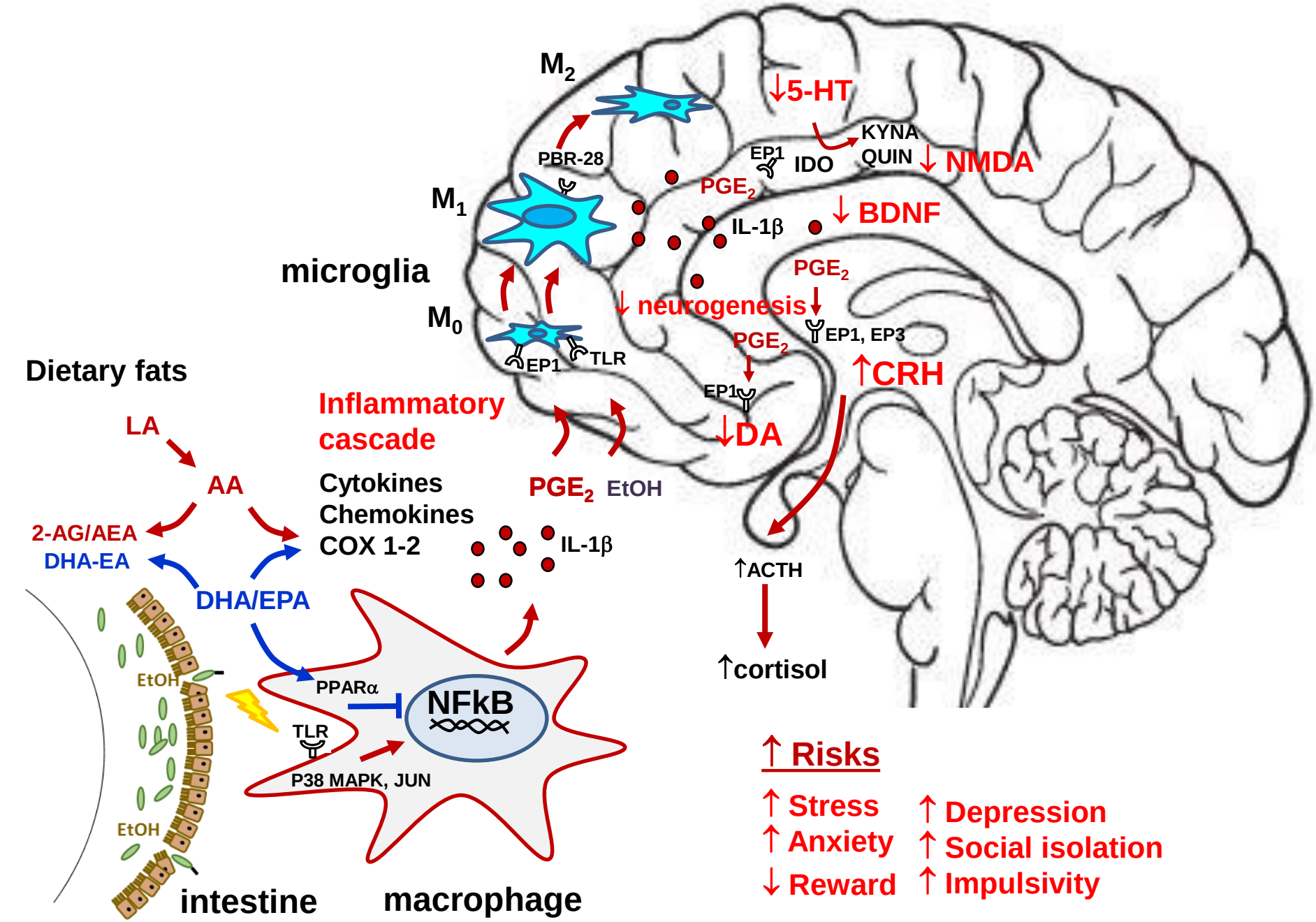
Omega-3 in Body	70%	60%	50%	40%	30%	20%	17%
	ACHIEVABLE Trad. Innuit	SUPERB Trad. Japanese	HEALTHY Mediterranean	ACTION BENEFICIAL	REMEDIAL ACTION	URGENT ACTION	US NOW DANGER

Soy oil Consumption Increased 1,000 fold in the 20th Century, USA



Blasbalg et al.(Hibbeln group), AJCN 2011; 93: 950-962.

Dietary fats and neuro-inflammation in mental ill health



↑ Risks

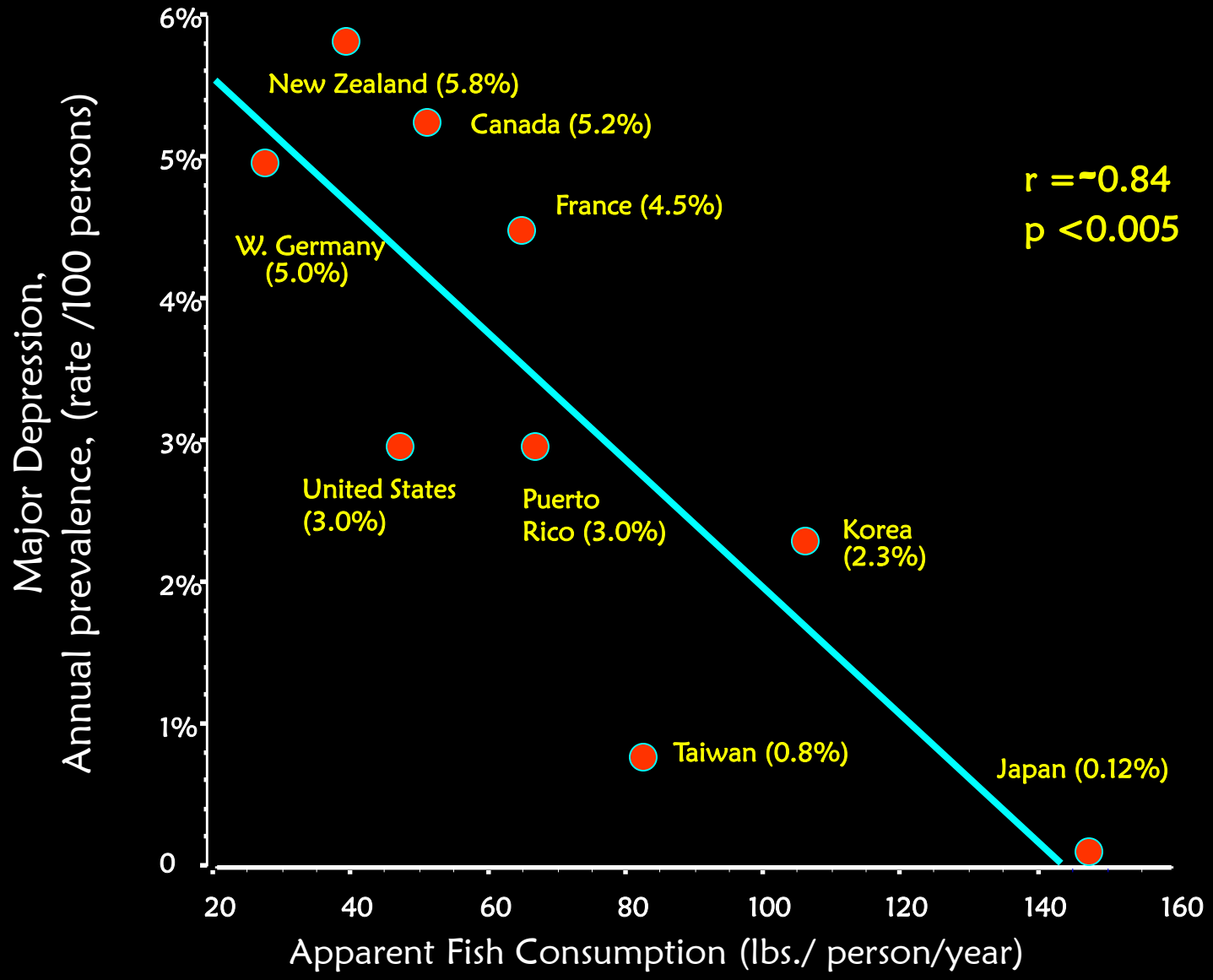
- ↑ Stress
- ↑ Anxiety
- ↓ Reward
- ↑ Depression
- ↑ Social isolation
- ↑ Impulsivity

Omega-3 HUFAs and Dysphoric Disorders?

Overview of human data

Disorder	Plausible mechanism	Epidemiological Ecological	Case control (Tissue)	RCT's	Meta-analyses	Positive clinical effect? Size?
Major depression	Yes	54	17	52	6	Yes Large effect
ADHD	Yes	6	15	10	2	Yes Less than stimulants
Aggression violence/conduct	Yes	8	5	10	2	Replicates Large effect ↓ 40 % in felony violence
Anxiety	Yes	2	5	3	-	Probable -
Alcohol/ Sub. use	Yes	-	4	1	-	Hopeful Large effect
Suicide	Yes	6	4	1	-	Hopeful

Fish Consumption and Major Depression
Annual Prevalence by Country



Hibbeln, The Lancet 1998;351;1213

Mediterranean dietary patterns to reduce depression? fish, olive oil and n-3 HUFAs as causal agents

1. Dietary patterns
Healthy
Mediterranean

2015 Dietary Guidelines for Americans Scientific committee evaluated ONLY data on dietary patterns for depression.

2. Specific foods
Fish
Olive oil

Fish consumption: a meta-analysis including **n=26** studies, **n=150,278** - lower risks of depression. **RR= 0.83** (95% CI 0.74 to 0.93)
Li F, et al. J Epidemiol Community Health 2015;0:1–6

3. Specific nutrients
n-3 HUFAs

Blood levels: a meta-analysis of **n=14** studies with **n=3,318** participants indicate higher blood levels of n-3 HUFAs are associated with lower risks of depression. **g= 0.85,** $p<0.0000$ Lin et al, Biol Psychiatry 2010;68:140–147

4. RCTs
n-3 HUFAs vs. placebo

Causal testing: a meta-analysis of **n=52** study conditions with **n=11,038** participants indicate **EPA rich**, n-3 HUFAs treat symptoms in major depressive disorders. **g=0.61** Hallahan , Hibbeln et al, Br J Psychiatry, 2015

5. Mechanistic basis

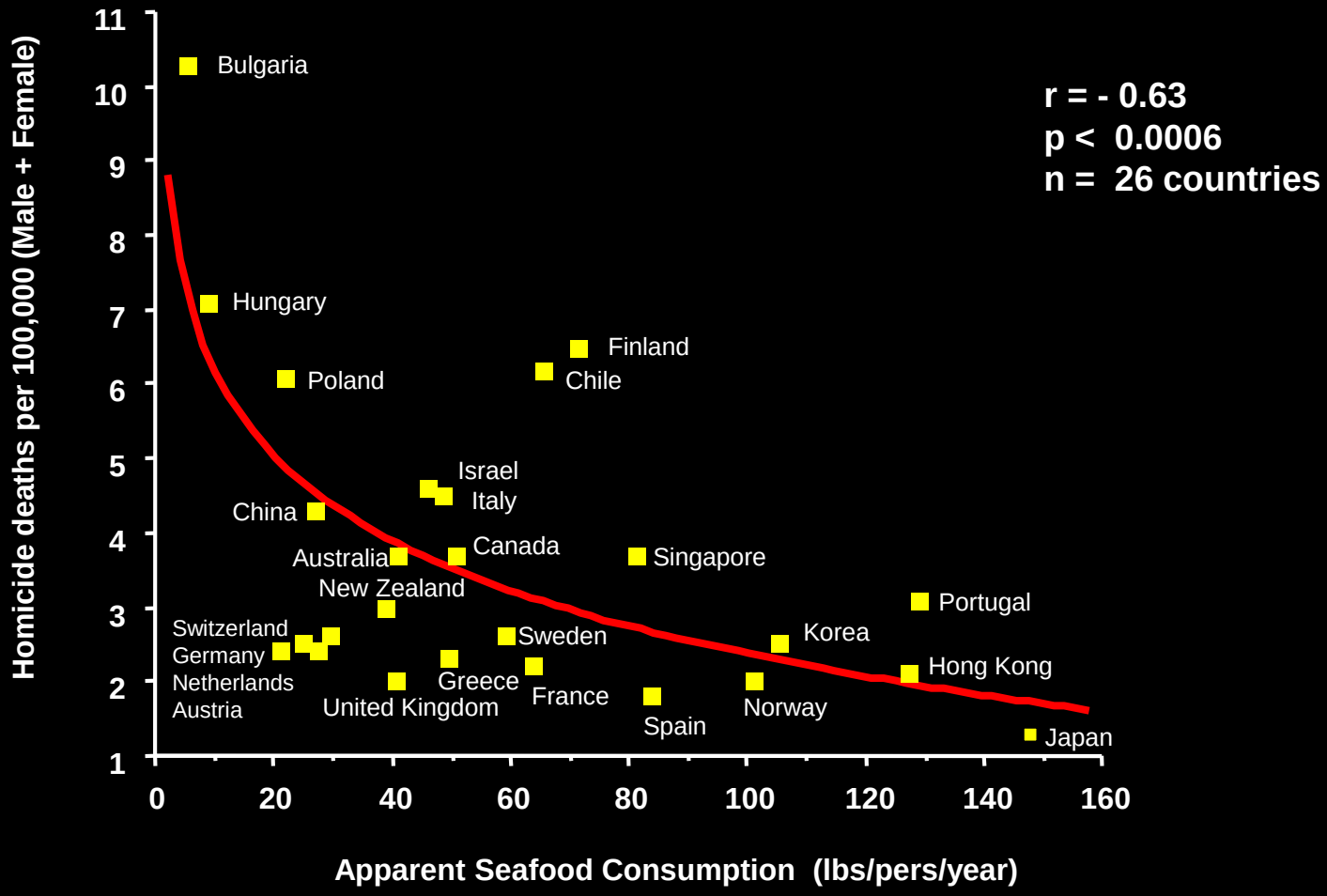
Multiple synergistic biological processes: n-3 HUFAs in neuroinflammation, dopaminergic and serotonergic function, neurogenesis and the stress axis

6. Olive oil

Olive oil, instead of vegetable oils, lowers intake of omega-6 fats and raises blood levels of **EPA** and is associated with lower risk of depression.
Wolfe et al Prog Neuropsychopharmacol Biol Psych. 2009 31;33(6):972-7

Can we stop this?

Homicide Mortality Rates[1] and Seafood Consumption



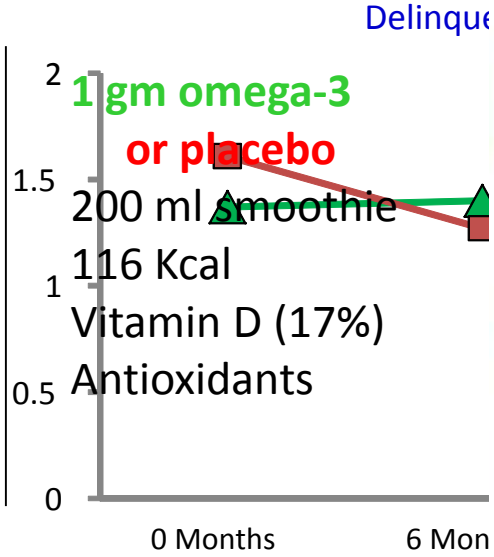
[1]World Health Statistics Annual 1995, WHO, Geneva Switzerland **Hibbeln, JR World Rev Nutr Diet, 2001; 88; 41-46**

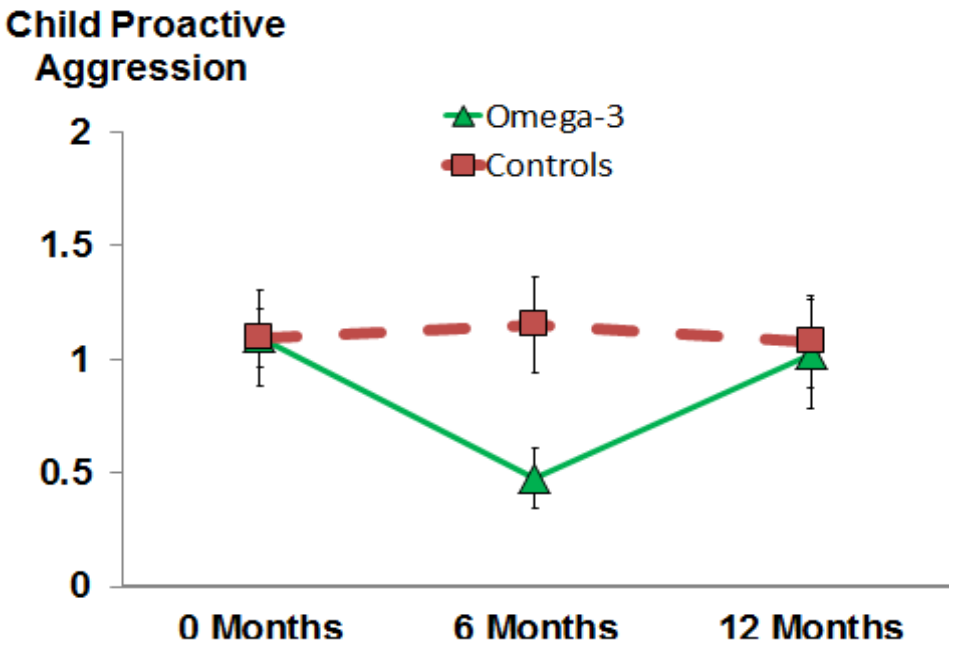
Mauritius Child Health Project

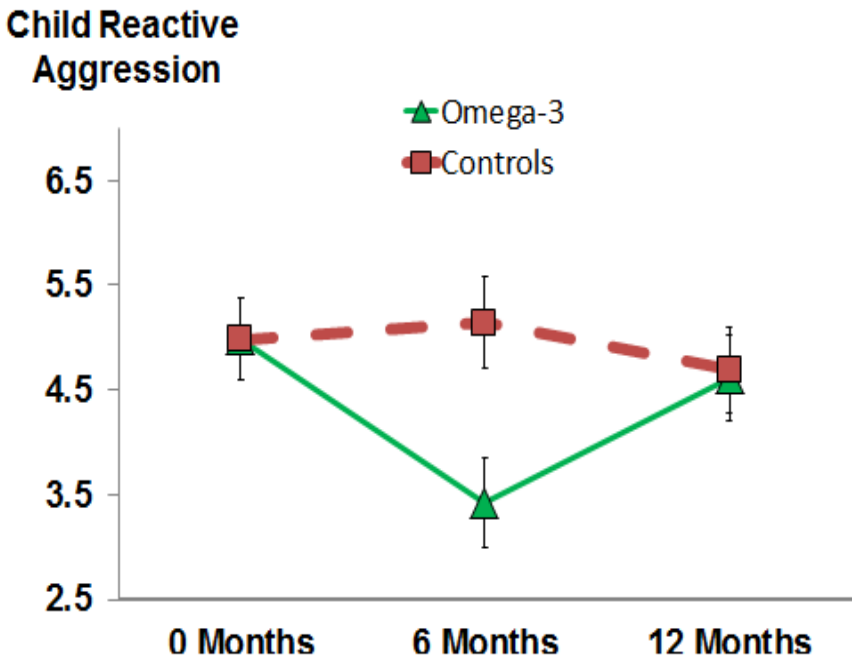
Age 8-16,
Randomized, stratified by age, gender
Blinded, 38.7% Creole, 61.3% Indian

n=95 omega-3, n= 89 placebo
6 mo. intervention, 6 mo. follow up
Child Behavior Checklist (parent)

Omega-3 specific



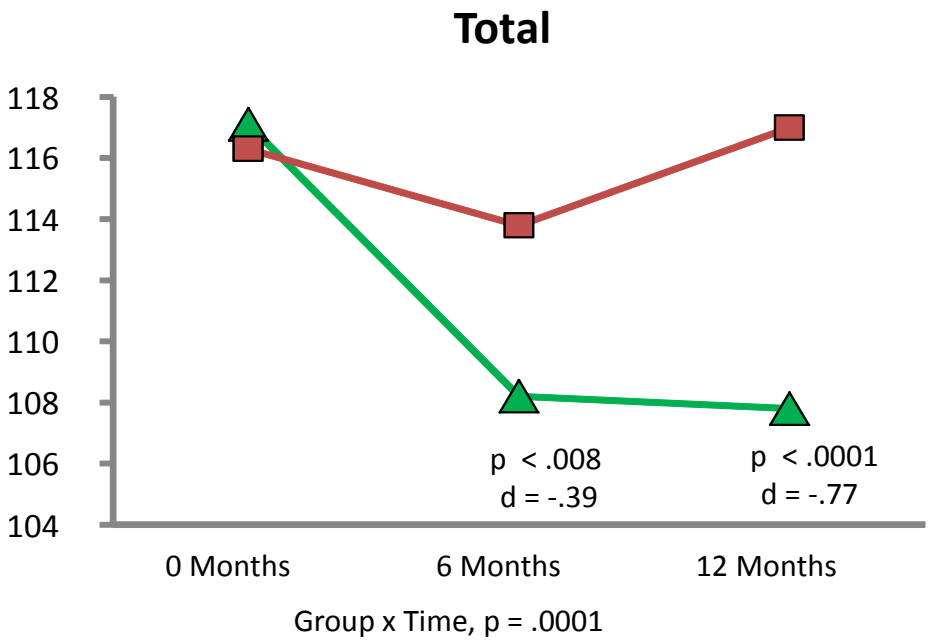




Raine, Hibbeln et al 2014

Parents were less psychopathic when their children took omega-3's

Parent Psychopathic Personality Inventory

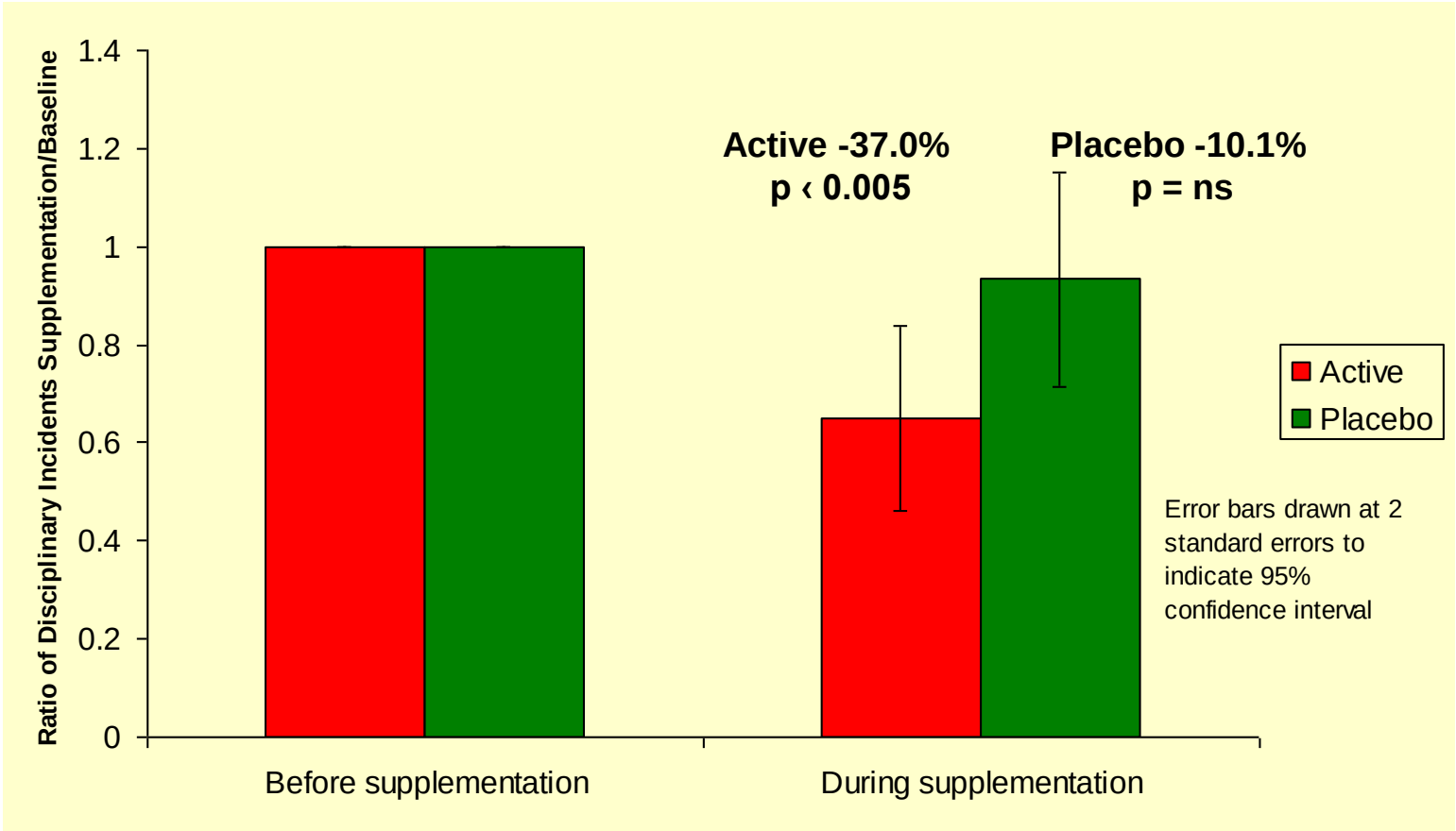


Raine, Hibbeln et al, 2014

portfolio

Reduced Felony Violent Offences Among Prisoners

with recommended daily amounts of vitamins, minerals and essential fatty acids

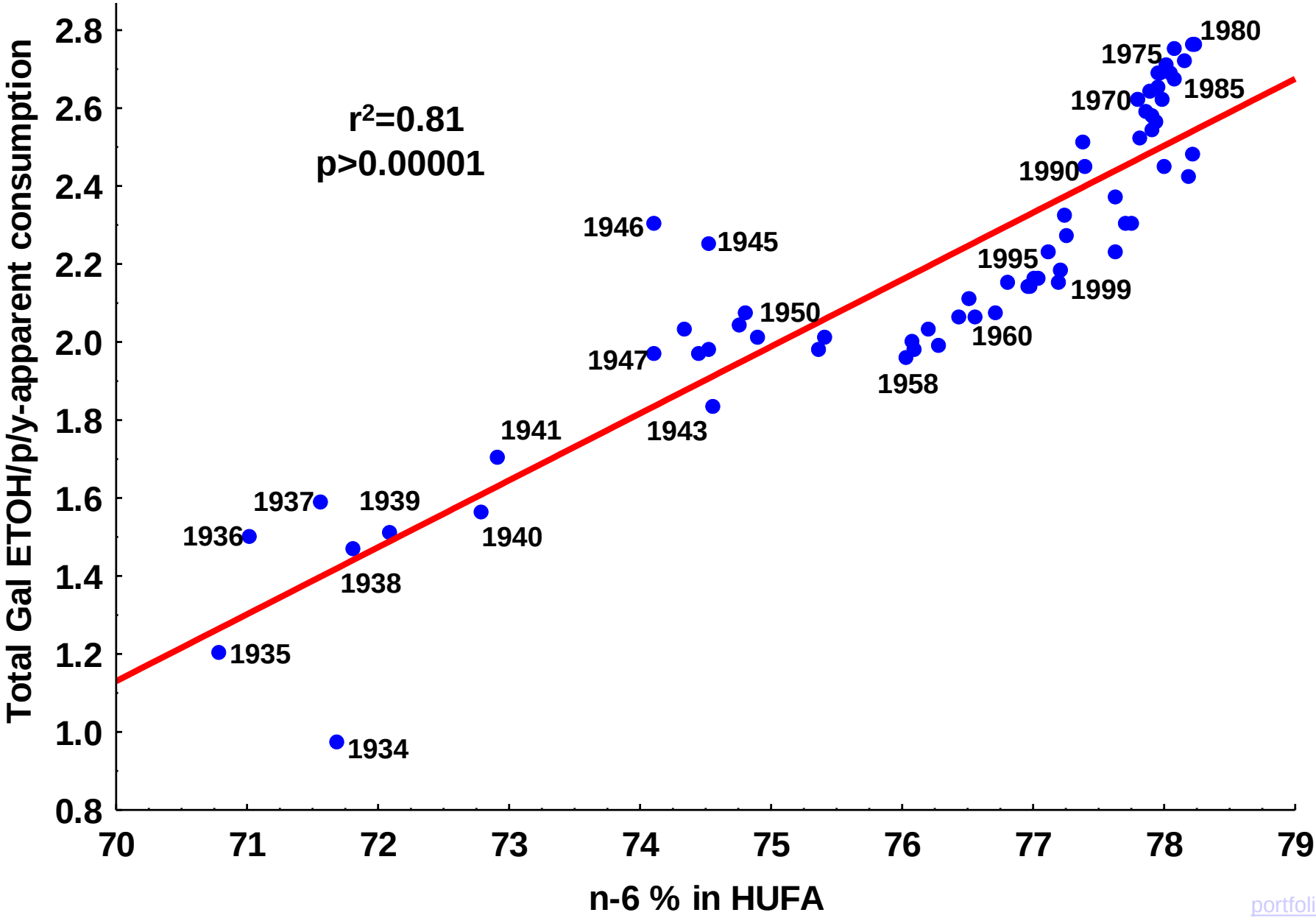


UK maximum security prison - 338 offences among 172 prisoners over 9 months treatment in a compared to 9 months baseline.

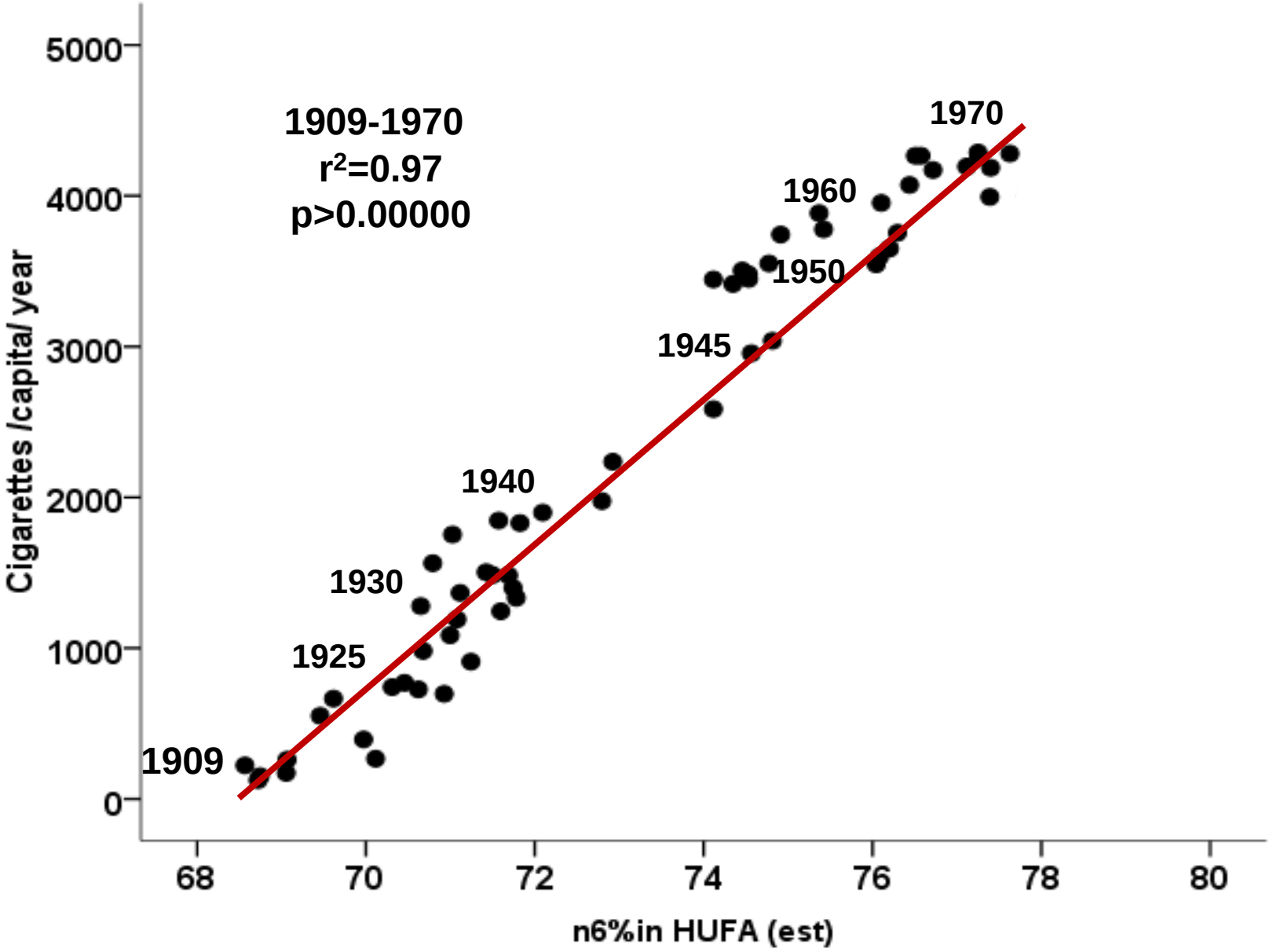
Gesch et al. Br J Psychiatry 2002, 181:22-28

How about addictions?

Alcohol consumption and increasing omega-6 fatty acids in tissue compositions (est) in the 20th century



Cigarette consumption and increasing omega-6 fatty acids in tissue compositions (est) in the 20th century



Current US Diet

Short n-6 LA 8 en%	Short n-3 α-LA 1 en%
Long n-6 HUFA	Long n-3 HUFA

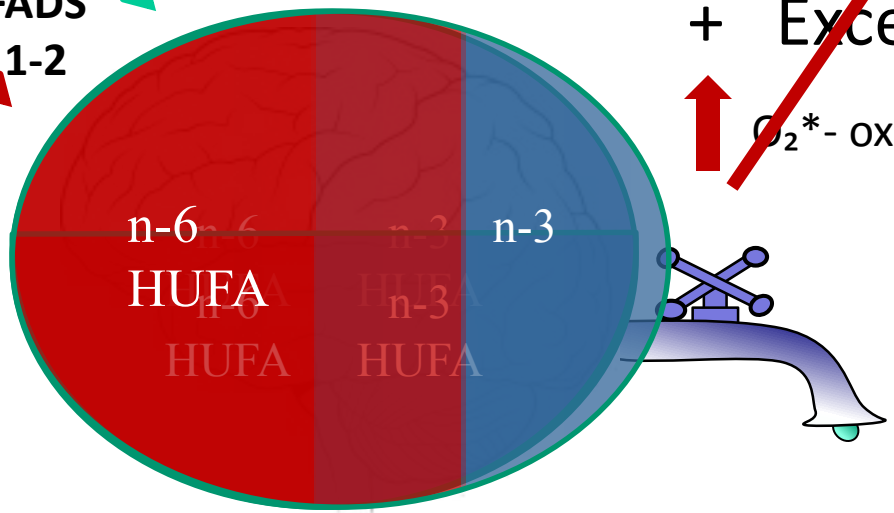
Brain

FADS
1-2

Desaturation

+ Excess Alcohol

O_2*- oxygen reactive species

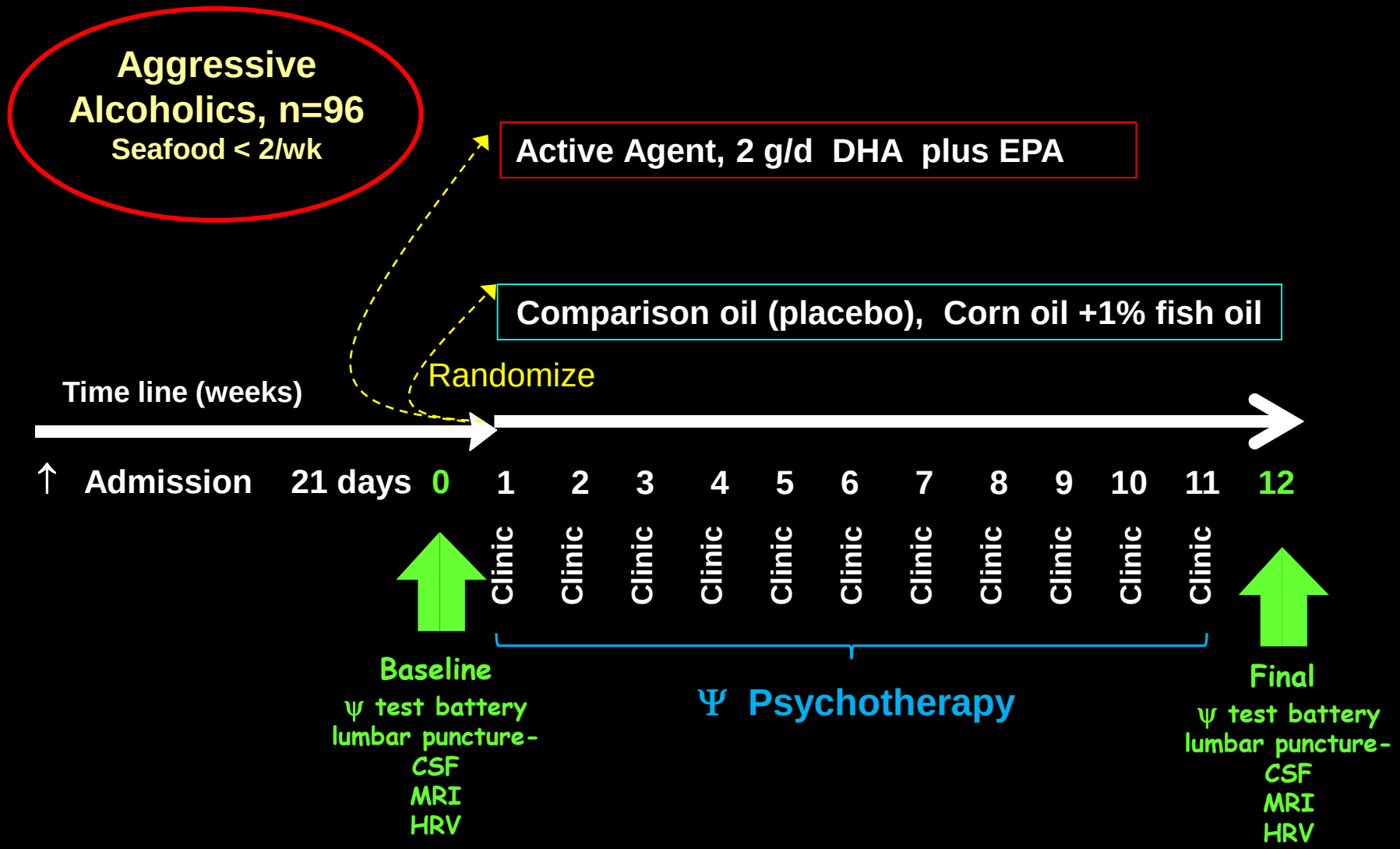


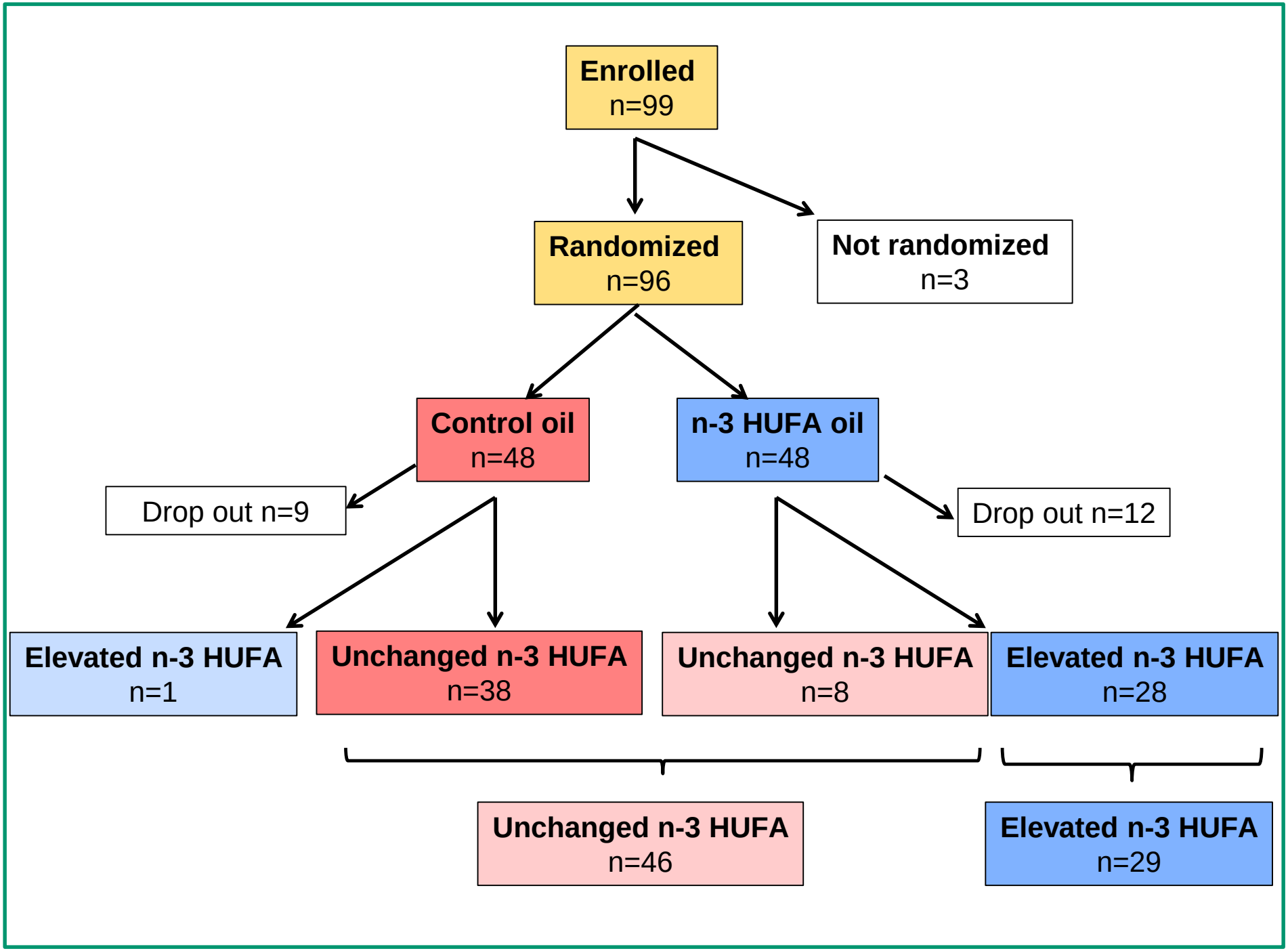
Depletes Brain
HUFAs

Replaces n-6 HUFA
but n-3 DHA ↓ by 50%

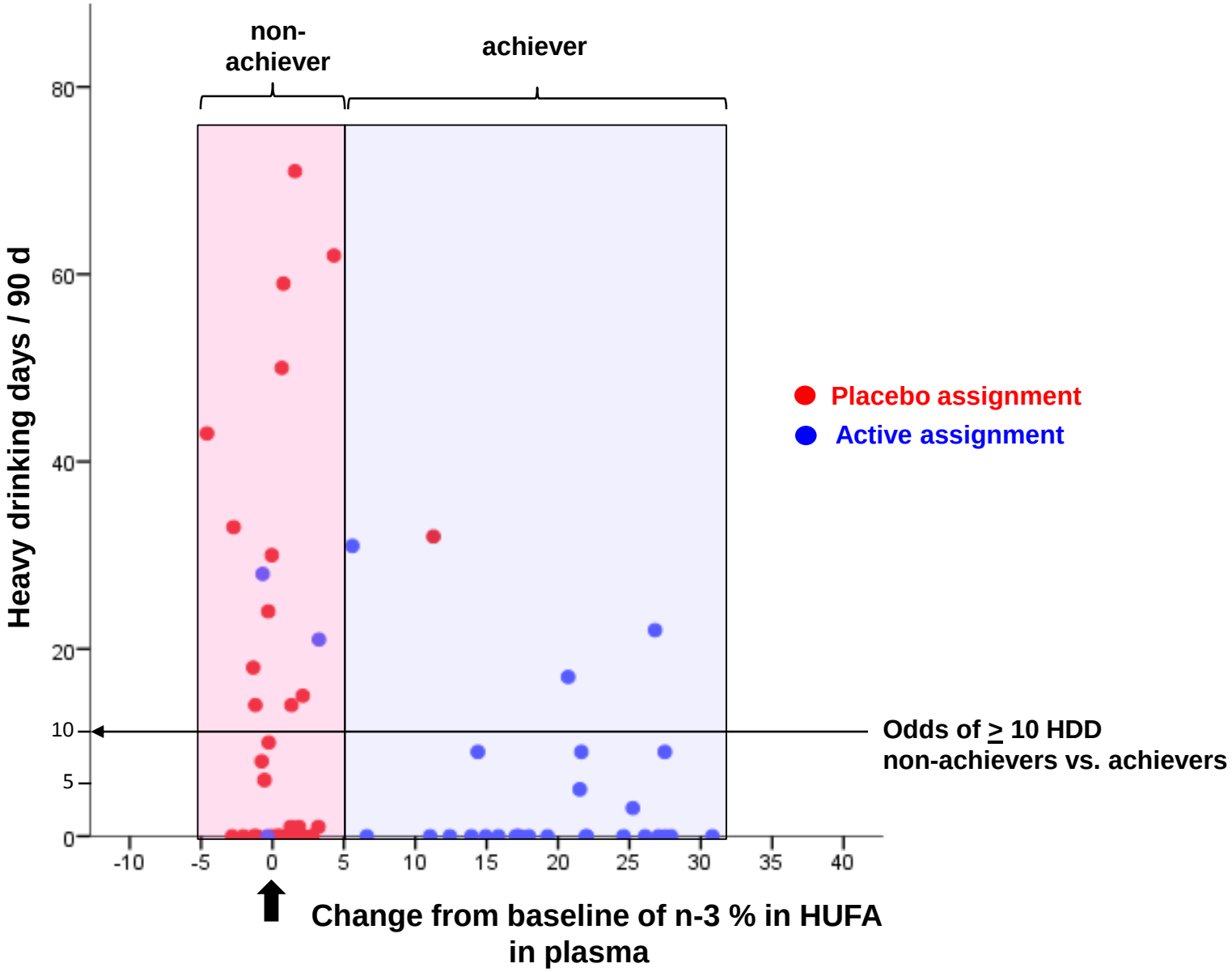
Pawlosky et al
Alcohol Clin Exp Res, 2001

N-3 HUFA intervention trial
NIH Clinical Protocol # 01-AA-0141




Enrolled
n=99
Randomized
n=96
Not randomized
n=3
Control oil
n=48
n-3 HUFA oil
n=48
Drop out n=9
Drop out n=12
Elevated n-3 HUFA
n=1
Unchanged n-3 HUFA
n=38
Unchanged n-3 HUFA
n=8
Elevated n-3 HUFA
n=28
Unchanged n-3 HUFA
n=46
Elevated n-3 HUFA
n=29

Biomarker defined compliance (change in n-3 HUFAs) and risk of heavy drinking days (HDD) in the first 90 days of recovery



Risk of heavy drinking days by n-3 HUFA compliance

(unadjusted)					(adjusted)				
		95% C.I					95% C.I.		
	OR	Lower	Upper	p<		OR	Lower	Upper	p<
5 or more HDD					***5 or more HDD***				
No n-3 HUFA elevation	**2.40**	0.88	6.56	0.089	No n-3 HUFA elevation	**3.05**	0.88	10.53	0.078
					No sober housing	**2.71**	0.86	8.56	0.089
10 or more HDD					***10 or more HDD***				
No n-3 HUFA elevation	**6.59**	1.73	25.05	0.006	No n-3 HUFA elevation	**9.59**	1.77	52.05	0.009
					No sober housing	**5.52**	1.33	22.86	0.018
20 or more HDD					***20 or more HDD***				
No n-3 HUFA elevation	**5.06**	1.04	24.63	0.045	No n-3 HUFA elevation	**8.05**	1.13	57.51	0.038
					No sober housing	**7.29**	1.17	45.32	0.033

HDD indicates Heavy Drinking Days.
> 5 std drinks for women > 6 std drinks for men

"Achiever" defined as n-3 HUFA elevation $\geq$5% change in CSF/ plasma n-3% in HUFA

Chronic Daily Headache Diet Trial

Why study pain?

$300 billion/y in healthcare costs (IOM, 2013)

↑ Risk for suicide

↑ Risk for substance abuse

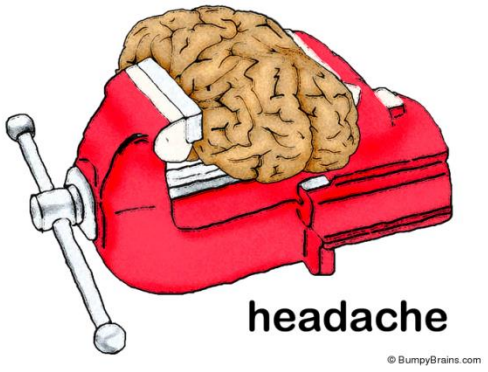
Treatments are inadequate

Patient population

Chronic Daily Headache

Severely impaired **23** d/month, **10** h/day

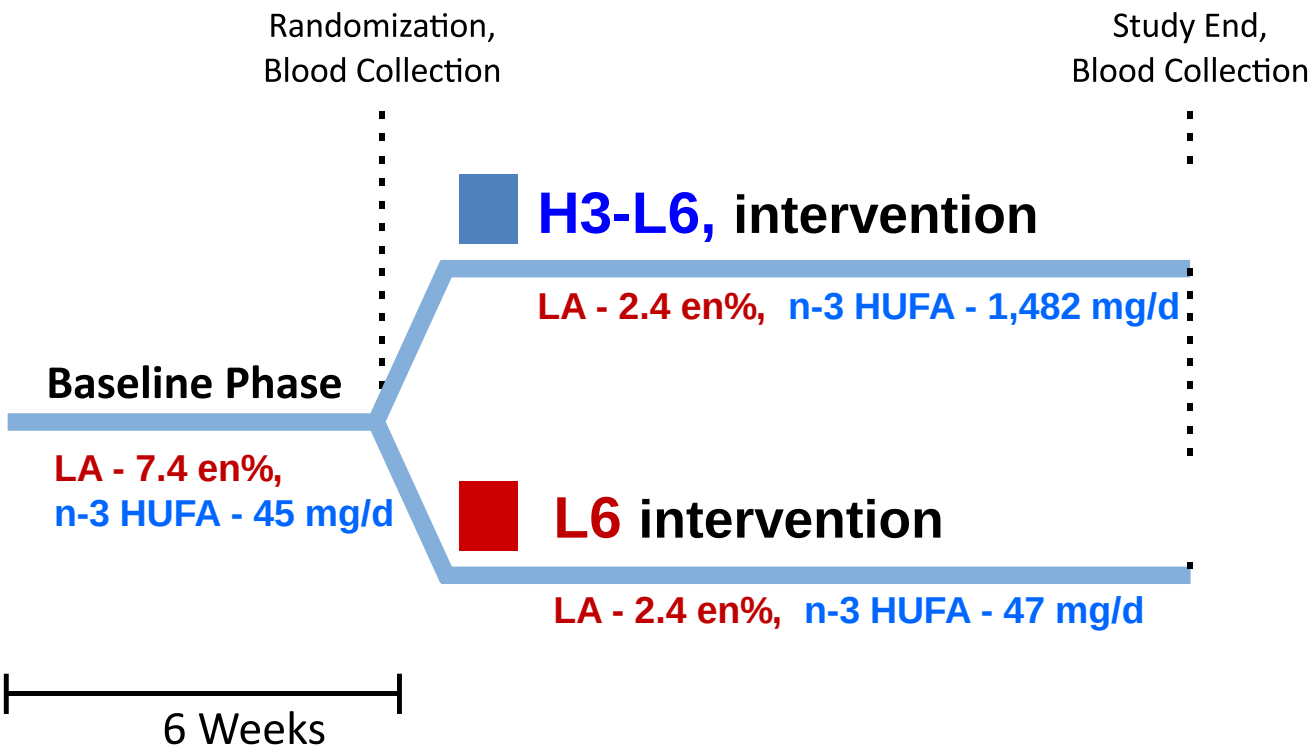
Treatment resistant > **6** meds



Ramsden CE, (Hibbeln) et al., *Trials* 2011

Chronic Daily Headache Diet Trial

Does total dietary ↓ n-6 LA and/or ↑n-3 HUFA reduce headache pain, frequency and disability?



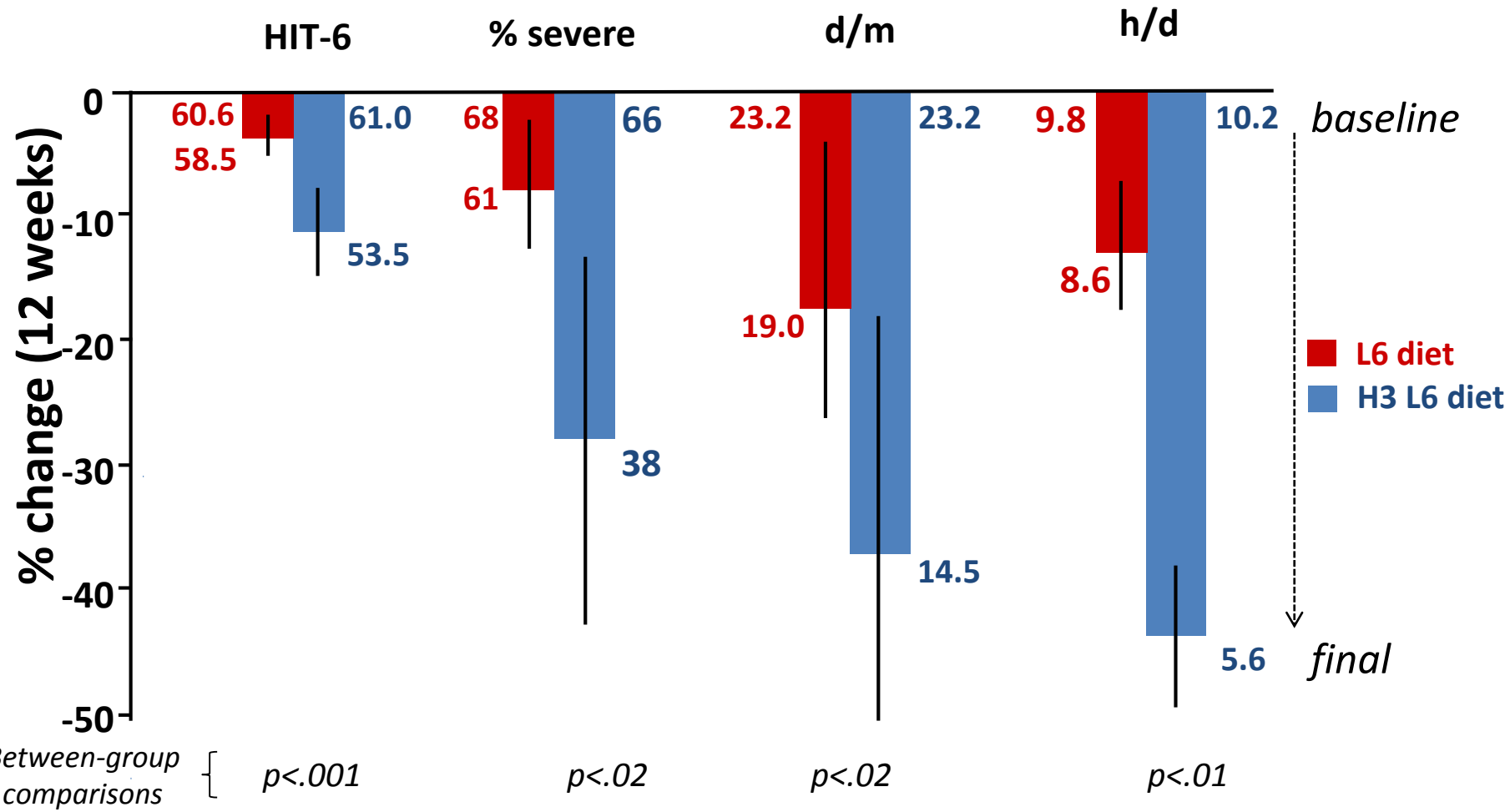
Patients continued usual headache care throughout trial

Ramsden CE, (Hibbeln) et al., *Trials* 2011

portfolio

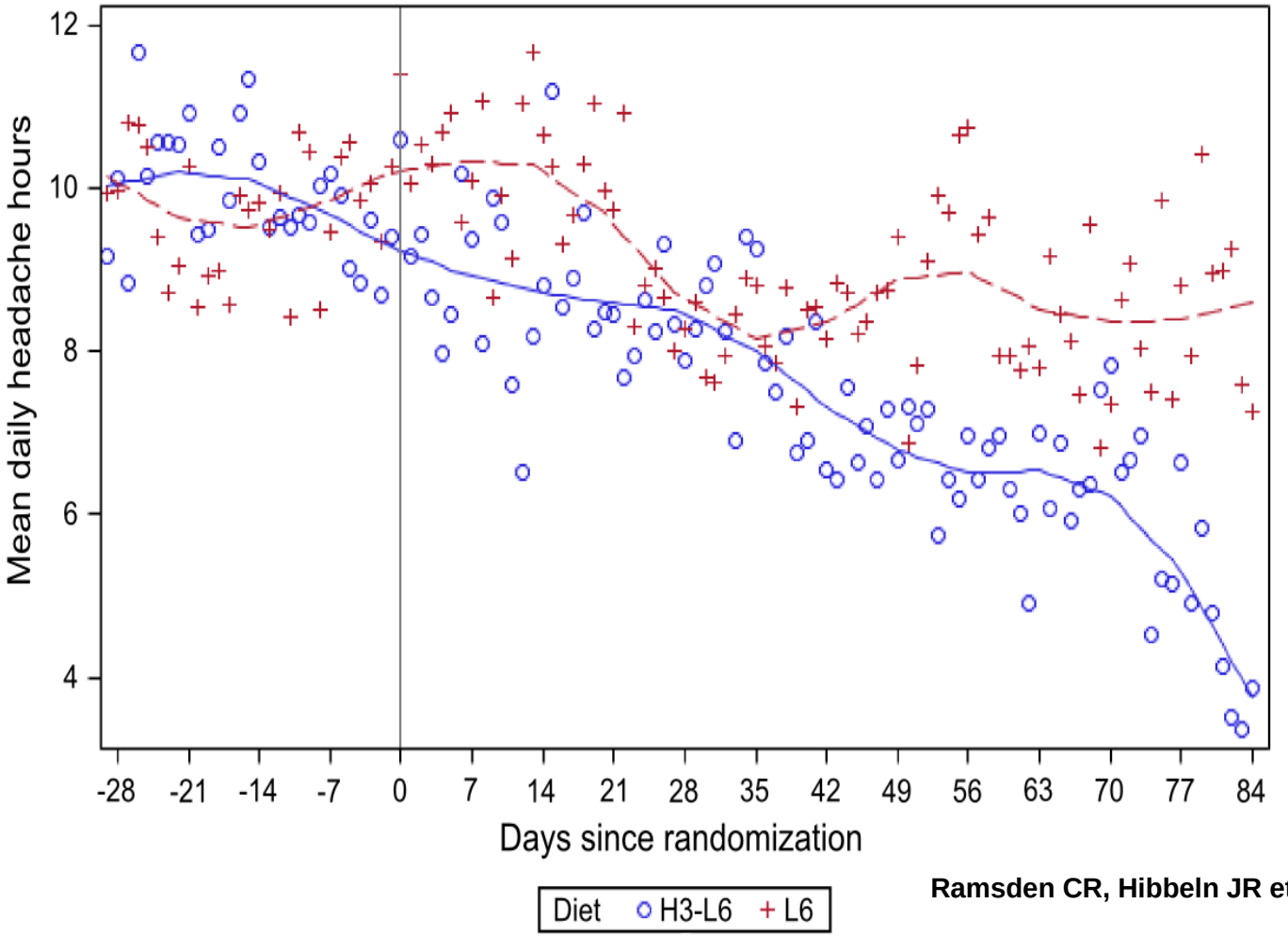
Chronic Daily Headache Diet Trial

Dietary essential fats reduce severe headache pain



Ramsden CR, (Hibbeln JR) et al, Pain 2013

The H3-L6 intervention reduces hours of daily headaches compared to n-6 LA lowering alone



Ramsden CR, Hibbeln JR et al, Pain 2013

Consult a Dietician?

Hi Doc,
I heard that changing my diet can improve my mental health.

Can you help?

Great idea!
But, I'm not an expert on diet or nutrition.

Let me consult a dietician.

Great idea!

But, I don't have any guidance from anyone as to what improves mental health or <u>how</u> to advise these clients.

What diet for mental health?

The Mediterranean Dietary Pattern

Fish 2-3 times per week
Olive oil, <u>not</u> vegetable oils

Avoid processed carbohydrates
More fruits and vegetables
Less red meat?
No fried foods

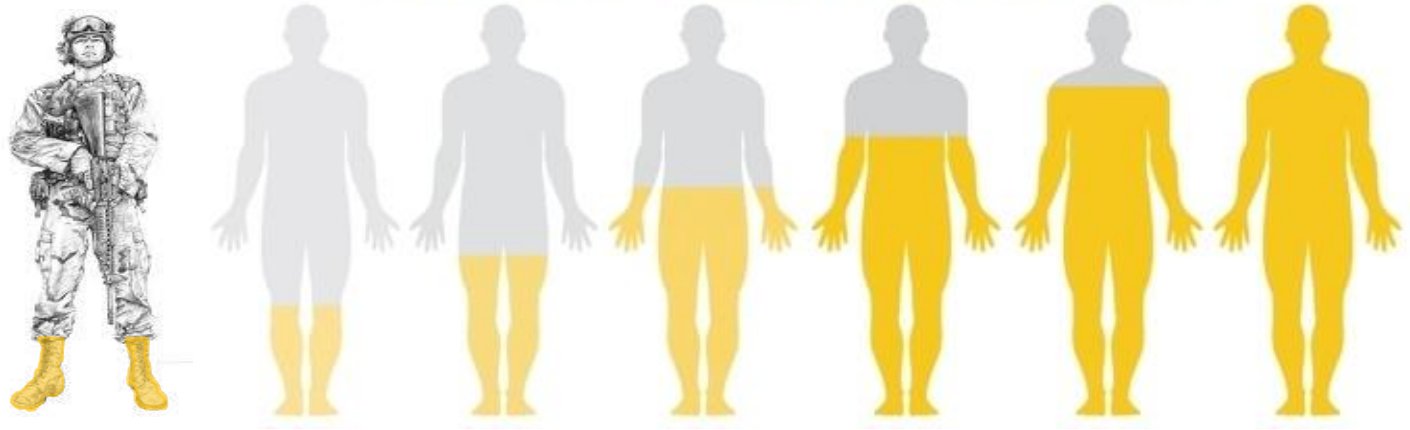
Linoleic acid is 2-3% of energy in traditional Mediterranean diets

"One common feature of Mediterranean diets was the use of olive oil as the principle fat, "

"Given a requirement of **~2-3 % of energy**, the amount of linoleic acid in olive oil would alone provide sufficient intake, if olive oil constituted 25% of energy."

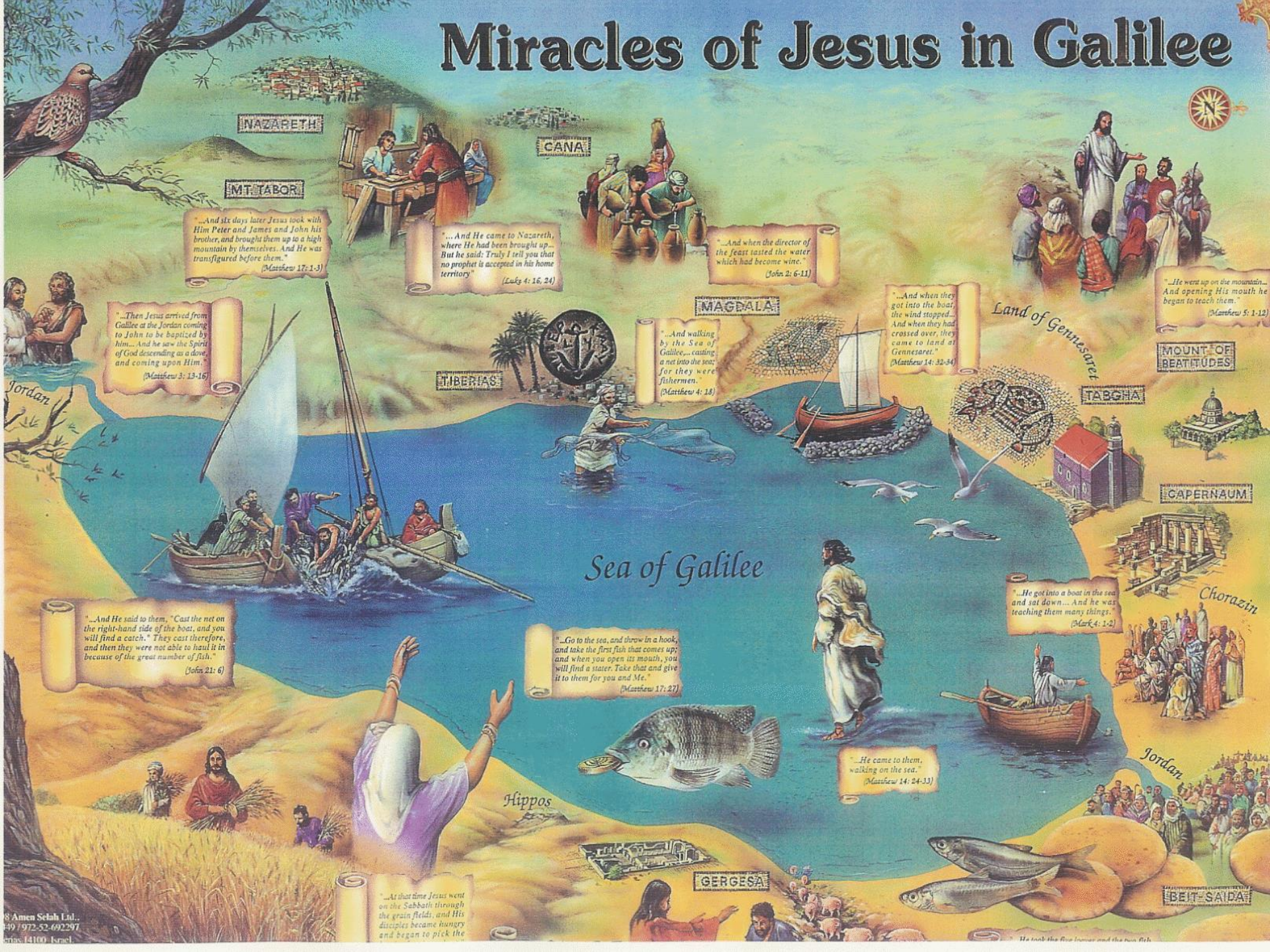
Kushi LH, Lenart EB, Willett WC. Am J Clin Nutr. 1995 Jun;61(6 Suppl):1416S-1427S

Eat less n-6 LA to help raise body n-3 HUFAs



n-3 % in HUFA	17%	20%	30%	40%	50%	60%	70%
	US MILITARY ACTIVE DUTY	TAKE URGENT ACTION	TAKE REMEDIAL ACTION	ACTION BENIFICIAL	HEALTHY OMEGA-3 LEVEL	ADJUST FOR OPTIMAL	OPTIMAL OMEGA-3 LEVEL
Omega-3 Index	2	3	6	9	12	15	18
Soy — 8 en% n-6 LA + n-3 HUFA	50 mg/d	250 mg/d	750 mg/d		2,000 mg/d		
Olive — 3 en% n-6 LA + n-3 HUFA							

Miracles of Jesus in Galilee

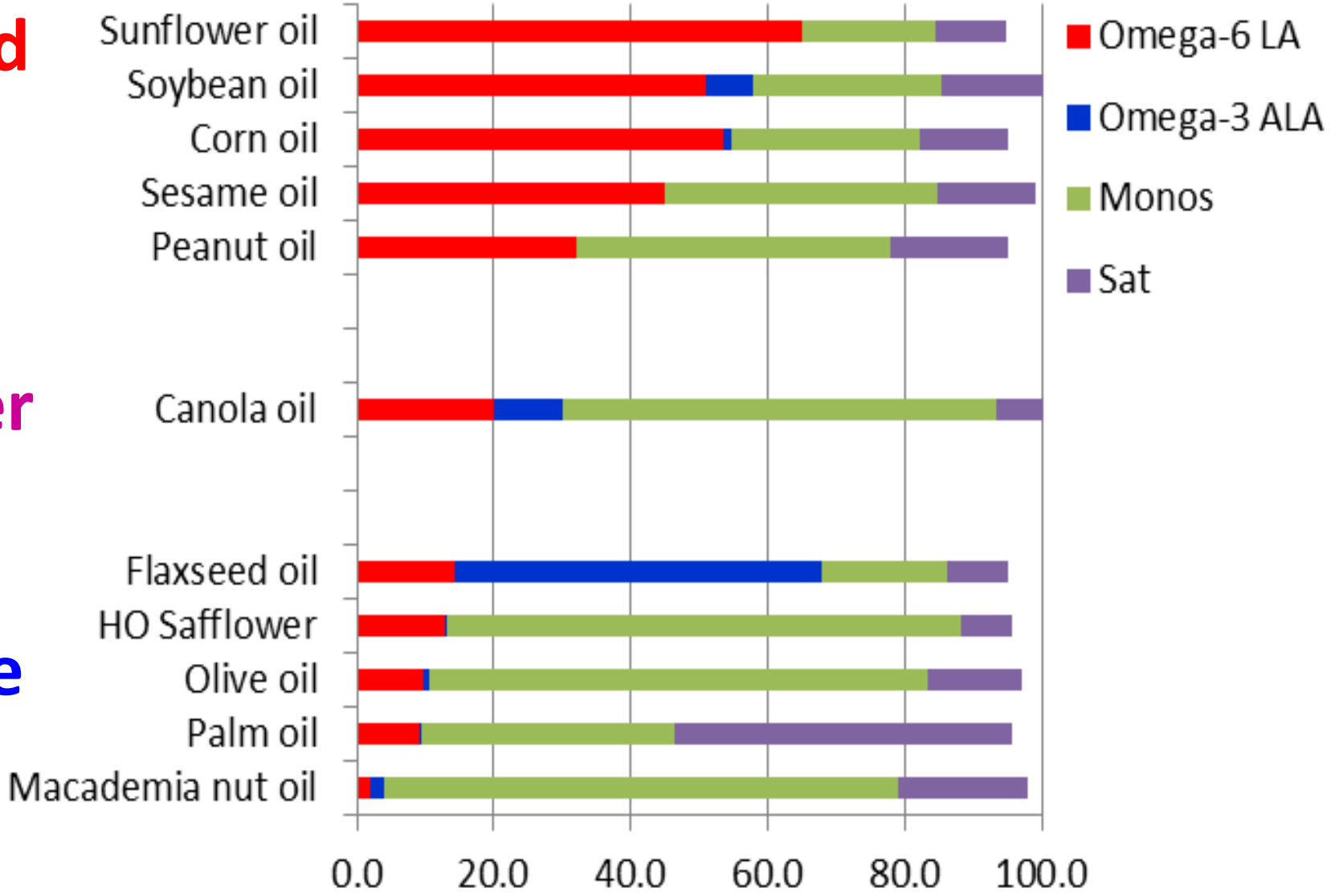


Nix the omega-6

Avoid

Better

Eat these



Quick fix

The USDA 100 most frequently consumed foods for Americans have a combined average score of -6

Eliminating these 10 non-Mediterranean foods will bring the remaining 90 foods down to a combined average score of -3

The ten most negative key foods for Americans

Soybean oil	-50
Mayonnaise	-46
Tub margarine	-39
Microwave popcorn	-37
“Italian salad” dressing	-35
Potato chips	-29
Stick Margarine	-28
Vegetable shortening	-28
Peanut butter	-24
Tortilla chip snacks	-24

The Brain Food Scale (BFS)

Given the high burden of disability due to mental disorders and the clear role that food choice can play in mitigating mental health risk, a scale to rank foods most likely to support brain health was developed.

Specific nutrients such as vitamin B12, long-chained omega-3 fatty acids, and iron are frequently deficient in mental health patients.

Scales of nutrient density, antioxidant capacity, and "power house" fruits and vegetables have ranked foods before, but no current scale based on specific brain essential nutrients (BEN) has been developed to our knowledge.

Several BEN are only found in meat, seafood, eggs, and dairy, which are generally excluded from lists of "superfoods" and rankings of nutrient density.

The objective of the current study was to determine which plant and animal based foods contain the highest nutrient density of brain essential nutrients.

Drew Ramsey, et al, ISNPR draft

Top 20 Brain Foods: Animals

	BFS
Oysters	51%
Clams	32%
Beef Spleen	31%
Chicken Liver	28%
Mussels	26%
Crab	24%
Poultry Giblets	23%
Octopus	22%
Fish Eggs (Caviar)	21%
Beef Kidney	20%
Seal	19%
Caribou	18%
Cuttlefish	18%
Whale	17%
Bluefin Tuna	17%
Rainbow Trout (wild)	17%
Bluefish	17%
Elk	16%
Smelts	16%
Herring	15%

Top 20 Brain Foods: Plants

	BFS
Mustard Greens	74%
Spinach	69%
Turnip Greens	61%
Green Bell Pepper	60%
Swiss Chard	54%
Red Cabbage	50%
Kohlrabi	48%
Cauliflower	46%
Red Bell Pepper	45%
Collard Greens	44%
Broccoli	43%
Acerola	40%
Scotch Kale	40%
Lemon	38%
Strawberry	38%
Brussels Sprouts	37%
Pummelo	36%
Asparagus	33%
Papaya	32%
Dandelion Greens	31%

BFS *Brain Food Score, Mean % daily value of brain essential nutrients per 100 calories

Efaeducation.com

Omega Foods Apps plus Tools

Omega Foods Apps plus Tools Inform Your Food Choices

Apps with Omega 3-6 Balance Scores – Apps help you find foods with more positive Scores that will increase the omega-3 in your tissue HUFA . When you know the Score, it helps you eat less food with a big negative Score (that will increase the omega-6). Plan to NIX6 and EAT3.

Finger-tip blood-spot test – This health risk assessment biomarker tells your current balance of HUFA and informs .you how much change you need to make to meet your personal wellness goals.

NEW, Free Software to Plan Meals – **Omega Meals** is a new interactive personal computer program that replaces KIM-2 (Keep It Managed). It uses Omega 3-6 Balance Scores to let you see a food's impact. **Omega Meals** manages EFA contents of over 9,000 food servings,fitting them to each person's taste, lifestyle and risk aversion. Download for either a Mac or Windows computer.

"Unless we prioritize brain nutrition, we will become a race of morons. The future health and intelligence of humanity is at stake, and it's the most serious threat of our times"

- 1972 -

Prof. Michael Crawford. PhD, FRSB, FRCPath,

Order of the Rising Sun, 2015, Tokyo, Japan.

Chevreul Medal, 2015, Paris, France.

Alexander Leaf Distinguished Scientist Award for Lifetime Achievement. ISSFAL, 2016

Thank you

2015 Dietary Guidelines for Americans

- **Strong evidence** … has shown that **eating patterns that include seafood** are associated with **reduced risk of CVD**,

- Moderate evidence indicates that **these eating patterns** are associated with **reduced risk of obesity.**

- Emerging evidence also suggests that relationships may exist between **eating patterns** and some **neurocognitive disorders** and congenital anomalies

- **Omega-3 (n-3)** fatty acids are a type of polyunsaturated fats found in **seafood**, such as salmon, trout, herring, tuna and mackerel and in flax seeds and walnuts. EPA and DHA are long chain n-3 fatty acids found in seafood.

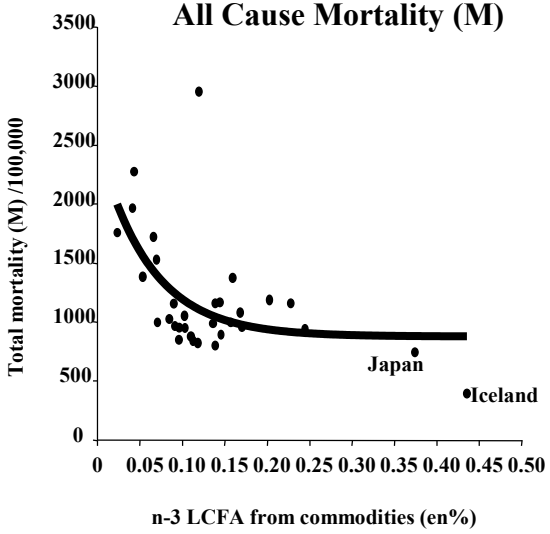
2015 Dietary Guidelines for Americans

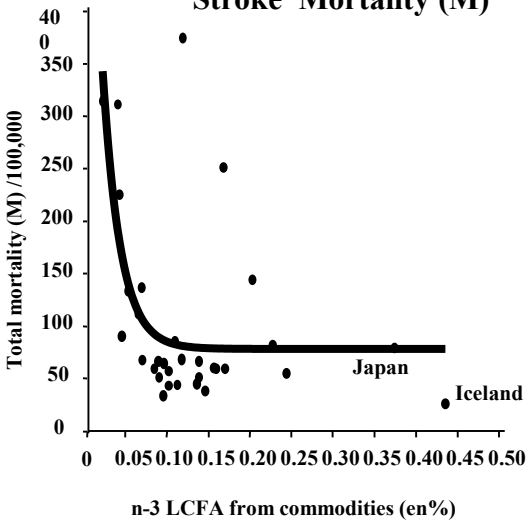
- Average intake of **total protein foods** is close to recommendations,

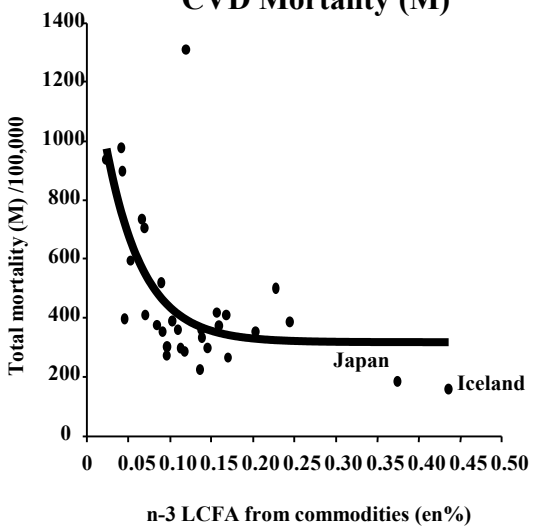
- But, **average seafood intake is below recommendations** for all age-sex groups.

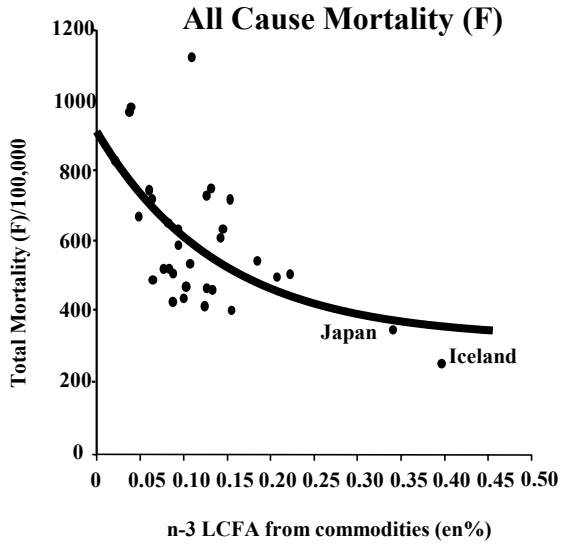
- Shifts are needed within the protein foods group to **increase seafood intake**.

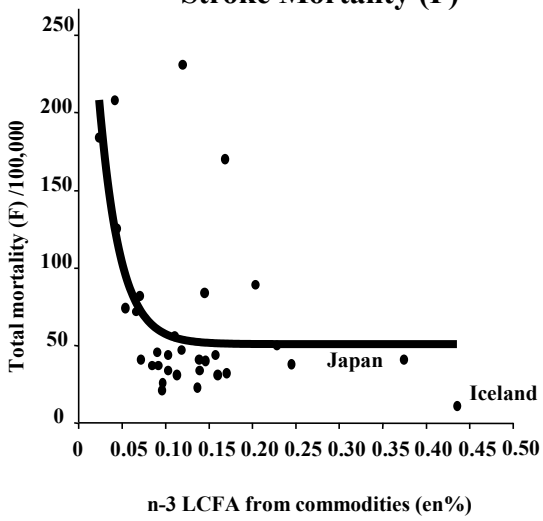
- Seafood as the protein foods choice in meals twice per week **in place of** meat, poultry, or eggs.

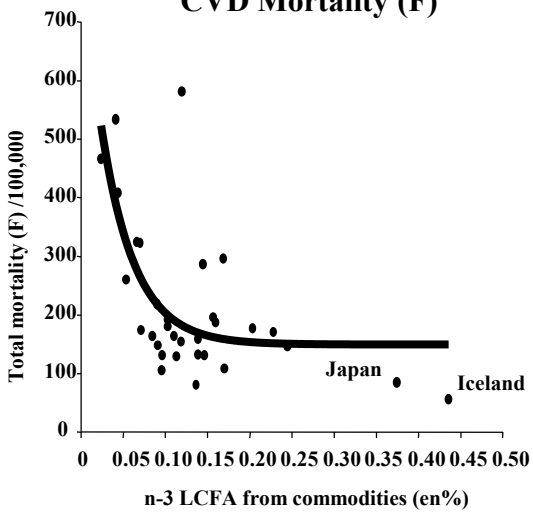




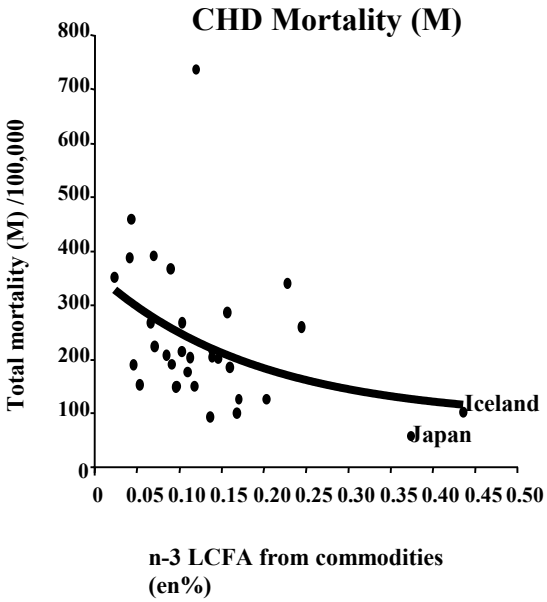


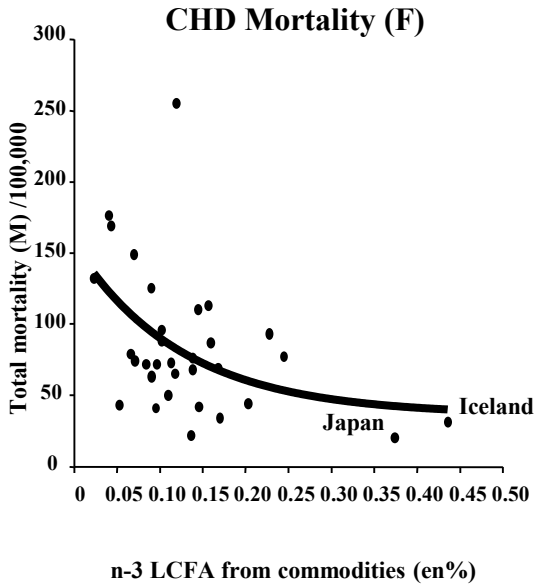


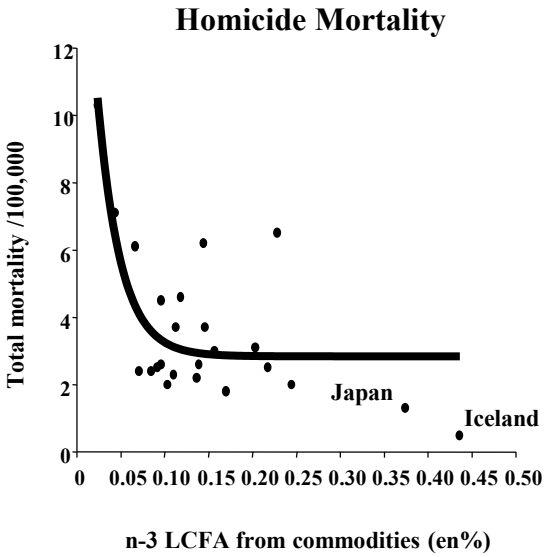


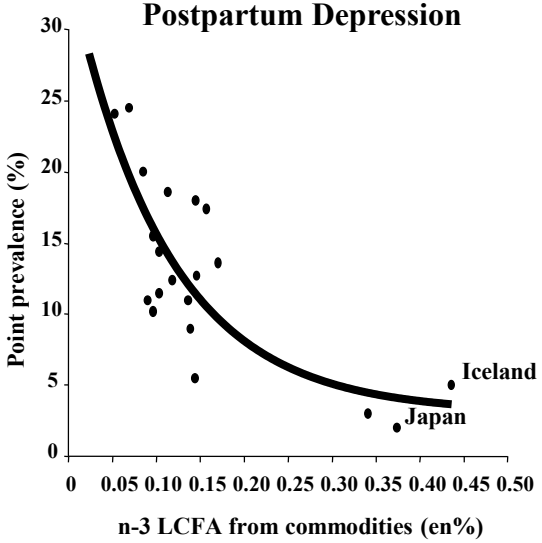


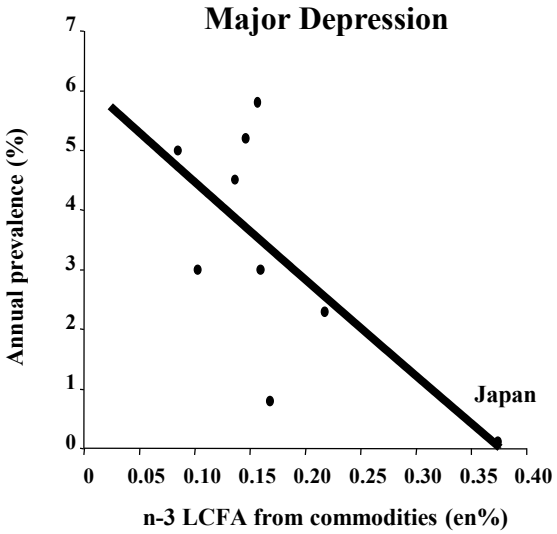
Hibbeln et al Am J Clin Nutr 2006; 83; 1483S-93S

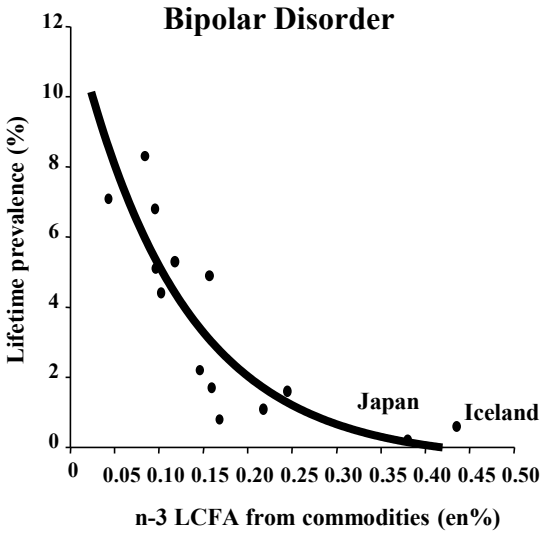












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