Ernährung: ein paar Mythen zerstört durch Fakten?

Online, 23. Februar 2021

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Interessenskonflikte

- Omegametrix
- Honorare für Vorträge und Beratung:
  BASF/Pronova, Huntsworth Medical,
  EPAX, Norsan

Präventionsleitlinien der Europäischen Kardiologengesellschaft

Table 12 Healthy diet characteristics

• Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
• <5 g of salt per day.
• 30–45 g of fibre per day, preferably from wholegrain products.
• ≥200 g of fruit per day (2–3 servings).
• ≥200 g of vegetables per day (2–3 servings).
• Fish 1–2 times per week, one of which to be oily fish.
• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Konventionelle Nomenklatur der Fettsäuren

Gesättigt

Einfach ungesättigt

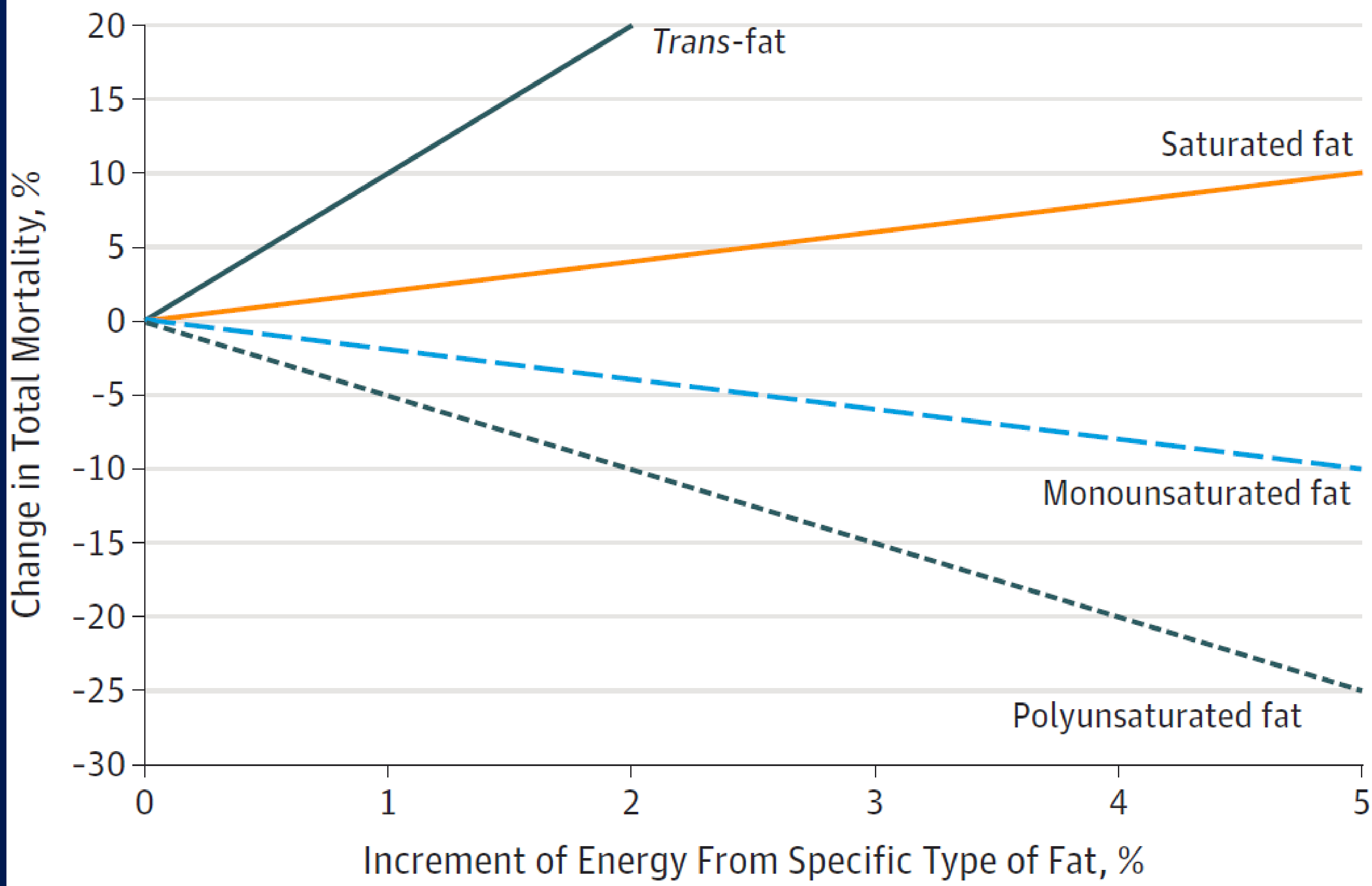
Vielfach ungesättigt

omega-6

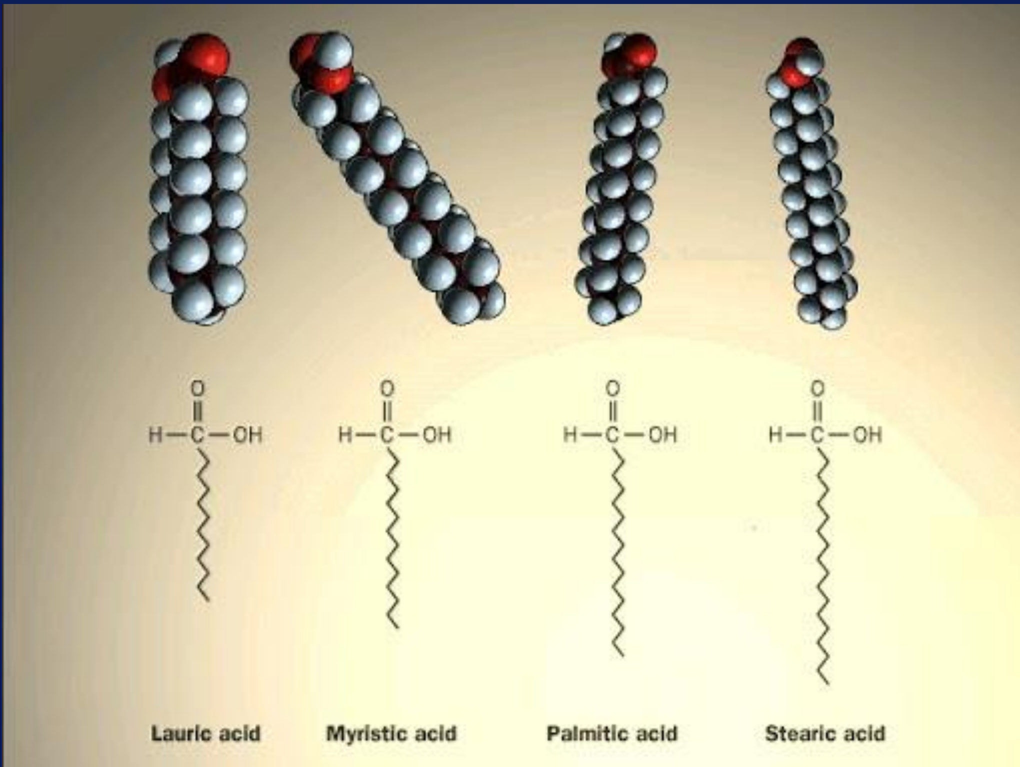
omega-3

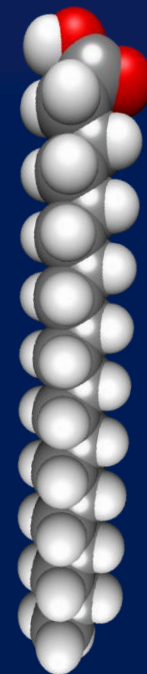
Trans-Fettsäuren

Figure 1. Change in Total Mortality Associated With Increases in the Percentage of Energy From Specific Types of Fat



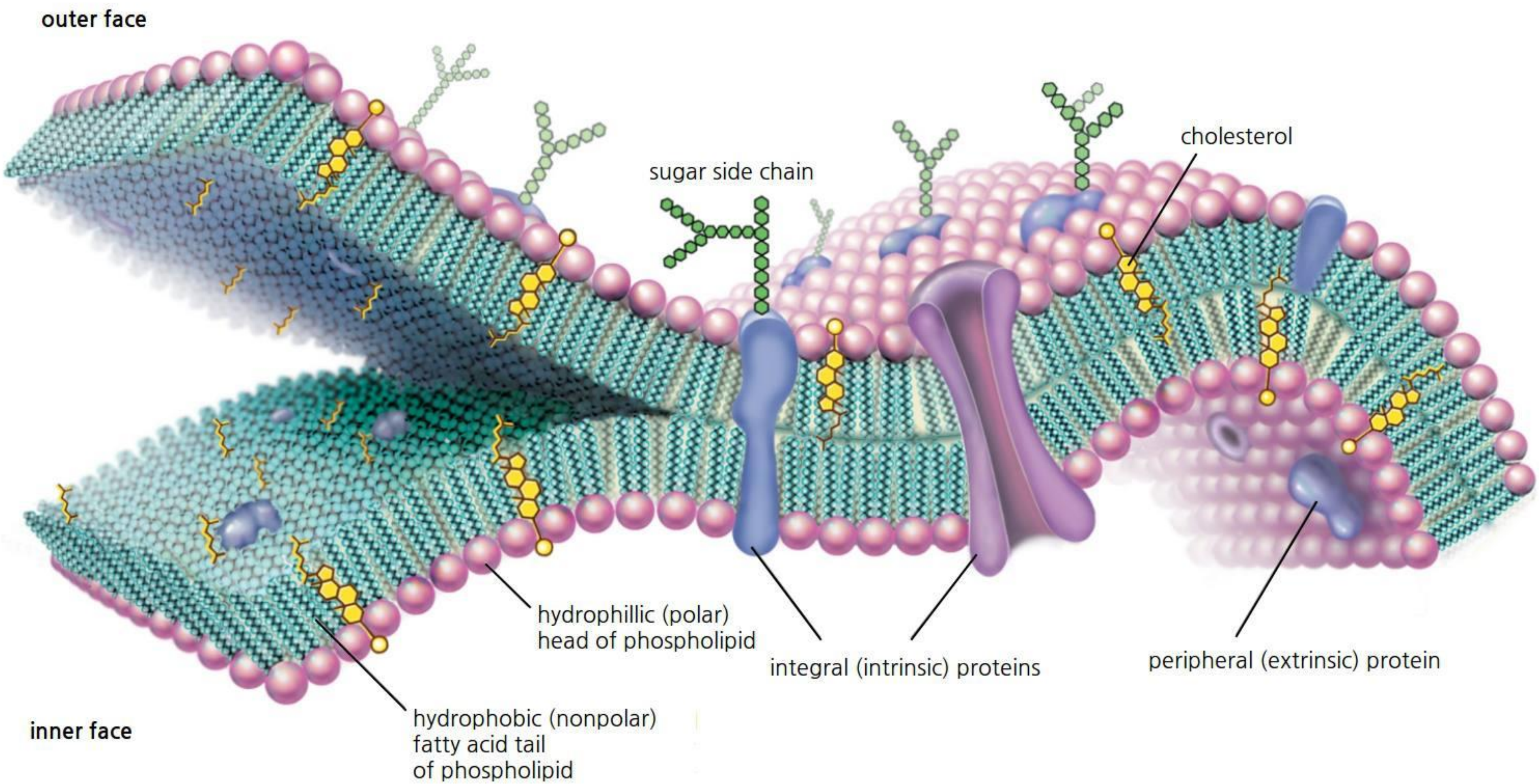
Wang et al JAMA Int Med 2016; e-pub Juli 5





C16:0 C18:0 C20:0

Dreidimensionale Struktur einiger gesättigter Fettsäuren


outer face
sugar side chain
cholesterol
hydrophillic (polar)
head of phospholipid
integral (intrinsic) proteins
peripheral (extrinsic) protein
hydrophobic (nonpolar)
fatty acid tail
of phospholipid
inner face

Biologische Eigenschaften einiger SFA

C12:0 Laurinsäure stimuliert GLP-1 Ausschüttung, senkt postprandiale Glukose, senkt Herzfrequenz und Blutdruck

C15:0 Pentadecansäure aus Milchfett anti-inflammatorisch, anti-fibrotisch, stabilisiert Erythrozyten und aktiviert Reparaturmechanismen in Mitochondrien

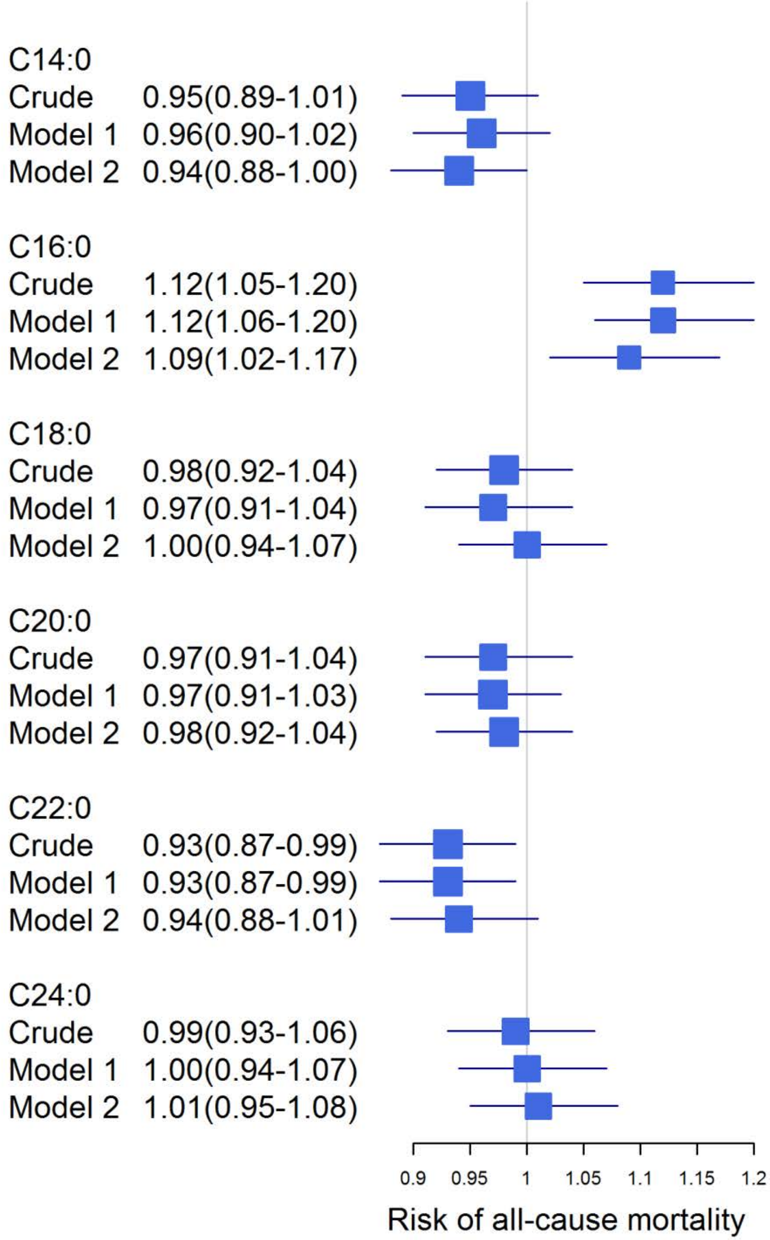
C16:0 Palmitinsäure: endogene Bildung DNL hohe Spiegel mit T2Dm assoziiert

C18:0 Stearinsäure: senkt LDL

usw.

Worm et al, eingereicht, van Rooijen & Mensink Nutrients 2020;12:615, Huang et al, Nutrients 2019;11:998

Gesamtmortalität



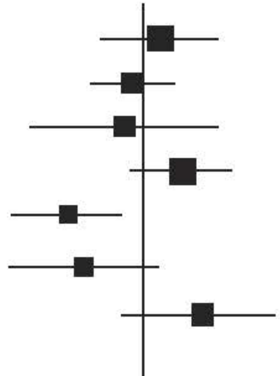
Model 1: adjustiert für Alter und Geschlecht

Model 2: zusätzlich adjustiert für LDL-C, HDL-C, logTG, BMI, Diabetes, Hochdruck, Rauchen, Fettsenkertherapie

Gesättigte Fettsäuren im Plasma und Koronare Ereignisse

Figure 2. RRs for coronary outcomes in prospective cohort studies of circulating fatty acid composition.

Circulating Blood Fatty Acid Composition	Studies, *n*	Participants, *n*	Events, *n*	RR (95% CI)*
Total saturated fatty acids	8	15 590	3758	1.06 (0.86–1.30)
14:0, Myristic	5	10 598	2932	0.96 (0.83–1.12)
15:0, Pentadecanoic	4	5490	2283	0.94 (0.67–1.32)
16:0, Palmitic	10	25 554	4318	1.15 (0.96–1.37)
17:0, Margaric	4	5490	2283	0.77 (0.63–0.93)
15:0, Pentadecanoic + 17:0, Margaric	4	5490	2283	0.81 (0.62–1.06)
18:0, Stearic	8	22 266	3654	1.23 (0.93–1.61)



Chowdhury et al, Ann Int Med 2014;160:398

Association of erythrocyte 20:0, 22:0 and 24:0 with incident sudden cardiac arrest (SCA).

	Q1	Q2	Q3	Q4	p-trend
A. 20:0					
Median [a]	0.32	0.36	0.39	0.43	
Model 1[b]	REF	0.63 (0.38–1.05)	0.53 (0.30–0.92)	0.51 (0.29–0.89	0.02
Model 2[b]	REF	0.61(0.36–1.02)	0.45 (0.25–0.81)	0.42 (0.23–0.77)	0.004
B. 22:0					
Median [a]	1.45	1.63	1.74	1.97	
Model 1[b]	REF	0.73 (0.43–1.22)	0.54 (0.31–0.94)	0.48 (0.27–0.85)	0.008
Model 2[b]	REF	0.72 (0.41–1.24)	0.49 (0.27–0.87)	0.35 (0.19–0.65)	<0.001
C. 24:0					
Median [a]	4.03	4.54	4.87	5.36	
Model 1[b]	REF	0.59 (0.34–1.02)	0.68 (0.39–1.18)	0.45 (0.25–0.83)	0.03
Model 2[b]	REF	0.58 (0.33–1.03)	0.71 (0.40–1.27)	0.52 (0.27–0.98)	0.10

[a]Median levels among controls, % of total fatty acids

LeMaitre RN et al PLEFA 2014;91:149

Zusammenfassung

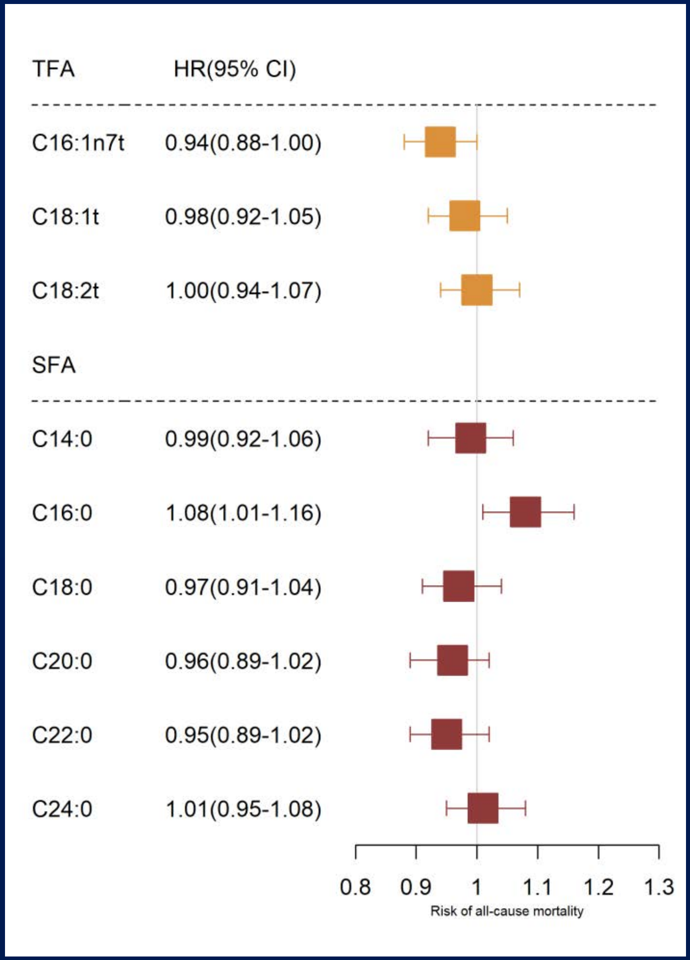
Individuelle SFA haben individuelle Struktur
Individuelle SFA haben individuelle biologische Wirkungen

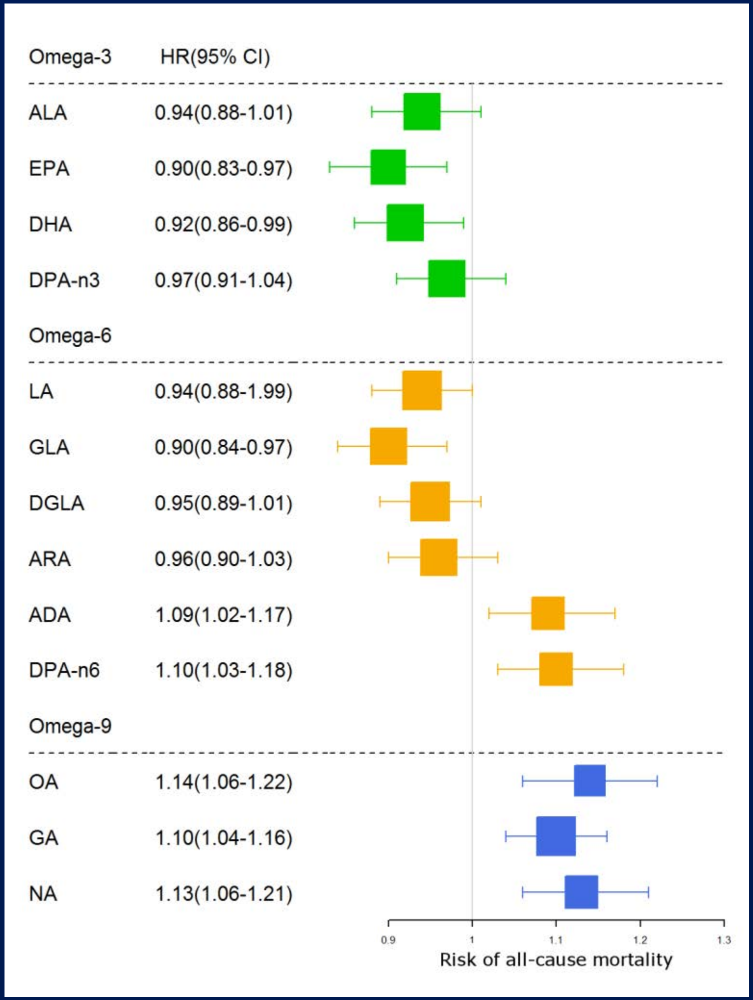
Assoziationen mit Lebenserwartung

16:0	verkürzt
15:0, 17:0, 22:0	verlängert
18:0, 20:0, 24:0	keine

Die kann man nicht alle in einen Topf werfen!

Assoziationen individueller Fettsäuren mit 10-Jahres-Mortalität in LURIC





Kleber et al Eur Heart J 2016;37:1072-82; Kleber et al Atherosclerosis 2016;252:157-81
Delgado et al J Clin Lipidol 2017;11:126-35; Delgado et al Clin Lipidol, 2017;11:1082-90
Kleber et al J Clin Lipidol 2018;12:455-63

Individuelle Fettsäuren haben
Individuelle Struktur
Individuellen Metabolismus
Individuelle Biologische Wirkungen
Individuelle Aussage für Prognose

Und müssen daher individuell betrachtet werden
Bisherige Nomenklatur falsch

Kleber et al, Eur Heart J 2016;37:1072-82
Kleber et al. Atherosclerosis 2016;252:157-81
Delgado et al, J Clin Lipidol 2017;11:126-35
Delgado et al, J Clin Lipidol, 2017;11:1082-90
Kleber et al, J Clin Lipidol 2018;12:455-63

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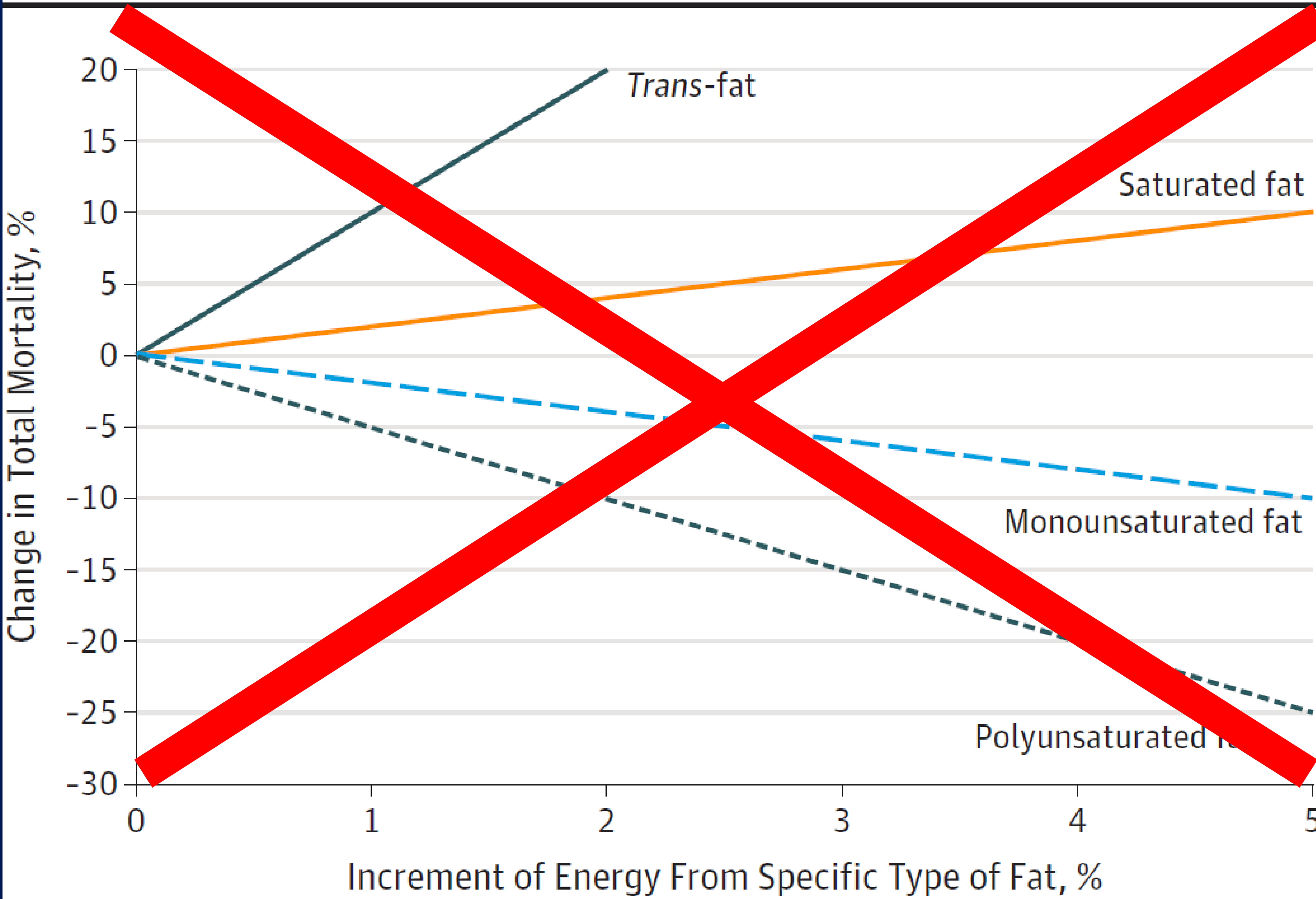
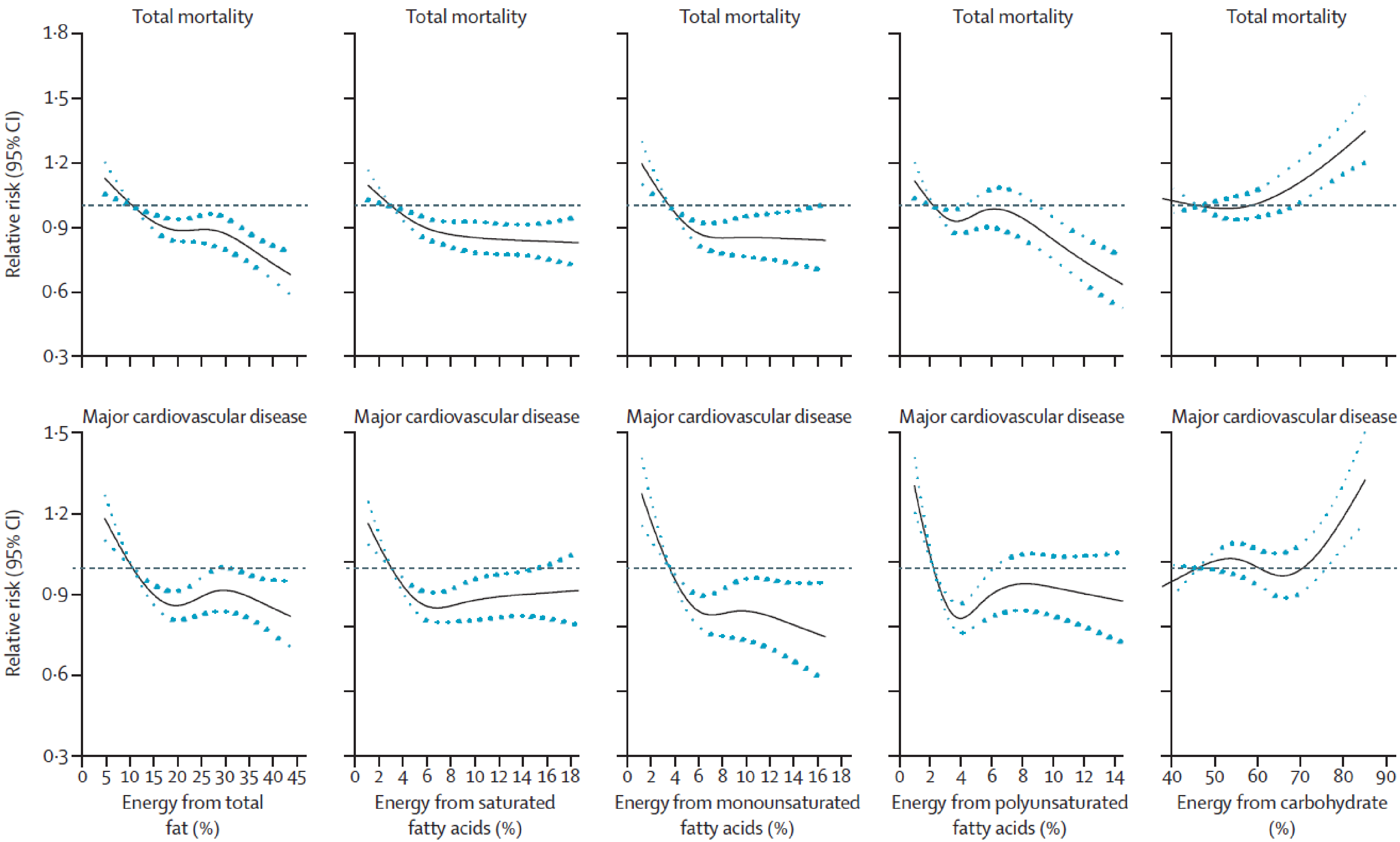


Wang et al JAMA Int Med 2016; e-pub Juli 5

PURE: Kohortenstudie, 18 Länder, 135 335 Teilnehmer, 7,4 Jahre verfolgt, Ernährungsfragebögen



Dehghan et al PURE Lancet 2017;390:2050

Mit anderen Worten: Konventionelle Nomenklatur der Fettsäuren

Gesättigt

Einfach ungesättigt

Vielfach ungesättigt

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omega-3

Trans-Fettsäuren

ist Unsinn

Methode der konventionellen Ernährungsforschung.

Konventionelle Methode

der Ernährungs-Epidemiologie:

Fragebogen zum Verzehr von Speisen

International Journal of Epidemiology
Vol. 26, No. 1(Suppl. 1)
Printed in Great Britain

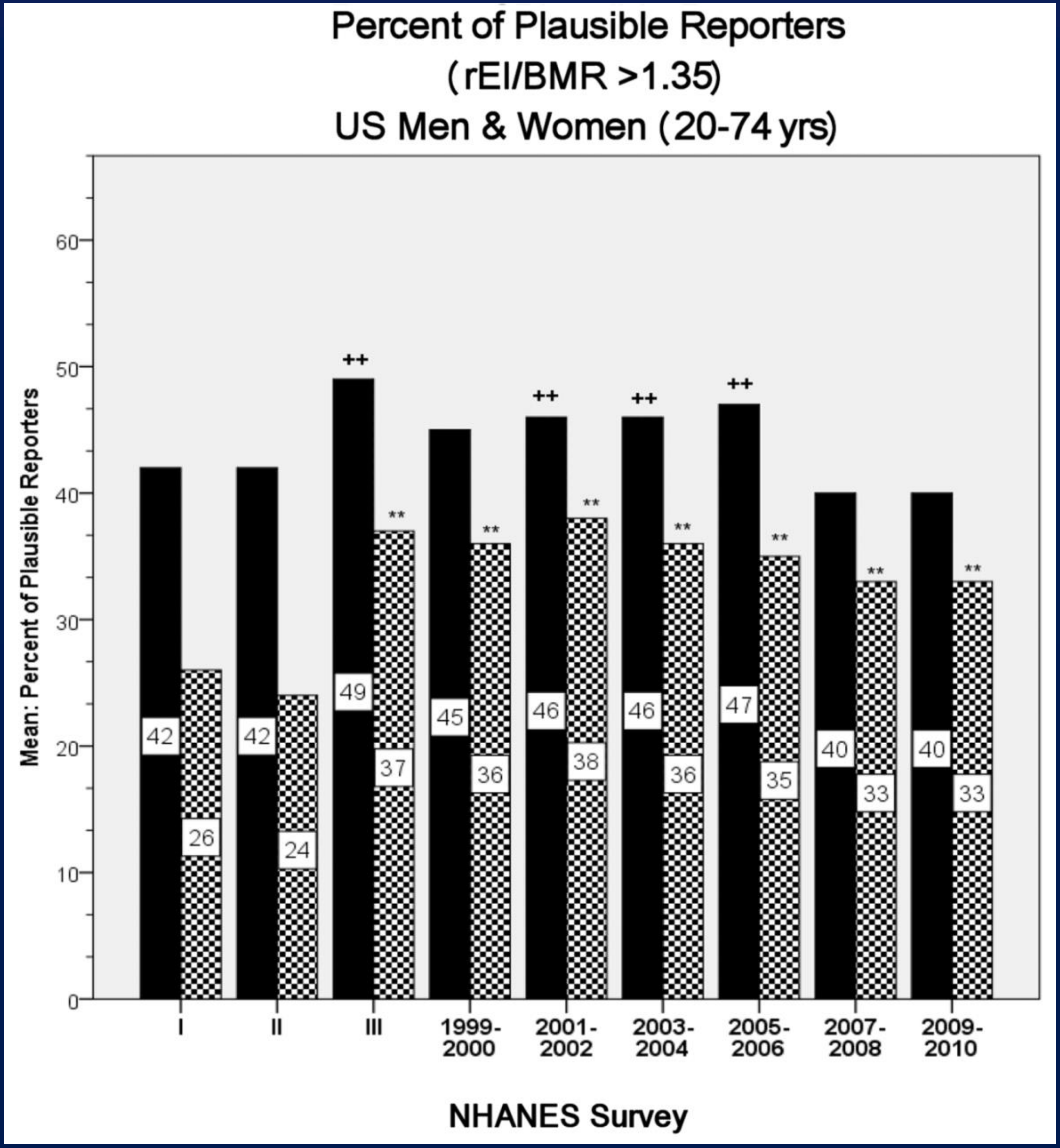
The Dutch EPIC Food Frequency Questionnaire. II. Relative Validity and Reproducibility for Nutrients

MARGA C OCKÉ,* H BAS BUENO-DE-MESQUITA,* MARGREET A POLS,** HENRIETTE A SMIT,*
WIJA A VAN STAVEREN† AND DAAN KROMHOUT‡

Schlussfolgerung: Ernährungsfragebögen scheinen angemessen um Personen
In eine Reihenfolge zu bringen, was Energie, Macronährstoffe, Faser und Retinol
Angeht, aber nicht so gut für ß-Carotin, und andere…

Mit anderen Worten: keine absoluten Messungen möglich.

Absolute Messung: Plausibilität um 50%



Archer et al PLOSOne 2013;8:76632

MAYO
CLINIC

SPEC

The Inadmissibility of What We Eat in America and NHANES Dietary Data in Nutrition and Obesity Research and the Scientific Formulation of National Dietary Guidelines

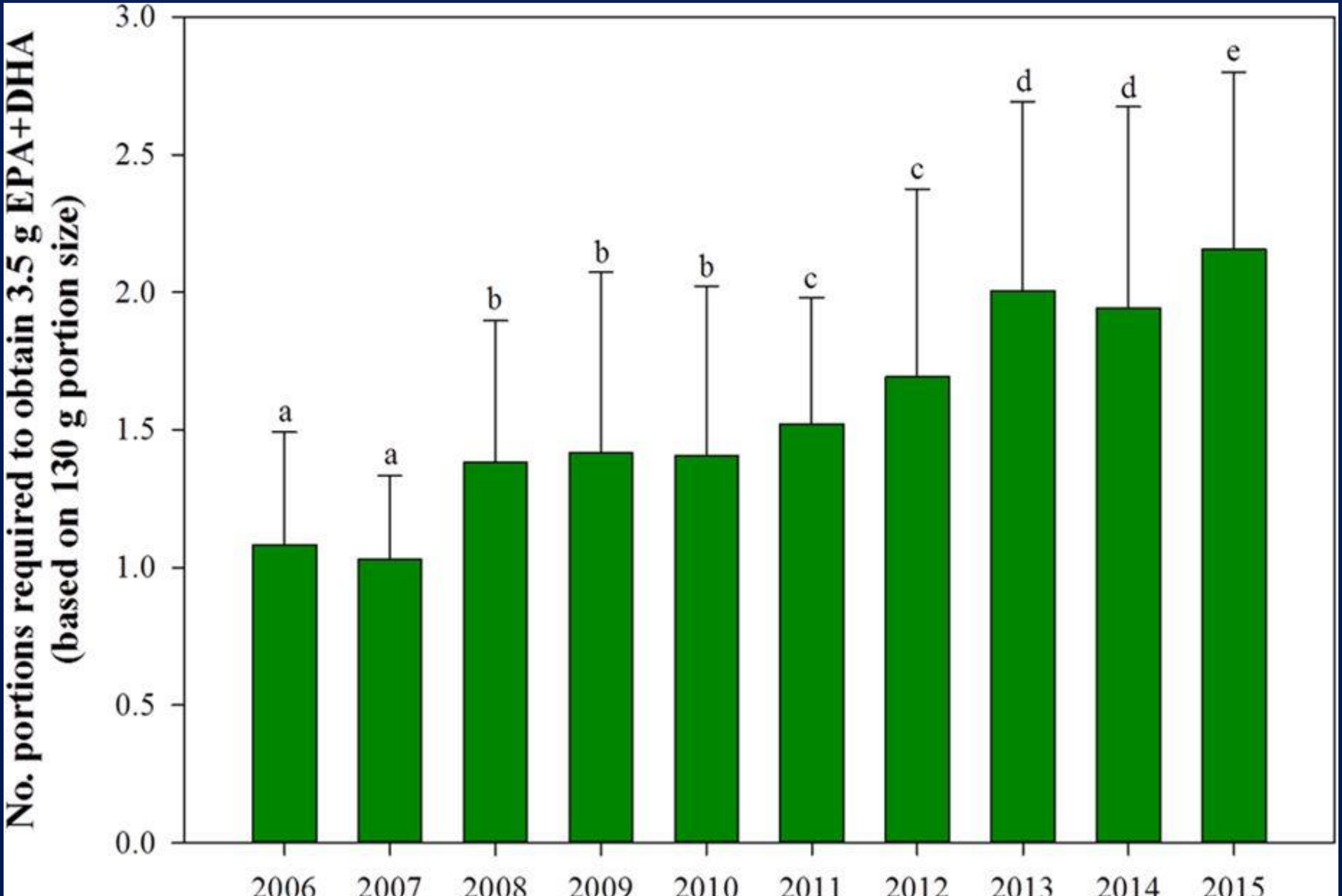
Edward Archer, PhD; Gregory Pavela, PhD; and Carl J. Lavie, MD

Schlussfolgerung: Methoden, wie Ernährungsfragebögen können nicht die Grundlage für nationale Leitlinien sein. Solche Forschung weiter zu fördern ist unwissenschaftlich und eine Verschwendung von Forschungsmitteln.“

Mayo Clin Proc 2015;90:911

Fisch – die typische Quelle

Immer weniger EPA & DHA in Fisch, z.B. Zuchtlachs



Sprague M et al, Scientific Reports 2016;6: 21892

Konventionelle Methode

der Ernährungs-Epidemiologie:

Fragebogen zum Verzehr von Speisen

auch ziemlicher Unsinn

ESC
European Society of Cardiology
European Heart Journal (2018) **0**, 1
doi:10.1093/eurheartj/ehy736

DISCUSSION FORUM

Is the PURE study pure fiction?

Edward Archer[1]* and Carl J. Lavie[2]

[1]EvolvingFX, Jupiter, FL 33468, USA; and [2]Cardiac Rehabilitation and Preventive Cardiology, John Ochsner Heart and Vascular Institute, 1514 Jefferson Hwy, Jefferson, LA 70121, USA

Cochrane Meta-Analyse RCT's weniger SFA vs. mehr SFA

Outcomes	Relative effect (95% CI)	Anticipated absolute effects (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)
		Risk with higher SFA intake	Risk with lower SFA intake		
All-cause mortality follow-up mean duration 56 months[1]	**RR 0.96** (0.90 to 1.03)	62 per 1000	60 per 1000 (56 to 64)	55,858 (12)	⊕⊕⊕⊝ **Moderate[2,3,4,5,6]**
Cardiovascular mortality follow-up mean duration 53 months[1]	**RR 0.94** (0.78 to 1.13)	19 per 1000	18 per 1000 (15 to 22)	53,421 (11)	⊕⊕⊕⊝ **Moderate[2,3,4,6,7]**
Combined cardiovascular events follow-up mean duration 52 months[1]	**RR 0.83** (0.70 to 0.98)	85 per 1000	70 per 1000 (59 to 83)	53,758 (13)	⊕⊕⊕⊝ **Moderate[4,8,9,10,11]**
Myocardial infarctions follow-up mean duration 55 months	**RR 0.90** (0.80 to 1.01)	32 per 1000	29 per 1000 (25 to 32)	53,167 (11)	⊕⊝⊝⊝ **Very Low[3,4,5,11,12]**

Hooper et al Cochrane Database Syst Rev 2020 Aug 21;8:CD011737

Selbst wenn man Nomenklatur und Methode der konventionellen Ernährungsforschung akzeptiert, gibt es keinen Beweis dafür, dass SFA schlecht sind.

Ernährung

Gesättigte Fette nicht verteufeln

Ist das schlechte Image der gesättigten Fettsäuren tatsächlich gerechtfertigt? Der genaue Blick auf eine Vielzahl von Studien wirft Fragen auf. Einige Ernährungswissenschaftler fordern daher, die strikten Grenzwerte zu lockern und wieder mehr auf Vollmilch, Käse und rotes Fleisch zu setzen.

Holstein T, Deutsches Ärzteblatt 2021;118:A359 vom 19.02.21

Präventionsleitlinien der Europäischen Kardiologengesellschaft

Table 12 **Healthy diet characteristics**

[redacted]
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
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Piepoli et al Eur Heart J 2016;37:2315

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Piepoli et al Eur Heart J 2016;37:2315

- Trans-unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.

TABLE 4. Relative Risk (95% CI) of Coronary Heart Disease Associated With *Trans* Fatty Acid Content in Erythrocytes*

	Quartile of *Trans* Fatty Acid Content (%)				
Trans Fatty Acid†	1 (Lowest)	2	3	4 (Highest)	P for Trend‡
Total *trans* fatty acids					
Mean (range)	1.17 (0.76 to 1.36)	1.50 (1.37 to 1.59)	1.72 (1.60 to 1.87)	2.23 (1.88 to 3.42)	
Model 1 (matching factors)	1.0	1.8 (1.0 to 3.4)	1.7 (0.9 to 3.1)	2.7 (1.5 to 5.0)	<0.01
Model 2 (multivariable)	1.0	1.6 (0.7 to 3.4)	1.4 (0.7 to 3.0)	2.7 (1.3 to 5.6)	0.01
Model 3 (model 2 plus n-3 and n-6 fatty acids)	1.0	1.6 (0.7 to 3.6)	1.6 (0.7 to 3.4)	3.3 (1.5 to 7.2)	<0.01
Total 18:1 *trans* isomers					
Mean (range)	0.77 (0.48 to 0.93)	1.03 (0.94 to 1.10)	1.21 (1.11 to 1.32)	1.62 (1.33 to 2.68)	
Model 1 (matching factors)	1.0	1.3 (0.7 to 2.4)	1.5 (0.8 to 2.7)	2.4 (1.4 to 4.3)	<0.01
Model 2 (multivariable)	1.0	1.1 (0.5 to 2.3)	1.2 (0.6 to 2.5)	2.5 (1.2 to 5.0)	<0.01
Model 3 (model 2 plus n-3 and n-6 fatty acids)	1.0	1.1 (0.5 to 2.4)	1.3 (0.6 to 2.7)	3.1 (1.5 to 6.7)	<0.01
Total 18:2 *trans* isomers					
Mean (range)	0.25 (0.14 to 0.28)	0.31 (0.29 to 0.34)	0.38 (0.35 to 0.41)	0.50 (0.42 to 0.78)	
Model 1 (matching factors)	1.0	1.2 (0.6 to 2.2)	2.1 (1.2 to 3.9)	2.2 (1.2 to 4.1)	<0.01
Model 2 (multivariable)	1.0	1.5 (0.7 to 3.2)	2.3 (1.1 to 5.0)	2.2 (1.0 to 4.8)	0.03
Model 3 (model 2 plus n-3 and n-6 fatty acids)	1.0	1.5 (0.7 to 3.4)	2.5 (1.1 to 5.7)	2.8 (1.2 to 6.3)	<0.01

Sun et al, Circulation 2007;115:1858

LURIC

LUdwigshafen RIsk and Cardiovascular Health Study

3316 Patienten zur Koronarangiographie überwiesen ins
Ludwigshafener Herzzentrum 1997 – 2000

>20% Stenose im Angiogramm

Patienten genau charakterisiert, viele Biomarker gemessen

9.9 Jahre Follow-up

975 (29.9%) der Teilnehmer verstorben

- plötzlicher Herztod: 254 (7.8%)
- tödlicher Herzinfarkt: 104 (3.2%)
- Herzinsuffizienz: 148 (4.5%)
- Revaskularisation: 26 (0.8%)
- Schlaganfall: 60 (1.8%)
- andere KHE: 19 (0.6%)
- unbekannt: 19 (0.6%)

3259 Erythrozyten-Proben auf Fettsäuren analysiert

Trans-Fettsäuren und Mortalität

	Sum TFA		C16:1t		C18:1t		18:2t	
Total mortality, adj age, sex								
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
1st tertile	1reference		1reference		1reference		1reference	
2nd tertile	0.87 (0.74-1.01)	0.065	0.85 (0.73-0.99)	0.037	0.87 (0.74-1.01)	0.073	0.89 (0.76-1.03)	0.139
3rd tertile	0.86 (0.73-1.01)	0.072	0.81 (0.69-0.94)	0.005	0.90 (0.77-1.05)	0.186	0.96 (0.81-1.14)	0.63
Cardiovascular mortality, adj age, sex								
1st tertile	1reference		1reference		1reference		1reference	
2nd tertile	0.77 (0.64-0.93)	0.008	0.87 (0.71-1.05)	0.14	0.82 (0.67-0.99)	0.042	0.86 (0.71-1.05)	0.139
3rd tertile	0.79 (0.64-0.98)	0.029	0.75 (0.62-0.91)	0.003	0.89 (0.74-1.09)	0.257	0.88 (0.71-1.08)	0.222
Sudden Death adj age, sex								
1st tertile	1reference		1reference		1reference		1reference	
2nd tertile	0.52 (0.39-0.71)	<0.001	0.74 (0.55-1.00)	0.05	0.70 (0.51-0.96)	0.027	0.85 (0.63-1.14)	0.27
3rd tertile	0.68 (0.50-0.92)	0.013	0.55 (0.41-0.76)	<0.001	0.92 (0.70-1.24)	0.594	0.87 (0.63-1.22)	0.426

Erythrozyten Transfettsäuren und Gesamtmortalität

obere Tertile vs. untere Tertile, adjustiert für Alter und Geschlecht

Natürlich

16:1n-7t	0.81; 95% CI 0.69-0.94; p=0.012

Industriell

18:1t	0.90; 95% CI 0.77-1.05, n.s.
18:2t	0.96; 95% CI 0.81-1.14, n.s.

Kleber et al, Eur Heart J 2016;37:1072

In LURIC

Trans-Fettsäuren aus der Lebensmittelproduktion:

18:1n-9t

18:2n-6t,c

18:2n-6c,t

18:2n-6t,t

Niedrige Spiegel, keine Assoziation mit Mortalität

Kleber et al, Eur Heart J 2016;37:1072

Natürliche Trans-Fettsäure: Längeres Überleben mit höheren Spiegeln

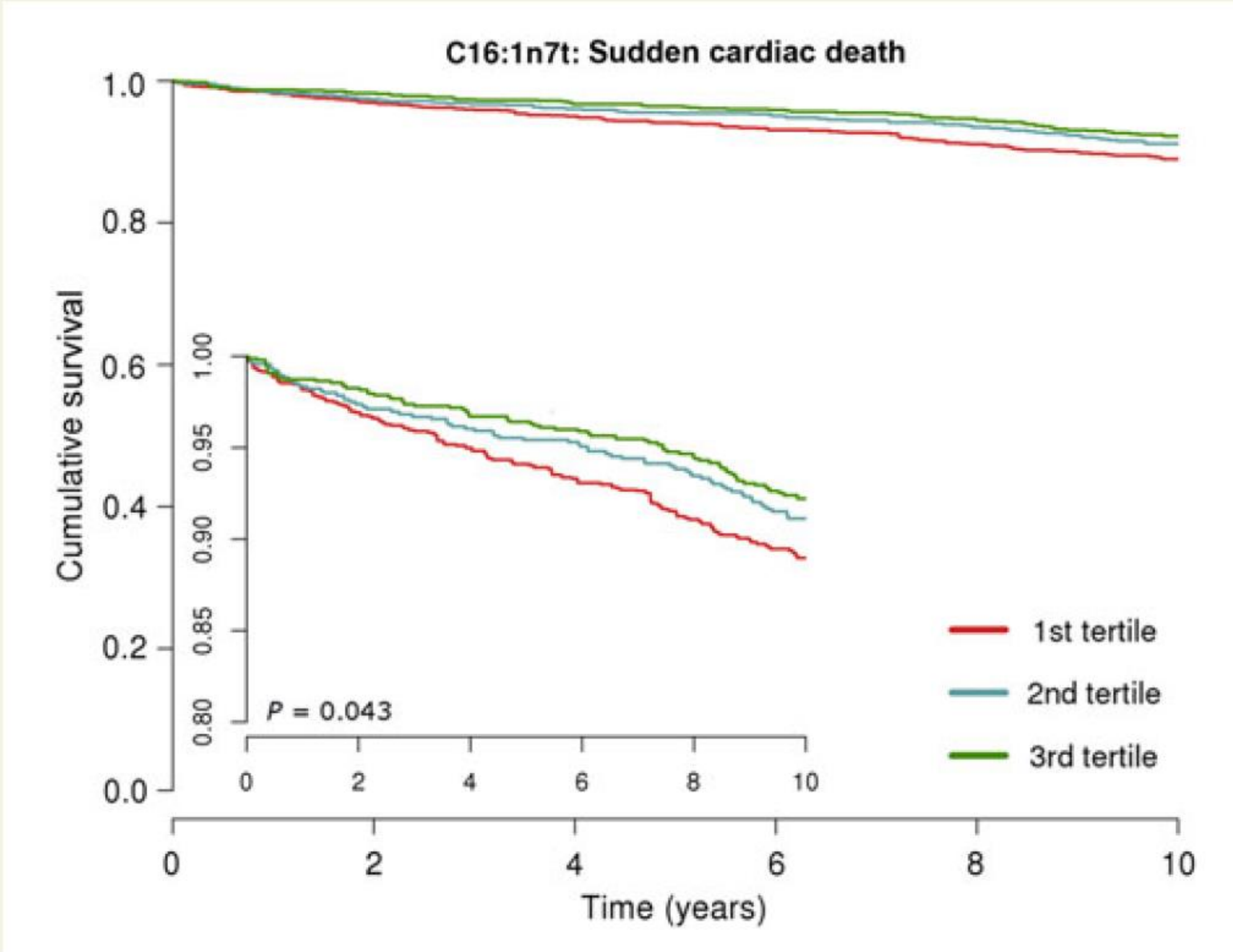

Figure 1 Adjusted survival curves for sudden cardiac death.

Kleber et al, Eur Heart J 2016;37:1072

Trans-Fettsäure-Spiegel in Deutschland über die Zeit

		Natürlich	HS-Trans Index	
	n	C16:1n-7t	Sum 18:1t + 18:2n-6trans	% > 1.04 %
2008	511	0.25 ± 0.33	0.99 ± 0.62	29.5
2009	720	0.15 ± 0.12	0.78 ± 0.34	9.3
2010	657	0.22 ± 0.20	0.75 ± 0.25	5.9
2011	812	0.20 ± 0.09	0.70 ± 0.27	3.8
2012	872	0.18 ± 0.07	0.71 ± 0.24	5.2
2013	1017	0.15 ± 0.06	0.65 ± 0.23	4.4
2014	1256	0.15 ± 0.05	0.56 ± 0.21	1.3
2015 (Jan–Sep)	909	0.15 ± 0.05	0.59 ± 0.19	1.3

von Schacky et al, Eur J Nutr 2017;56:1719

Wenn man alle Transfettsäuren in einen Topf wirft,

und entsprechende Gesetze erlässt (z.B. DK, nicht A)

dann verschwinden auch die, die das Leben verlängern.

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Piepoli et al Eur Heart J 2016;37:2315

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• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Üblicher vs. niedriger Na-Konsum und Gesamtmortalität

Study	Total	Weight	Hazard ratio, random (95% CI)
Lennie[35] mild heart failure	134	1.3%	0.44 (0.20 – 0.97)
Alderman,[19] M	1,900	5.4%	0.70 (0.52 – 0.94)
Ekinci[36]	620	6.0%	0.72 (0.55 – 0.94)
Cohen[26] (NH II)	7,154	9.2%	0.78 (0.67 – 0.91)
Stolarz-Skrypek[37]	2,454	5.8%	0.82 (0.62 – 1.08)
Tunstall-Pedoe,[20] M	3,453	6.5%	0.82 (0.64 – 1.05)
Cohen[29] (NH III)	6,525	9.9%	0.83 (0.73 – 0.94)
Thomas[15]	2,105	1.7%	0.87 (0.45 – 1.68)
Alderman[21] (NH I)	11,346	10.7%	0.88 (0.80 – 0.97)
Gardener[16]	2,099	8.2%	0.89 (0.74 – 1.07)
Tuomilehto,[24] F	1,263	2.8%	0.91 (0.56 – 1.48)
O'Donnel[38]	23,327	10.9%	0.92 (0.84 – 1.01)
Tunstall-Pedoe,[20] F	4,700	5.4%	0.93 (0.69 – 1.25)
Yang,[30] NW (NH III)	4,000	0.0%	0.93 (0.73 – 1.18)
He,[22] NW (NH I)	6,797	0.0%	0.98 (0.88 – 1.09)
Geleijnse[27]	1,578	6.2%	1.12 (0.86 – 1.46)
Taylor[41] (Appel 43)	291	2.8%	1.14 (0.70 – 1.86)
Alderman,[19] F	1,037	3.1%	1.17 (0.74 – 1.85)
He,[22] OW (NH I)	2,688	0.0%	1.32 (1.16 – 1.50)
Yang,[30] OW (NH III)	5,200	0.0%	1.44 (1.06 – 1.96)
Lennie[35] severe heart failure	163	1.1%	2.54 (1.10 – 5.87)
Costa[41]	372	1.8%	2.86 (1.50 – 5.44)
Arcand[34]	123	1.0%	3.54 (1.46 – 8.58)
Total (95% CI)	**70,644**	**100.0%**	**0.91 (0.82 – 0.99)**

Heterogeneity: $\tau^2 = 0.02$; $\chi^2 = 46.41$, df = 18 ($P = 0.0003$); $I^2 = 61\%$
Test for overall effect: $Z = 2.07$ ($P = 0.04$)

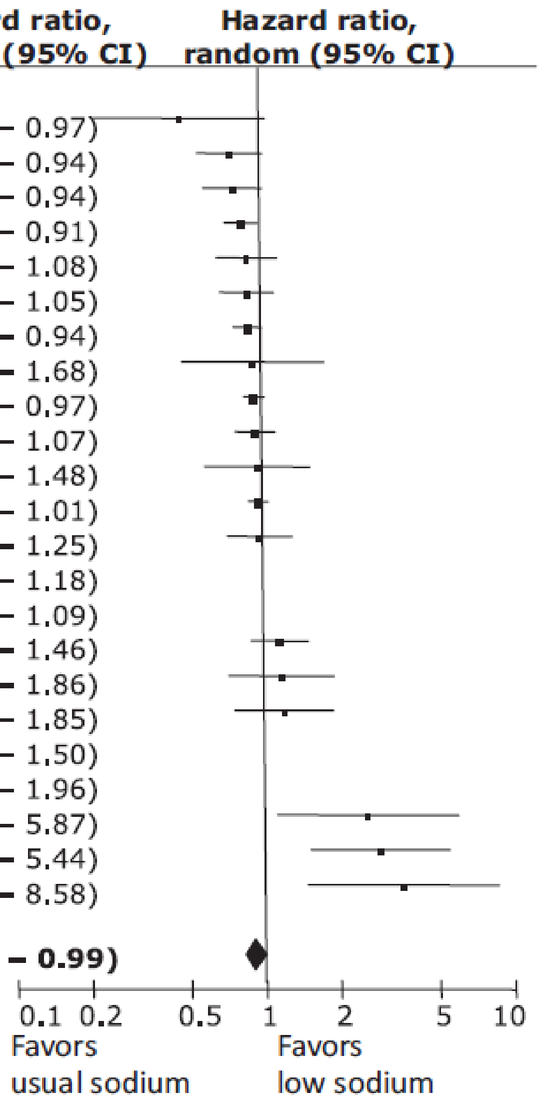

Figure 1. All-cause mortality, usual sodium vs. low sodium. Exchanging the first NHANES analyses[21,29] with the reanalyses:[22,30] (hazard ratio = 0.99; 95% confidence interval = 0.88–1.11; $P = 0.84$). CI, confidence interval; F, female; M, male; NH, NHANES, NW, normal weight; OW, overweight.

Graudal et al, Am J Hypertens. 2014;27:1129

Üblicher vs. hoher Na-Konsum und Gesamtmortalität

Study	Total	Weight	Hazard Ratio (95% CI)
Yang,[30] NW	2,667	0.0%	0.86 (0.51 – 1.45)
Cohen[29] (NH III)	6,525	15.5%	0.94 (0.79 – 1.12)
Tunstall-Pedoe,[20] M	4,604	12.7%	0.96 (0.77 – 1.20)
Tuomiletho,[24] M, NW	659	7.9%	0.98 (0.70 – 1.37)
Stolarz-Skrzypek[37]	2,454	6.5%	1.13 (0.77 – 1.66)
Tunstall-Pedoe,[20] F	3,525	7.3%	1.14 (0.80 – 1.62)
O'Donnel[38]	25,408	21.5%	1.20 (1.11 – 1.30)
Gardener[16]	2,337	10.0%	1.32 (1.00 – 1.74)
Thomas[15]	2,105	7.5%	1.43 (1.01 – 2.02)
Tuomilehto,[24] M, OW	514	11.0%	1.56 (1.21 – 2.01)
Yang,[30] OW	3,467	0.0%	2.07 (1.35 – 3.17)
Total (95% CI)	**48131**	**100.0%**	**1.16 (1.03 – 1.30)**

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 17.61$, df = 8 ($P = 0.02$); $I^2 = 55\%$
Test for overall effect: $Z = 2.46$ ($P = 0.01$)

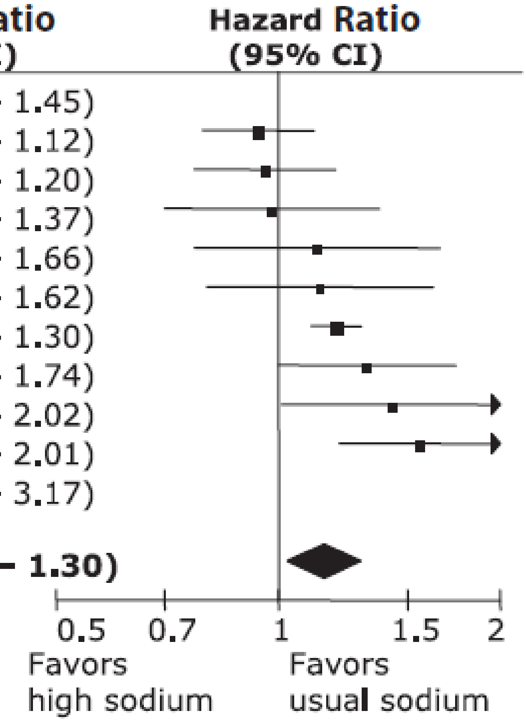

Figure 3. All-cause mortality, high sodium vs. usual sodium. Exchanging the first NHANES analysis[29] with the reanalysis[30] (hazard ratio = 1.22; 95% confidence interval = 1.08–1.39; $P = 0.002$). F, female; M, male; NH, NHANES; NW, normal weight; OW, overweight.

Graudal et al, Am J Hypertens. 2014;27:1129

Salz

U-förmig

Optimum bei 7-12 g/Tag

Meta-Analyse und Systematischer Review zur Salzaufnahme

CONCLUSIONS

Both low sodium intakes and high sodium intakes are associated with increased mortality, consistent with a U-shaped association between sodium intake and health outcomes.

Am J Hypertension 2014, e-pub April 1

Weniger als 5 g Salz pro Tag bringt die Leute um

Präventionsleitlinien der Europäischen Kardiologengesellschaft

Table 12 Healthy diet characteristics

• Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
[redacted]
• 30–45 g of fibre per day, preferably from wholegrain products.
• ≥200 g of fruit per day (2–3 servings).
• ≥200 g of vegetables per day (2–3 servings).
• Fish 1–2 times per week, one of which to be oily fish.
• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Präventionsleitlinien der Europäischen Kardiologengesellschaft

Table 12 Healthy diet characteristics

• Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
• <5 g of salt per day.
• 30–45 g of fibre per day, preferably from wholegrain products.
• ≥200 g of fruit per day (2–3 servings).
• ≥200 g of vegetables per day (2–3 servings).
• Fish 1–2 times per week, one of which to be oily fish.
• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Meta-Analyse 22 Kohorten-Studien:

pro zusätzliche 7 g Fasern / Tag

-Risiko für eine kardiovaskuläre Erkrankung 9% niedriger

(RR 0,91; 95%CI 0,88 - 0.94)

- Risiko for koronare Herzerkrankung 9 % niedriger

(RR 0,91 95%CI 0,87 - 0.94)

Aber: gilt nicht für Obst, keine Daten >30 g/Tag

Interventionsstudien: Surrogatparameter

Threapleton et al, BMJ. 2013 Dec 19;347:f6879.

Präventionsleitlinien der Europäischen Kardiologengesellschaft

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• Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
• <5 g of salt per day.
• 30–45 g of fibre per day, preferably from wholegrain products.
• ≥200 g of fruit per day (2–3 servings).
• ≥200 g of vegetables per day (2–3 servings).
• Fish 1–2 times per week, one of which to be oily fish.
• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Meta-Analyse 16 Kohorten-Studien:

pro zusätzliche 80 g Obst/ Tag

- Risiko für Gesamtmortalität 6% niedriger (HR 0,94; 95%CI 0,90 - 0.98)

Pro zusätzliche 80 g Gemüse pro Tag

- Risiko für Gesamtmortalität 5 % niedriger (HR 0,95 95%CI 0,92 - 0.99)

Plateau bei 400 g Obst und Gemüse

Interventionsstudien: Surrogatparameter

Wang et al BMJ 2014;349:g4490

Mediterrane Kost

Mediterrane Kost enthält

täglich
≥4 Esslöffel Polyphenol-reichen Olivenöls,
≥3 Portionen frisches Obst,
≥2 Portionen Gemüse

wöchentlich
≥3 Portionen Nüsse,
≥3 Portionen fetten Fisch,
≥3 Portionen Hülsenfrüchte,
≥2 Portionen „Sofrito“ (eine Soße aus Tomaten und Zwiebeln,
häufig mit Knoblauch und aromatischen Kräutern,
die langsam mit Olivenöl gekocht wird),

weißes statt rotes Fleisch, und zur Hauptmahlzeit,
wenn gewünscht, täglich ein Glas Wein.

Estruch et al Predimed NEJM 2013;368:1279

Cochrane Meta-Analyse Mediterrane Kost In der sekundären Prävention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with usual care	Risk with Mediterranean dietary intervention				
CVD mortality Follow-up: mean 46 months	Study population		RR 0.35 (0.15 to 0.82)	605 (1 RCT)	⊕⊕⊝⊝ LOW [1]	—
	63 per 1000	22 per 1000 (9 to 51)				
Total mortality Follow-up: mean 4 years	Study population		RR 0.44 (0.21 to 0.92)	605 (1 RCT)	⊕⊕⊝⊝ LOW [1]	—
	79 per 1000	35 per 1000 (17 to 73)				

Rees et al, Cochrane Database Sys Rev 2019;3:CD009825

Vitamin D

Meta-Analyse von Meta-Analysen Supplementation Vitamin D

Table 1. Summary characteristics of meta-analyses and the individual RCTs included in MA on non-skeletal effects of vitamin D supplementation.

			CVD	BP	T2D	Body Weight	Birth Weight	Cancer	RTI	Dep.	Death	ALL
Number of meta-analyses			7	9	1	3	6	5	7	4	12	54
	Results (main finding)											
		Beneficial response	0	2	0	0	2	0	3	1	8	16
		Harmful	0	1	0	0	1[a)]	0	0	0	0	2

			CVD	Death	ALL
Number of meta-analyses			7	12	54
	Results (main finding)				
		Beneficial response	0	8	16
		Harmful	0	0	2
		Null finding	7	4	36

Rejnmark et al PlosONE 2017; 12:e0180512

ESC-Leitlinie:

Epidemiologisch Gesamt- und CV Mortalität

ohne Supplementation mindestens 35% höher,

in RCT‘s 11% Reduktion Gesamtmortalität,

aber keine Reduktion CV-Mortalität, deshalb:

Keine Empfehlung zur Supplementation.

oder auch:

ESC nur für CV Mortalität zuständig…

m.E. unethisch.

Piepoli MF et al, Eur Heart J. 2016;37:2315

Meines Erachtens:

Vitamin D:

Spiegel messen, wenn niedrig anheben,

am ehesten mit Supplementen.

Präventionsleitlinien der Europäischen Kardiologengesellschaft

Table 12 Healthy diet characteristics

• Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids.
• Trans unsaturated fatty acids: as little as possible, preferably no intake from processed food, and <1% of total energy intake from natural origin.
• <5 g of salt per day.
• 30–45 g of fibre per day, preferably from wholegrain products.
• ≥200 g of fruit per day (2–3 servings).
• ≥200 g of vegetables per day (2–3 servings).
• Fish 1–2 times per week, one of which to be oily fish.
• 30 grams unsalted nuts per day.
• Consumption of alcoholic beverages should be limited to 2 glasses per day (20 g/d of alcohol) for men and 1 glass per day (10 g/d of alcohol) for women.
• Sugar-sweetened soft drinks and alcoholic beverages consumption must be discouraged.

Piepoli et al Eur Heart J 2016;37:2315

Omega-3-Fettsäuren

Der erhöhte Verzehr der langkettigen Omega-3-Fettsäuren ist nach einer neuen Cochrane-Untersuchung weitgehend nutzlos.

www.aerzteblatt.de/n96810

Deutsches Ärzteblatt, Jahrgang 115, Heft 35 – 36, 03. Sept. 2018, Seite 104

Gesamtmortalität, Tabelle 1a

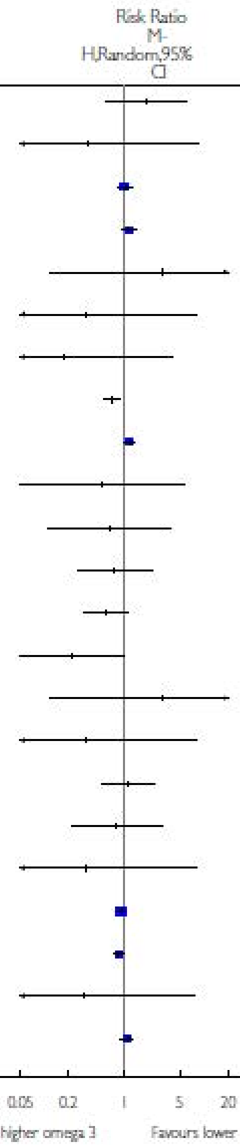
Analysis 1.1. Comparison 1 High vs low LCn3 omega-3 fats (primary outcomes), Outcome 1 All-cause mortality (overall) - LCn3.

Review: Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease

Comparison: 1 High vs low LCn3 omega-3 fats (primary outcomes)

Outcome: 1 All-cause mortality (overall) - LCn3

Study or subgroup	Favours higher omega 3 n/N	Lower omega 3 fats n/N	Weight	Risk Ratio M-H,Random,95% CI
ADCS 2010	11/238	4/164	0.2 %	1.89 [0.61, 5.85]
AFFORD 2013	0/153	1/163	0.0 %	0.35 [0.01, 8.65]
AlphaOmega - EPA+DHA 2010 (1)	186/2404	184/2433	6.0 %	1.02 [0.84, 1.24]
AREDS2 2014	200/2147	168/2056	6.0 %	1.14 [0.94, 1.39]
Bates 1989	1/155	0/157	0.0 %	3.04 [0.12, 74.02]
Berson 2004	0/105	1/103	0.0 %	0.33 [0.01, 7.94]
Brox 2001	0/80	1/40	0.0 %	0.17 [0.01, 4.05]
DART 1989	94/1015	131/1018	4.0 %	0.72 [0.56, 0.92]
DART2 2003	283/1571	242/1543	8.4 %	1.15 [0.98, 1.34]
Derosa 2016	1/138	2/143	0.1 %	0.52 [0.05, 5.65]
DIPP 2015	2/104	3/101	0.1 %	0.65 [0.11, 3.79]
DISAF 2003	6/201	8/206	0.3 %	0.77 [0.27, 2.18]
DO IT 2010	14/282	24/281	0.7 %	0.58 [0.31, 1.10]
Doi 2014	2/119	9/119	0.1 %	0.22 [0.05, 1.01]
EPIC-1 2008	1/183	0/180	0.0 %	2.95 [0.12, 71.97]
EPIC-2 2008	0/189	1/190	0.0 %	0.34 [0.01, 8.17]
FAAT 2005	13/200	12/202	0.5 %	1.09 [0.51, 2.34]
FORWARD 2013	4/289	5/297	0.2 %	0.82 [0.22, 3.03]
FOSTAR 2016	0/101	1/101	0.0 %	0.33 [0.01, 8.09]
GISSI-HF 2008	955/3494	1014/3481	18.8 %	0.94 [0.87, 1.01]
GISSI-P 1999	472/5666	545/5658	12.2 %	0.86 [0.77, 0.97]
HARP 1995	0/41	1/39	0.0 %	0.32 [0.01, 7.57]
JELIS 2007	286/9326	265/9319	7.8 %	1.08 [0.91, 1.27]



Abdelhamid et al Cochrane Database Syst Rev. 2018;11:CD003177

Gesamtmortalität, Tabelle 1b

(. . . Continued)

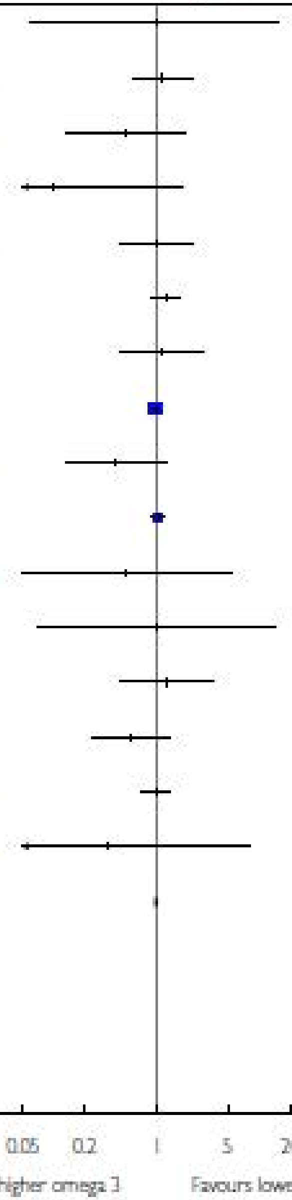
Study or subgroup	Favours higher omega 3 n/N	Lower omega 3 fats n/N	Weight	Risk Ratio M-H,Random,95% CI
Kumar 2013	1/39	1/39	0.0 %	1.00 [0.06, 15.43]
MAPT 2017	18/840	16/840	0.6 %	1.13 [0.58, 2.19]
NAT2 2013	3/150	6/150	0.2 %	0.50 [0.13, 1.96]
Nutristroke 2009	0/38	4/34	0.0 %	0.10 [0.01, 1.79]
OFAMI 2001	11/150	11/150	0.4 %	1.00 [0.45, 2.24]
OMEGA 2009	88/1919	70/1885	2.7 %	1.23 [0.91, 1.68]
OPAL 2010	9/434	8/433	0.3 %	1.12 [0.44, 2.88]
ORIGIN 2012	951/6281	964/6225	17.5 %	0.98 [0.90, 1.06]
Raitt 2005	4/100	10/100	0.2 %	0.40 [0.13, 1.23]
Risk % Prevention 2013	348/6239	337/6266	9.3 %	1.04 [0.90, 1.20]
SCIMO 1999	1/112	2/111	0.1 %	0.50 [0.05, 5.39]
Shinto 2014	1/13	1/13	0.0 %	1.00 [0.07, 14.34]
SHOT 1996	8/317	6/293	0.3 %	1.23 [0.43, 3.51]
SOFA 2006	8/273	14/273	0.4 %	0.57 [0.24, 1.34]
SU.FOL.OM3 2010	66/1253	68/1248	2.4 %	0.97 [0.70, 1.34]
Zhang 2017	0/120	1/120	0.0 %	0.33 [0.01, 8.10]
Total (95% CI)	**46479**	**46174**	**100.0 %**	**0.98 [0.93, 1.03]**

Total events: 4048 (Favours higher omega 3), 4141 (Lower omega 3 fats)

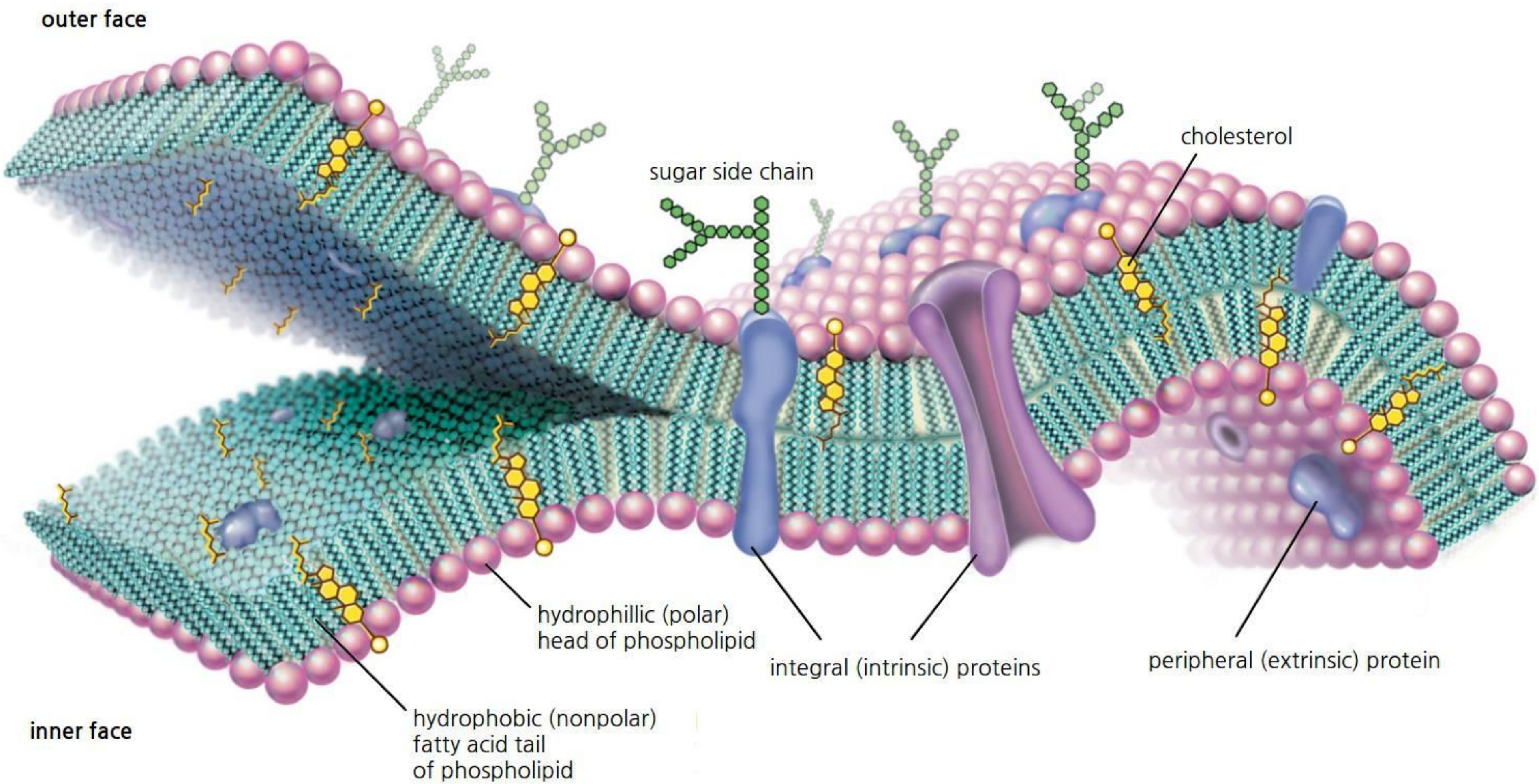
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 43.01$, df = 38 (P = 0.27); $I^2 = 12\%$

Test for overall effect: Z = 0.87 (P = 0.39)

Test for subgroup differences: Not applicable



Abdelhamid et al Cochrane Database Syst Rev. 2018;11:CD003177


outer face
sugar side chain
cholesterol
hydrophillic (polar)
head of phospholipid
integral (intrinsic) proteins
peripheral (extrinsic) protein
hydrophobic (nonpolar)
fatty acid tail
of phospholipid
inner face

https://www.handelszeitung.ch/beruf/veraltetes-wissen-vergessen-so-verlernt-man-richtig

Erkennen Sie den Unterschied?

ALA	ALA
↓	⇣
EPA	EPA
↓	⊥ ↑
DHA	DHA

von Schacky, Ann Int Med 1987; 107:890;
Plourde & Cunnane Appl Physiol Nutr Metab. 2007;32:619

Ratte ≠ Mensch

d.h. Mensch braucht DHA

Zufuhr = Aufnahme?

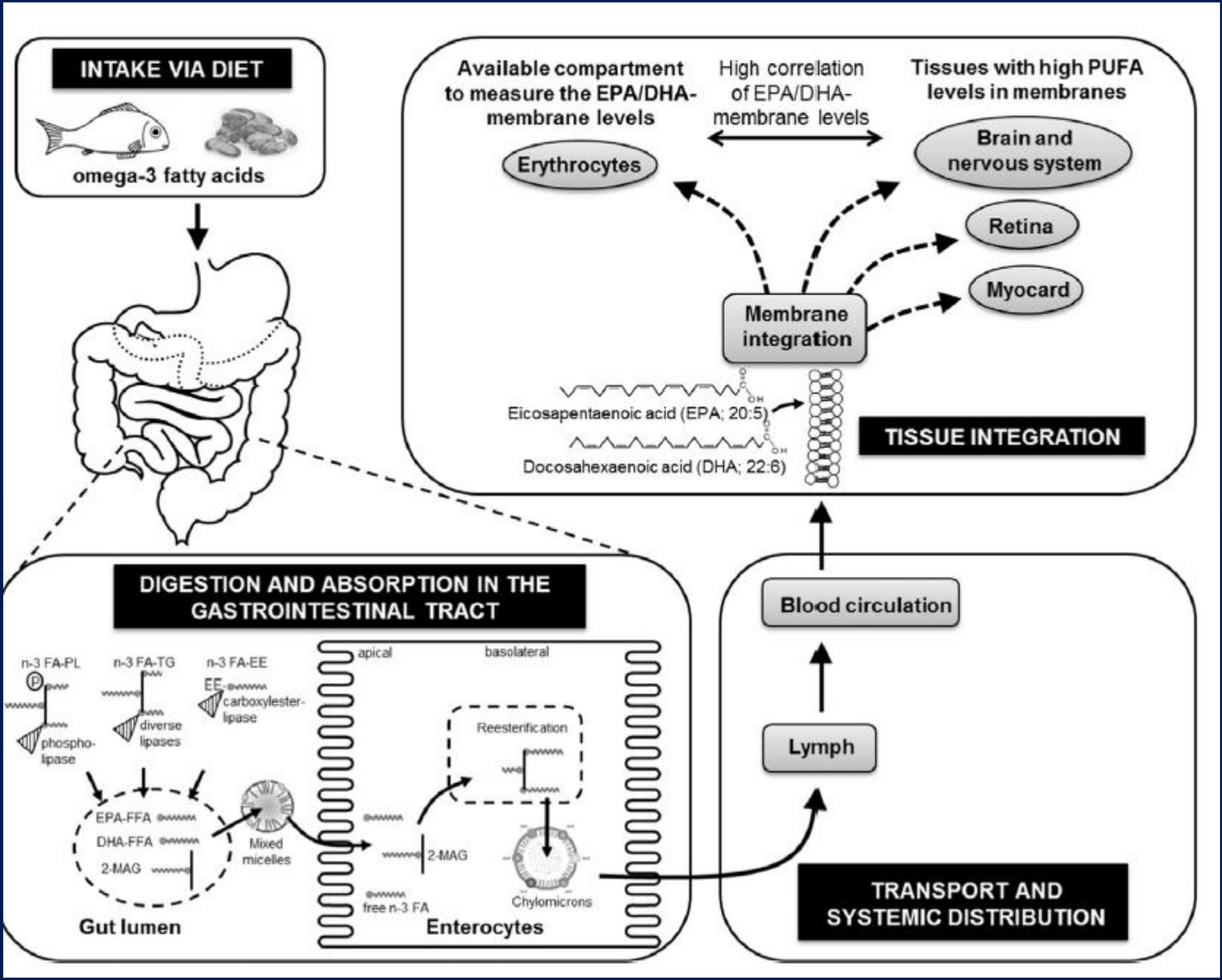
Omega-3 Absorption und Einbau in Gewebe - ein komplexer, mehrschrittiger Prozess

Wichtige Aspekte:

1. Emulsifizierung durch Gallensalze

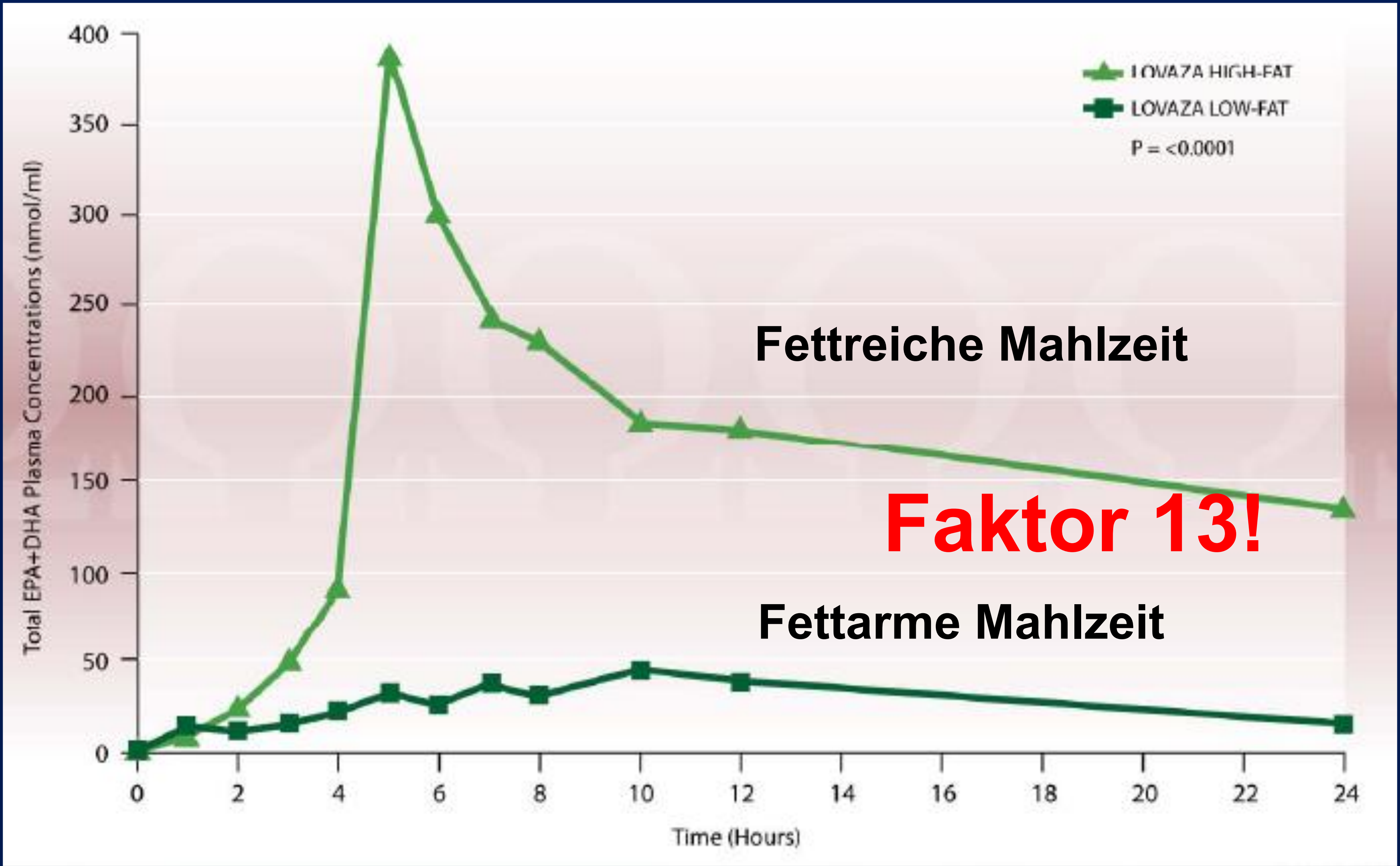
2. Verdauung durch Enzyme (z.B. Lipasen)

3. Absorption und Rekonstitution zum Transport



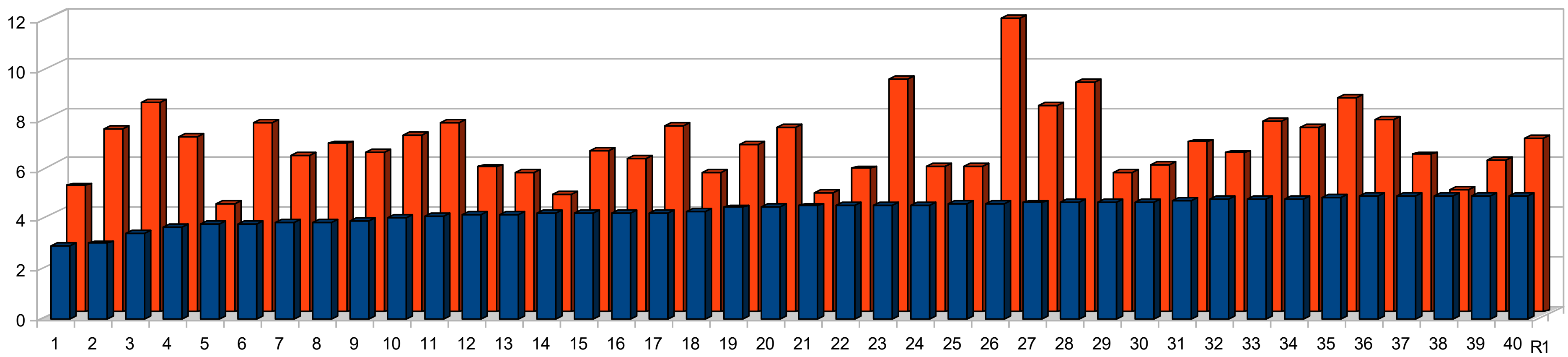
Schuchardt PLEFA 2013;89:1

Aufnahme von EPA+DHA Ethyl-Ester (Omacor®, Lovaza®, Zodin®)



Davidson et al J Clin Lipidol. 2012;6:573-84

HS-Omega-3 Index
Effekt von 500 mg EPA+DHA / Tag



Mittel vorher 4.37 <u>+</u> 0.51, nach 8 Wochen 6.80 <u>+</u> 1.45 %
in Interventionsgruppe, p<0.0001, gepaarter t-test
Unterschied in der Antwort: Faktor 13

Köhler et al, Br J Nutr 2010, 104:729-36

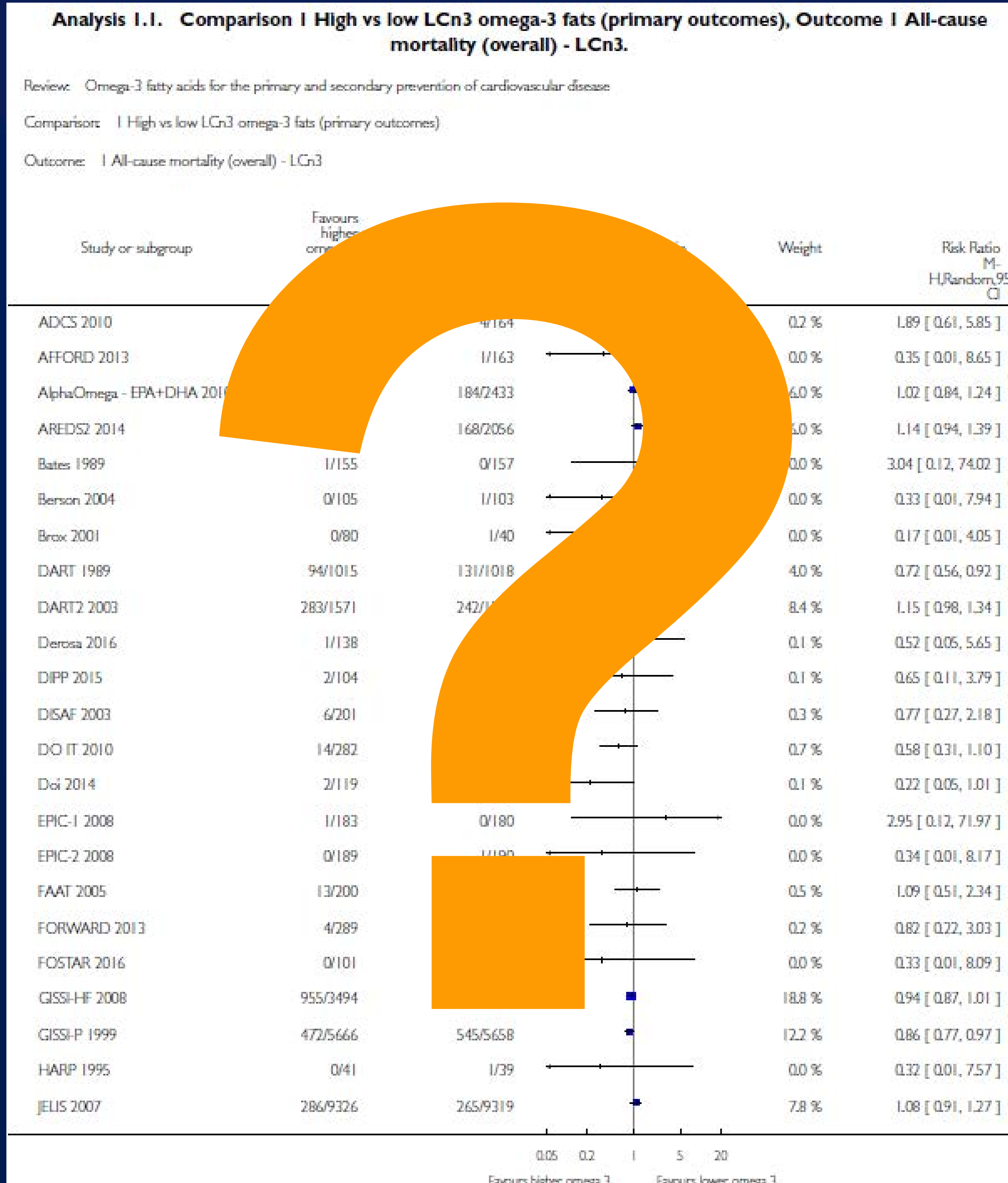
Variabilität der Aufnahme von EPA und DHA

- Fettarme / Fettreiche Mahlzeit:	bis Faktor 13
- Chemische Form:	bis Faktor 2
- Emulsion / Ethylester in Kapsel	bis Faktor 22
- Matrix-Effekte	bis Faktor 10
- Inter-individuell:	bis Faktor 13

Zufuhr ≠ Aufnahme

Dosis???

Gesamtmortalität, Tabelle 1a



Analysis 1.1. Comparison 1 High vs low LCn3 omega-3 fats (primary outcomes), Outcome 1 All-cause mortality (overall) - LCn3.

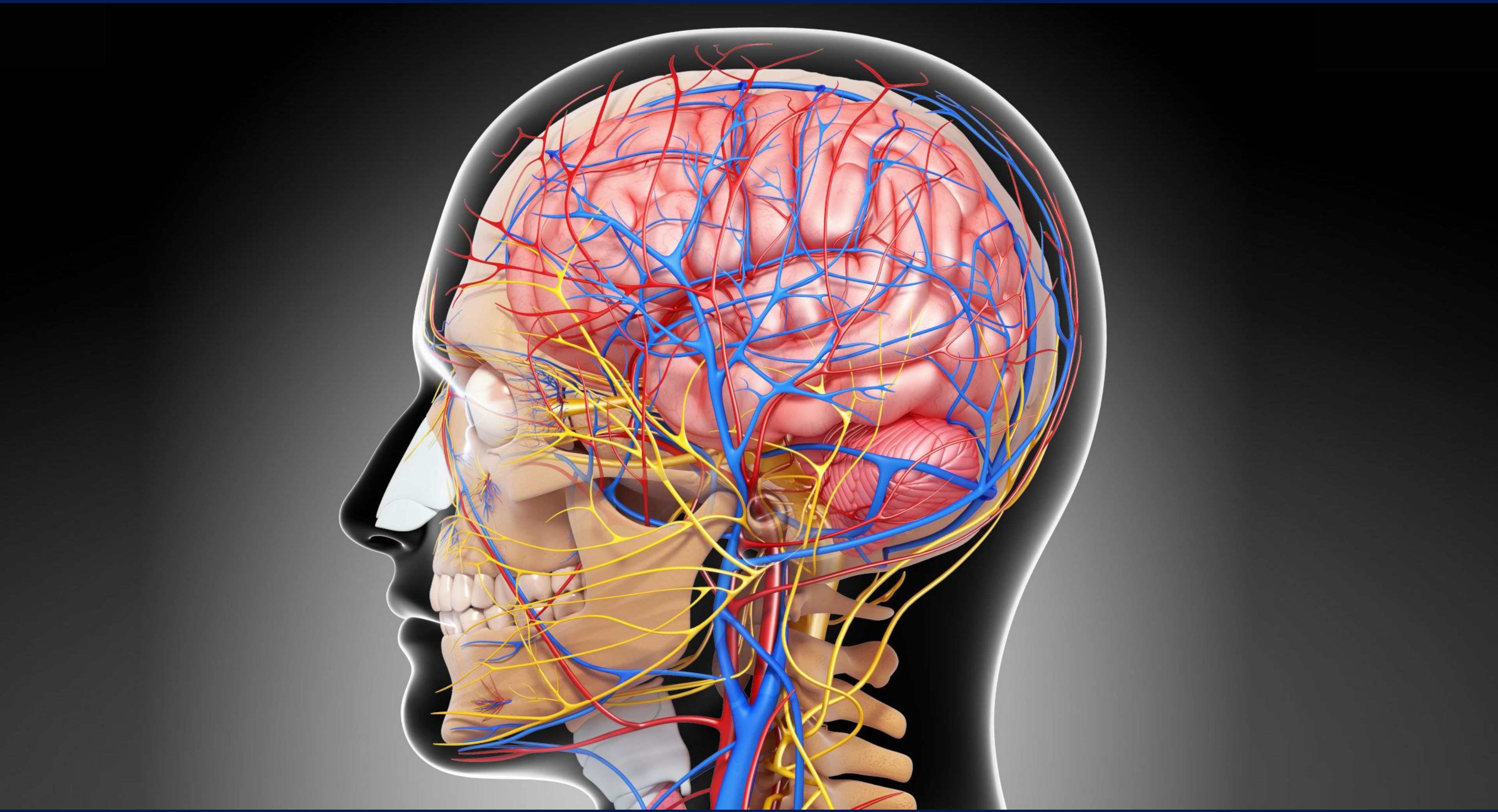
Review: Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease

Comparison: 1 High vs low LCn3 omega-3 fats (primary outcomes)

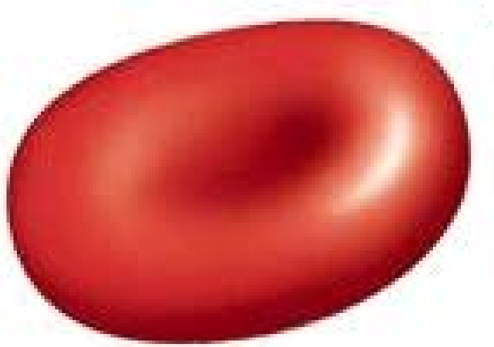
Outcome: 1 All-cause mortality (overall) - LCn3

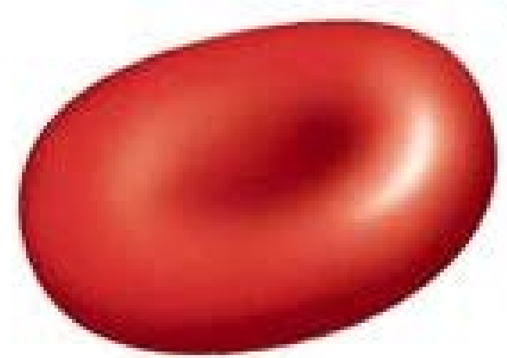
Study or subgroup	Favours higher [illegible]	[illegible]	[illegible]	Weight	Risk Ratio M-H,Random,95% CI
ADCS 2010	[illegible]	4/164		0.2 %	1.89 [0.61, 5.85]
AFFORD 2013	[illegible]	1/163		0.0 %	0.35 [0.01, 8.65]
AlphaOmega - EPA+DHA 201[illegible]	[illegible]	184/2433		[illegible]0 %	1.02 [0.84, 1.24]
AREDS2 2014	[illegible]	168/2056		[illegible]0 %	1.14 [0.94, 1.39]
Bates 1989	1/155	0/157		0.0 %	3.04 [0.12, 74.02]
Berson 2004	0/105	1/103		0.0 %	0.33 [0.01, 7.94]
Brox 2001	0/80	1/40		0.0 %	0.17 [0.01, 4.05]
DART 1989	94/1015	131/1018		4.0 %	0.72 [0.56, 0.92]
DART2 2003	283/1571	242/1[illegible]		8.4 %	1.15 [0.98, 1.34]
Derosa 2016	1/138	[illegible]		0.1 %	0.52 [0.05, 5.65]
DIPP 2015	2/104	[illegible]		0.1 %	0.65 [0.11, 3.79]
DISAF 2003	6/201	[illegible]		0.3 %	0.77 [0.27, 2.18]
DO IT 2010	14/282	[illegible]		0.7 %	0.58 [0.31, 1.10]
Doi 2014	2/119	[illegible]		0.1 %	0.22 [0.05, 1.01]
EPIC-1 2008	1/183	0/180		0.0 %	2.95 [0.12, 71.97]
EPIC-2 2008	0/189	[illegible]		0.0 %	0.34 [0.01, 8.17]
FAAT 2005	13/200	[illegible]		0.5 %	1.09 [0.51, 2.34]
FORWARD 2013	4/289	[illegible]		0.2 %	0.82 [0.22, 3.03]
FOSTAR 2016	0/101	[illegible]		0.0 %	0.33 [0.01, 8.09]
GISSI-HF 2008	955/3494	[illegible]		18.8 %	0.94 [0.87, 1.01]
GISSI-P 1999	472/5666	545/5658		12.2 %	0.86 [0.77, 0.97]
HARP 1995	0/41	1/39		0.0 %	0.32 [0.01, 7.57]
JELIS 2007	286/9326	265/9319		7.8 %	1.08 [0.91, 1.27]

Abdelhamid et al Cochrane Database Syst Rev. 2018;11:CD003177



HS-Omega-3 Index®





Langzeit-Biomarker für Fettsäuren

Gemessen in Erythrozyten (geringe biologische Variabilität)

Standardisierte und validierte Methode für 26 Fettsäuren

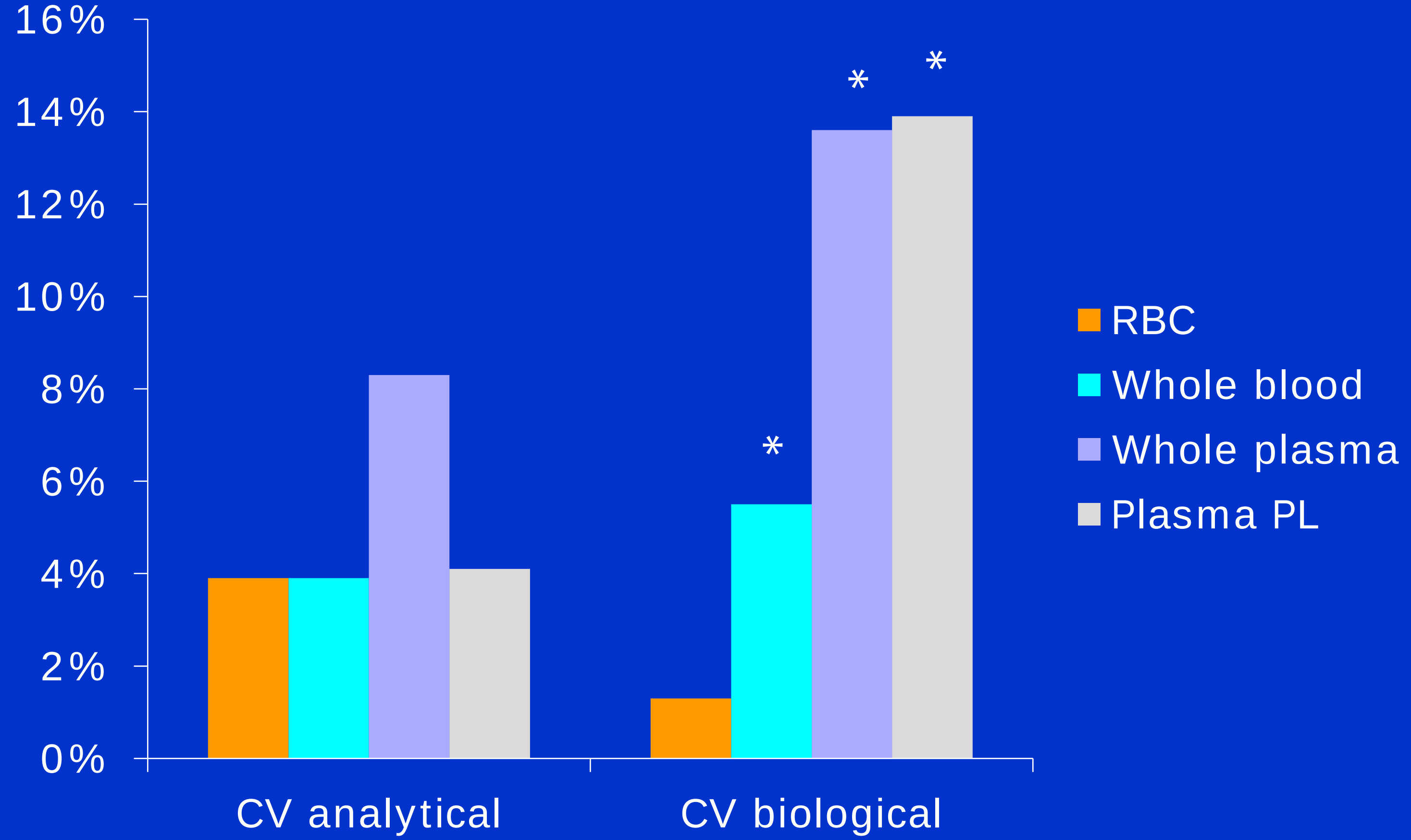
(niedrige analytische Variabilität)

> 320 Publikationen, >50 laufende Forschungsprojekte

QM nach DIN ISO 15189

Ω metrix®

Biologische Variabilität von Erythrocyten vs. Andere und Analytische Variabilität des HS-Omega-3 Index



* p<0.03 vs RBC

Harris WS, Thomas R Clin Biochem Clin Biochem 2010;43:338-340

…eine Probe in 6 Labors…

August 2018 – Omega-3 Index in Deutschland

	Ergebnis	Ziel	Empfehlung
Omegametrix:	6.43%	8 – 11%	mehr omega-3
Labor B1:	4.36%	>8%	ist normal
Labor B2:	7.29%	>8%	mehr omega-3
Labor G:	5.69%	>8%	mehr omega-3
Labor M:	3.70%	>4%	mehr omega-6
Labor W:	4.30%	6 – 8%	-

Standardisierung !!!
Ethische Probleme!!!

Ja, und?
Haben wir was gelernt?

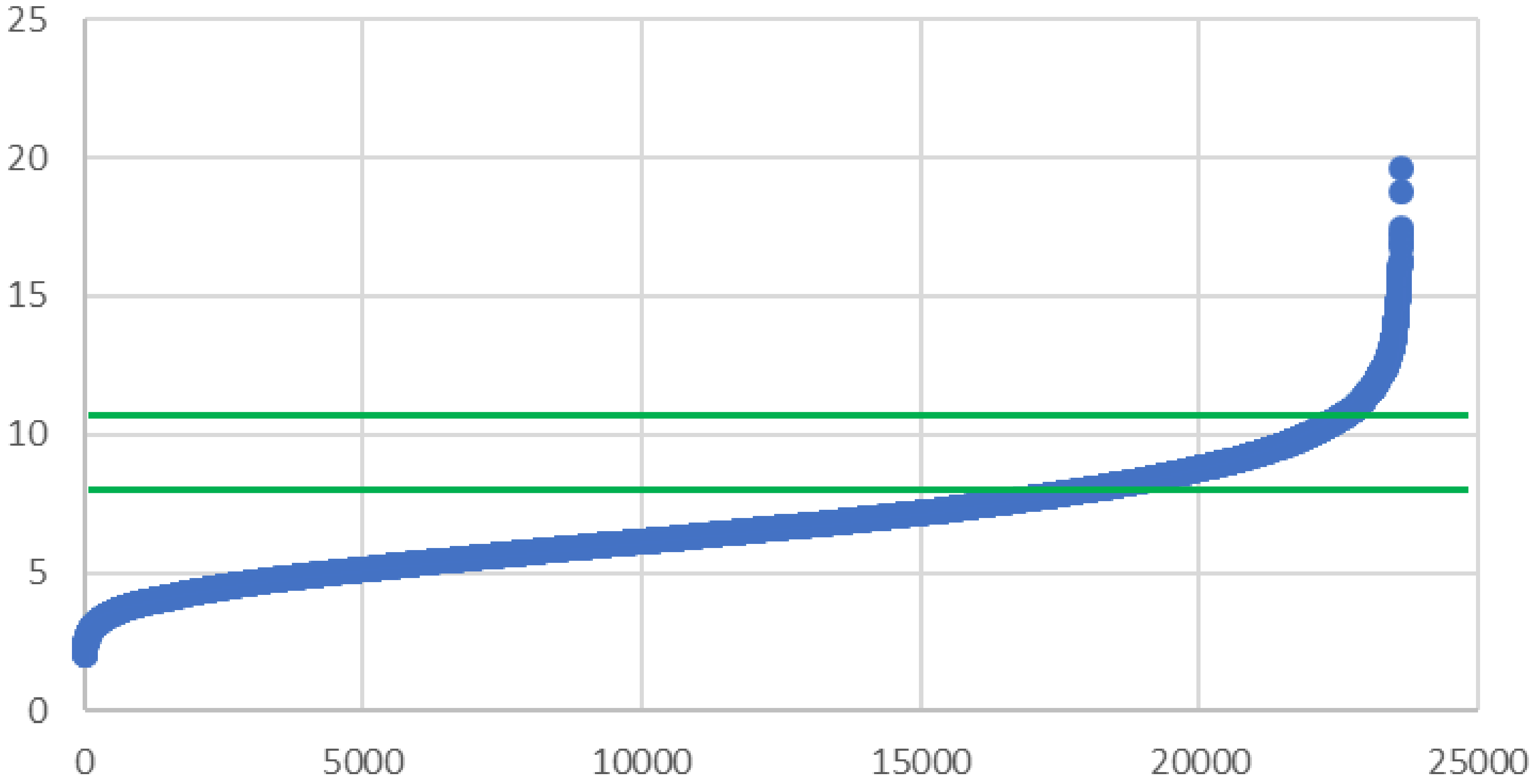
EPA+DHA in Erythrozyten repräsentativ für EPA+DHA in Myokard, Vorhof, Muskel weibliches Brustgewebe

Im Tierexperiment auch repräsentativ für

Nieren
Hirnrinde
Leber
Lunge
Pankreas
Darm

Harris WS et al Circulation 2004;110:1645; Arnold et al, JBC, 2010; 285:32720; Metcalf et al, Am J Clin Nutr. 2010;91:528 Gurzell et al, PLEFA 2014;91:87; Roy S et al, Int J Canc 2015;137:2934

Omega-3 Index in 23 615 Erythrozyten-Proben aus Europa



n < 2% = 0, n > 20% = 0

Bisher keinen Menschen gefunden,

der einen Omega-3 Index <2% hatte.

Menschliches Leben ohne EPA&DHA

gibt es nicht.

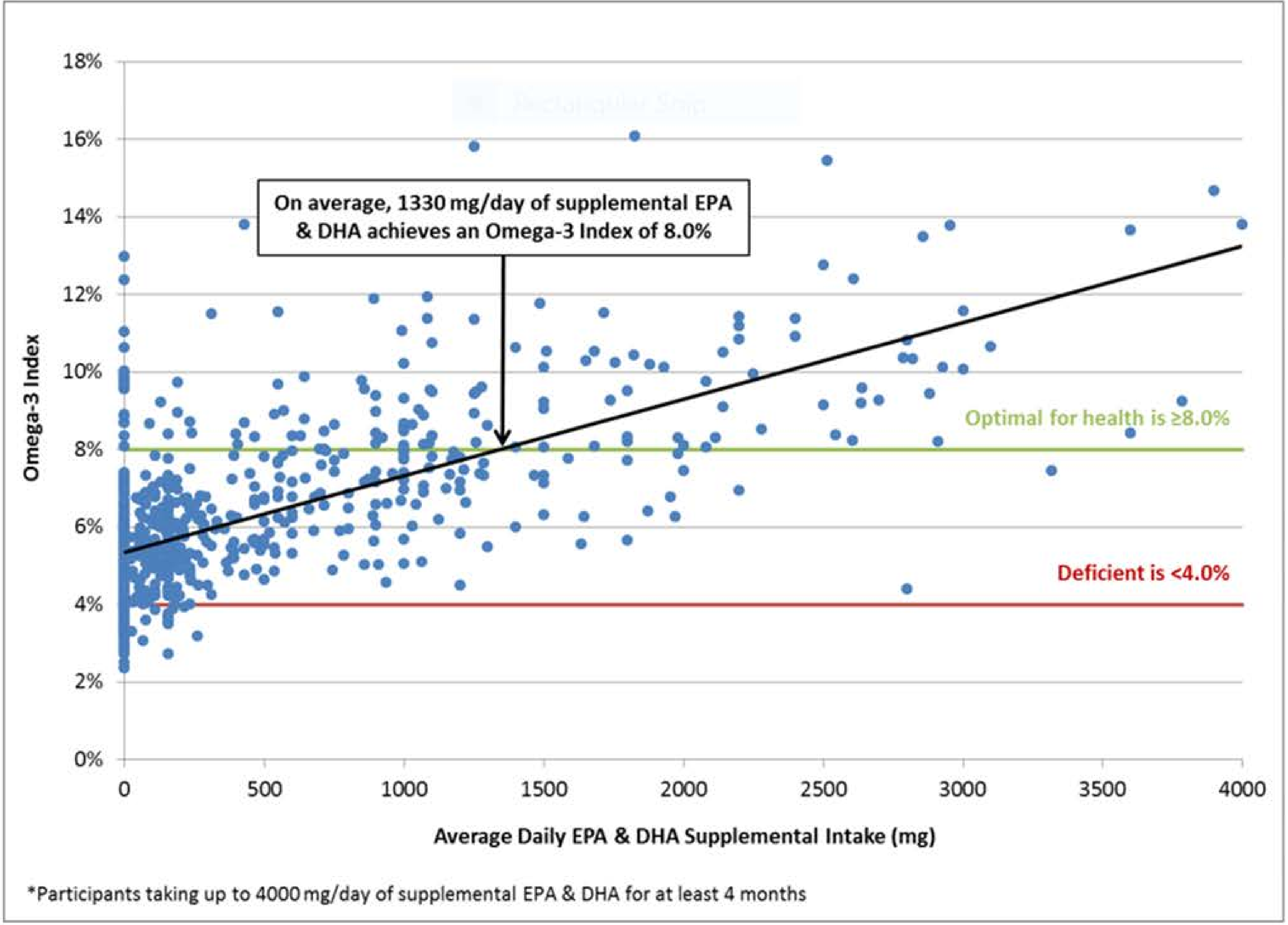


Figure 1© 2018 GrassrootsHealth

https://www.naturalproductsinsider.com/lipids/optimal-illusive-omega-3-level

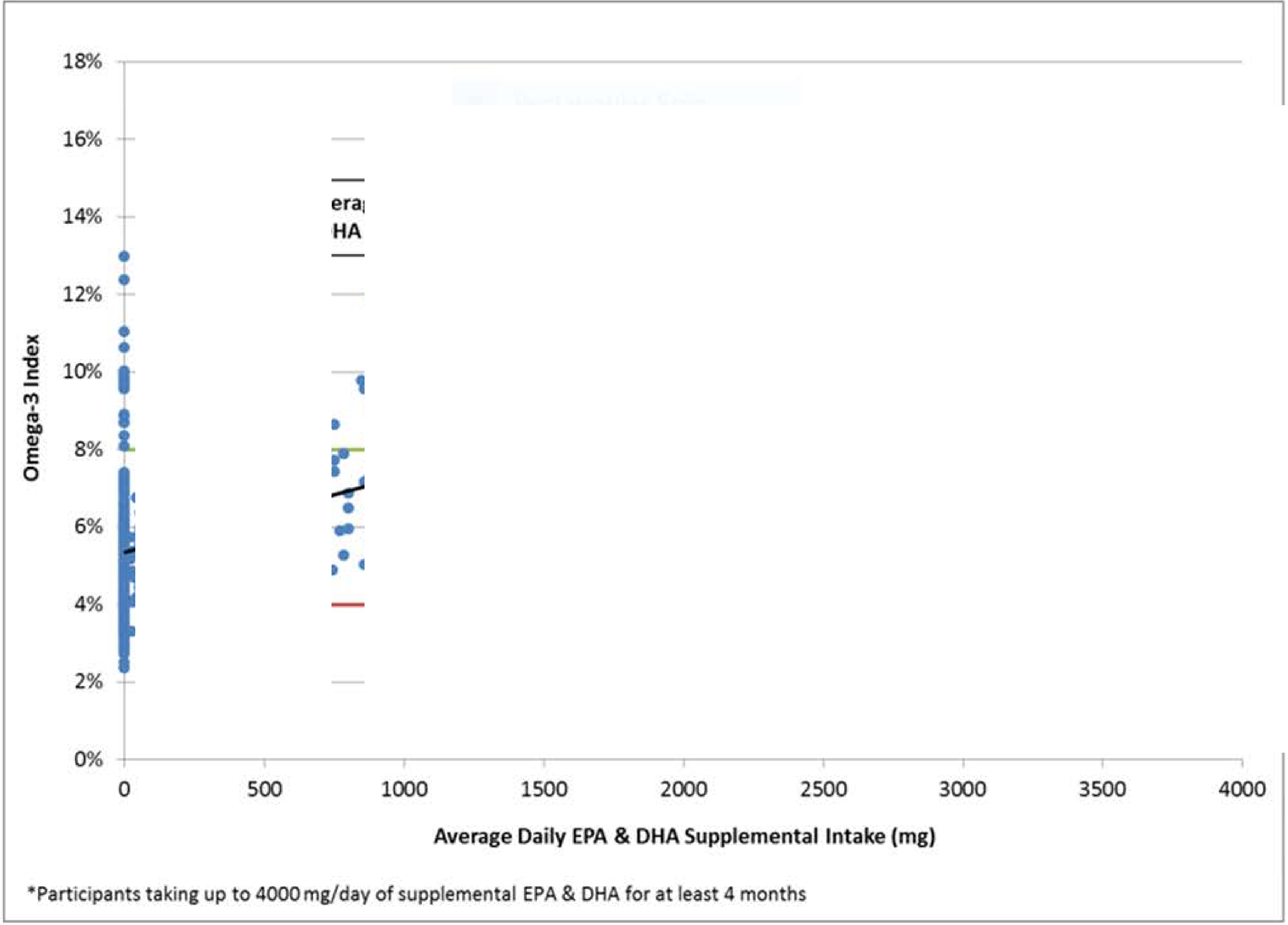
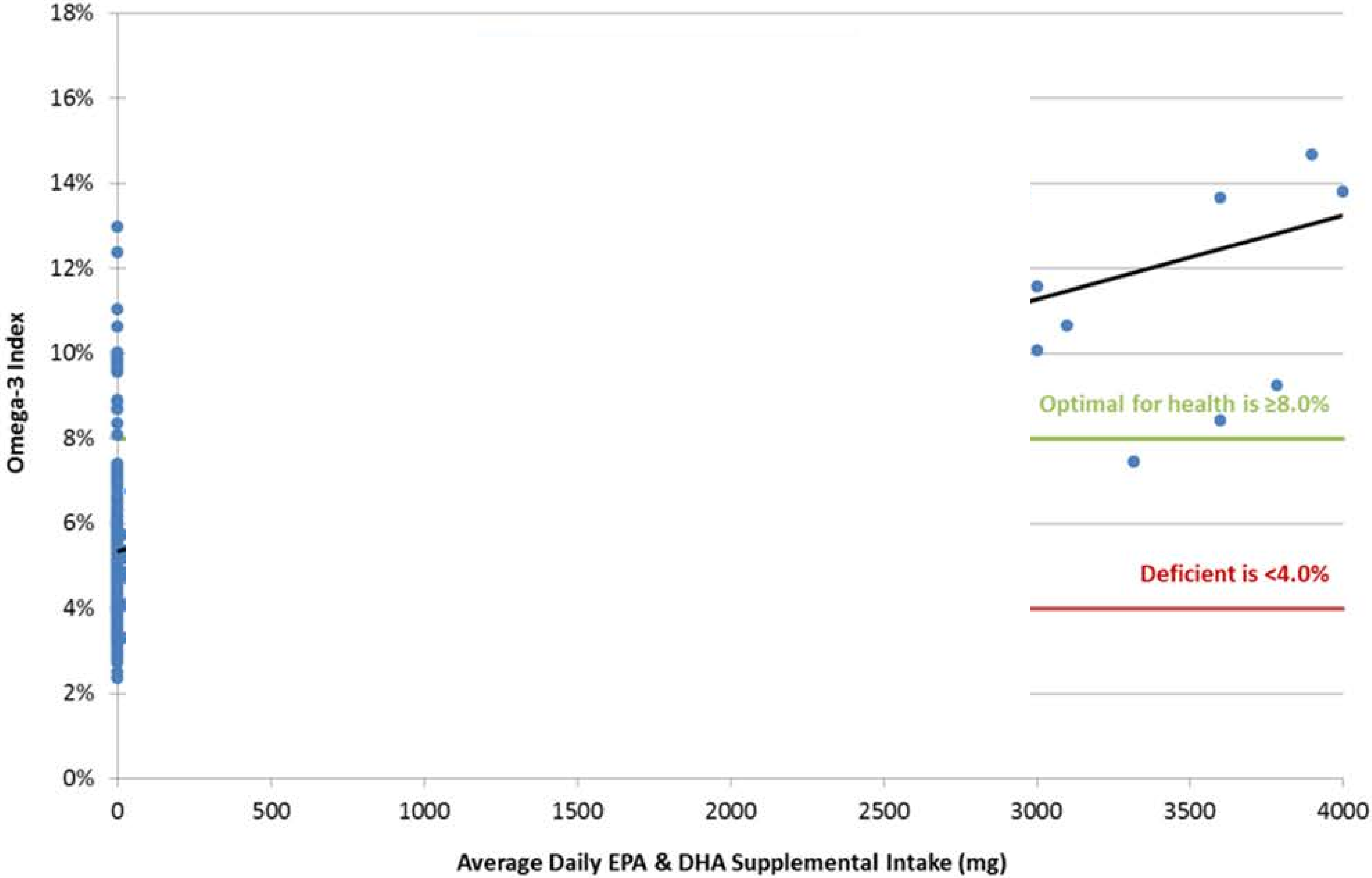


Figure 1© 2018 GrassrootsHealth

https://www.naturalproductsinsider.com/lipids/optimal-illusive-omega-3-level



*Participants taking up to 4000 mg/day of supplemental EPA & DHA for at least 4 months

Figure 1© 2018 GrassrootsHealth

https://www.naturalproductsinsider.com/lipids/optimal-illusive-omega-3-level

Spiegel entscheidend.

Weitaus am besten belegt: HS-Omega-3 Index

Individuell dosieren, um

Zielbereich HS-Omega-3 Index

8 – 11% zu erreichen.

Kardiologie

KHE

LURIC

LUdwigshafen RIsk and Cardiovascular Health Study

3316 Patienten zur Koronarangiographie überwiesen ins Ludwigshafener Herzzentrum 1997 – 2000

>20% Stenose im Angiogramm

Patienten genau charakterisiert, viele Biomarker gemessen

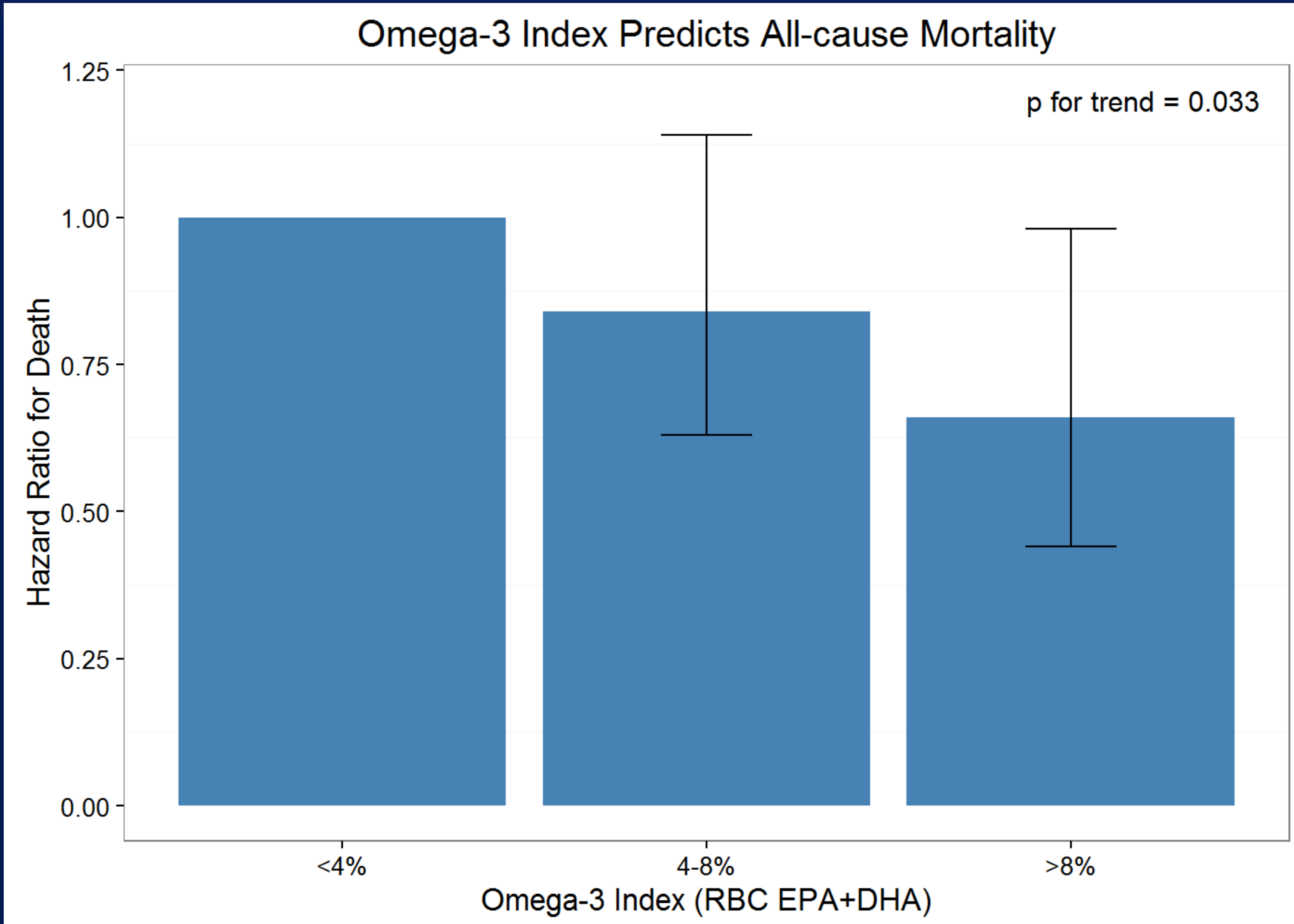
9.9 Jahre Follow-up

975 (29.9%) der Teilnehmer verstorben

- plötzlicher Herztod: 254 (7.8%)
- tödlicher Herzinfarkt: 104 (3.2%)
- Herzinsuffizienz: 148 (4.5%)
- Revaskularisation: 26 (0.8%)
- Schlaganfall: 60 (1.8%)
- andere KHE: 19 (0.6%)
- unbekannt: 19 (0.6%)

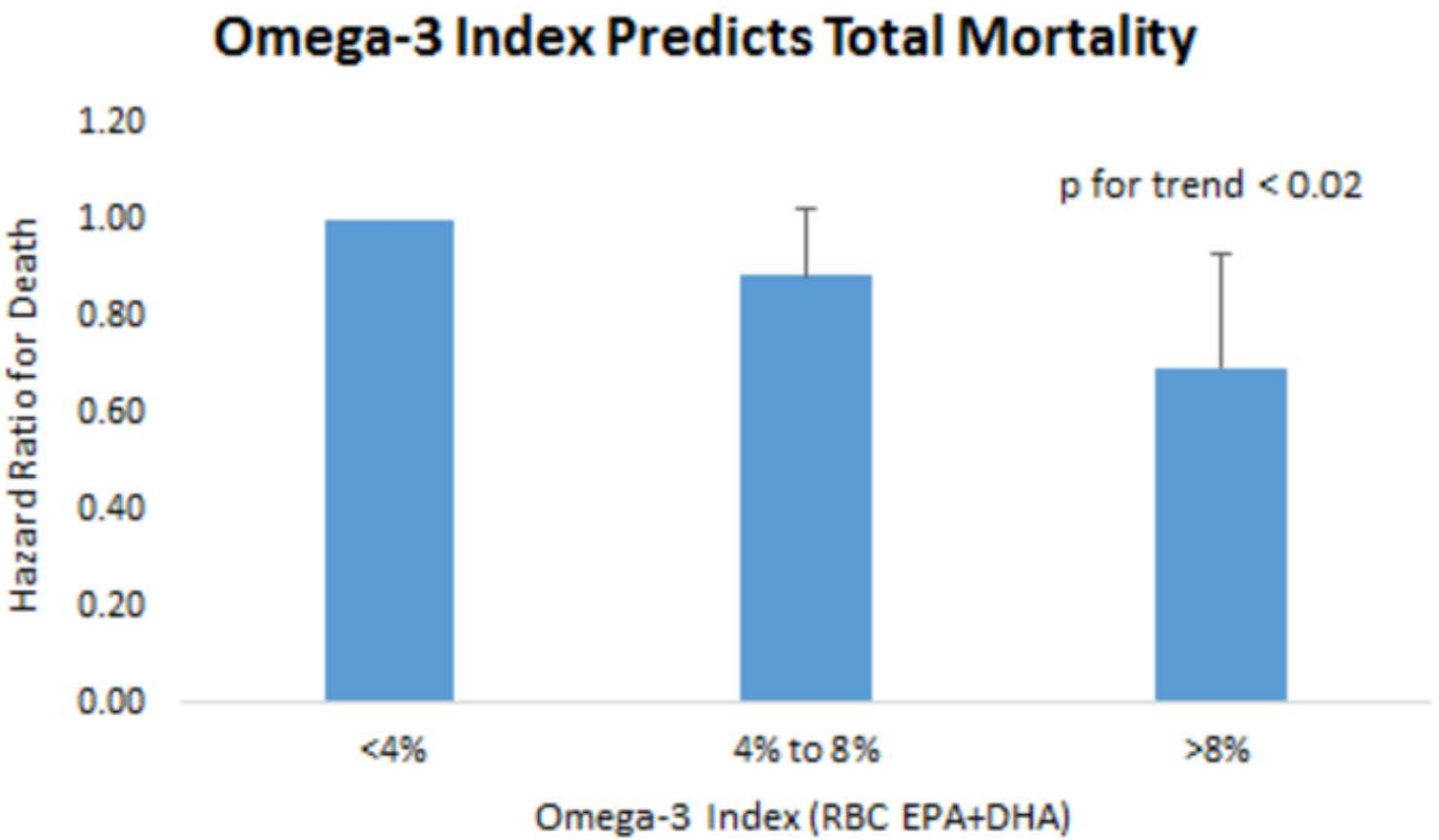
3259 Erythrozyten-Proben auf Fettsäuren analysiert

HS-Omega-3 Index und Risiko für Gesamtmortalität in LURIC



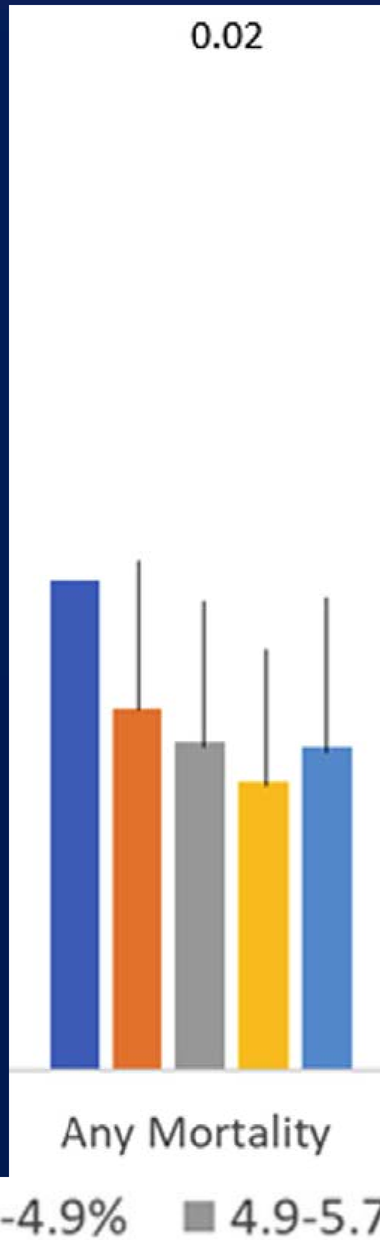
Kleber et al, Atherosclerosis 2016;252:157

Women's Health Initiative Memory Study: 6501 Frauen, Alter 65-80 Jahre, 15 Follow-up, 1851 (28,5%) verstorben



Harris et al, J Clin Lipidol 2017;11:250

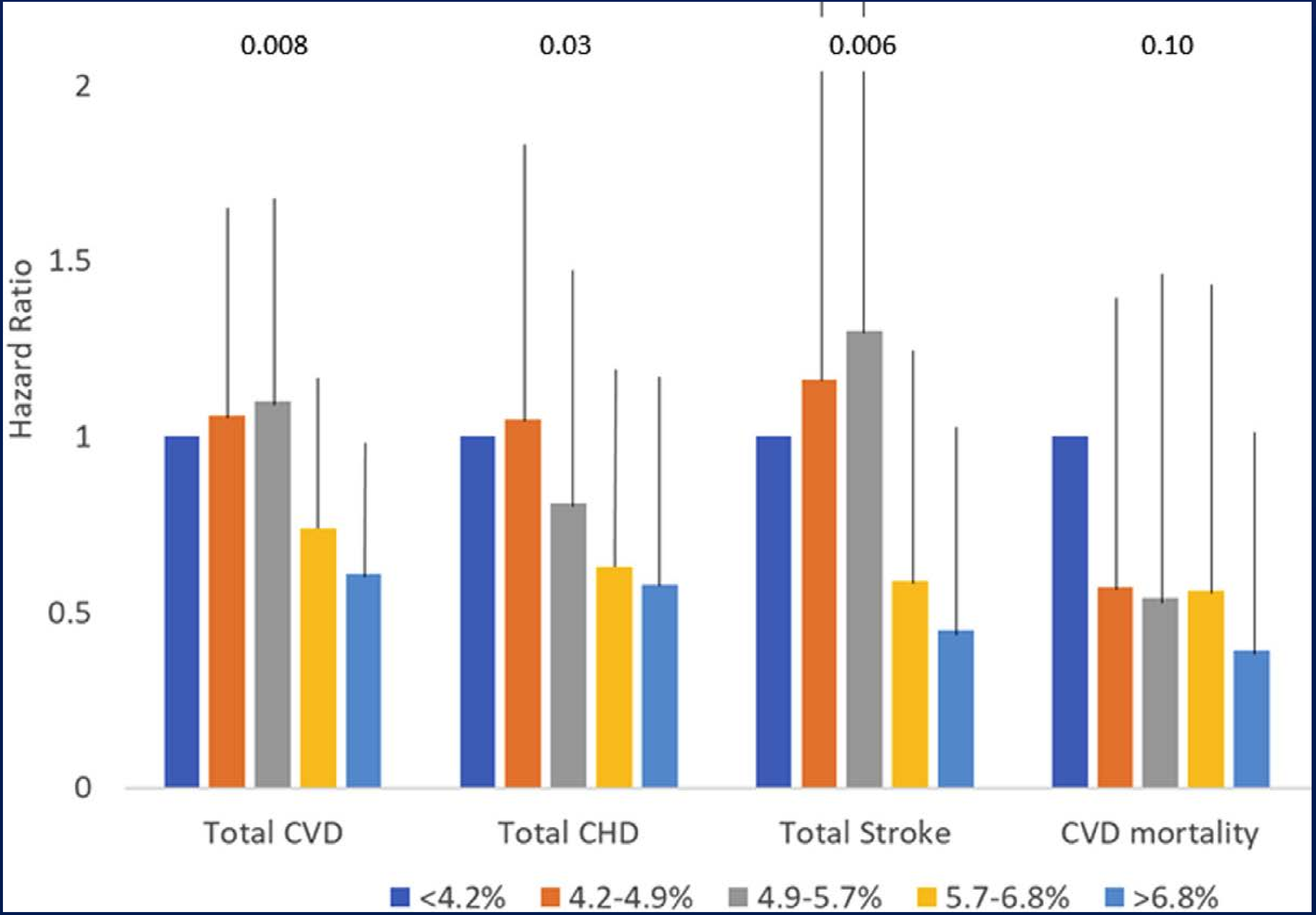
HS-Omega-3 Index und Gesamtmortalität in Framingham



Any Mortality	
1.0	
0.74 (0.53, 1.03)	
0.67 (0.47, 0.97)	Omega-3 Index
0.58 (0.41, 0.84)†	
0.65 (0.45, 0.94)	
.01*	
1.0	
0.73 (0.50, 1.05)	
0.72 (0.49, 1.06)	
0.91 (0.64, 1.31)	Cholesterin
0.96 (0.66, 1.40)	
.11	

Harris et al, J Clin Lipidol. 2018;12:718

Omega-3 Index und kardiovaskuläre Ereignisse in Framingham



Harris et al, J Clin Lipidol. 2018;12:718

HS-Omega-3 Index und kardiovaskuläre Ereignisse in Framingham

Table 4 Omega-3 Index and total cholesterol: Associations with risk for disease outcomes (n = 2500)

	Hazard ratios (95% CIs)				
	Total CVD	Total CHD	Total Stroke	CVD mortality	Any Mortality
Omega-3 Index[§]					
<4.2% (n = 506)	1.0	1.0	1.0	1.0	1.0
4.2%–4.9% (n = 500)	1.08 (0.70, 1.65)	1.06 (0.61, 1.85)	1.20 (0.63, 2.27)	0.65 (0.27, 1.54)	0.74 (0.53, 1.03)
4.9%–5.7% (n = 500)	1.11 (0.73, 1.68)	0.81 (0.44, 1.47)	1.32 (0.69, 2.50)	0.53 (0.19, 1.49)	***0.67 (0.47, 0.97)***
5.7%–6.8% (n = 502)	0.74 (0.47, 1.17)	0.63 (0.34, 1.19)	0.61 (0.29, 1.27)	0.58 (0.22, 1.55)	***0.58 (0.41, 0.84)***[†]
>6.8% (n = 489)	0.63 (0.39, 1.01)	0.59 (0.30, 1.17)	0.47 (0.21, 1.06)	0.44 (0.16, 1.91)	***0.65 (0.45, 0.94)***
P-value from linear trend test[‖]	***.009***[†]	***.03***[*]	***.006***[†]	.19	***.01***[*]
Total cholesterol[§]					
<154 (n = 406)	1.0	1.00	1.0	1.0	1.0
154–175 (n = 491)	1.03 (0.69, 1.56)	1.02 (0.55, 1.89)	0.88 (0.47, 1.66)	1.22 (0.53, 2.77)	0.73 (0.50, 1.05)
176–194 (n = 520)	0.95 (0.62, 1.45)	1.29 (0.71, 2.37)	0.63 (0.31, 1.27)	0.67 (0.26, 1.77)	0.72 (0.49, 1.06)
195–218 (n = 551)	0.89 (0.56, 1.39)	1.01 (0.53, 1.92)	0.69 (0.32, 1.40)	1.07 (0.30, 3.79)	0.91 (0.64, 1.31)
>218 (n = 530)	1.09 (0.66, 1.80)	1.59 (0.81, 3.11)	0.89 (0.41, 1.93)	0.31 (0.72, 1.34)	0.96 (0.66, 1.40)
P-value from linear trend test[‖]	.99	.26	.50	.27	.11

CVD, cardiovascular disease; CHD, coronary heart disease; CI, confidence interval.

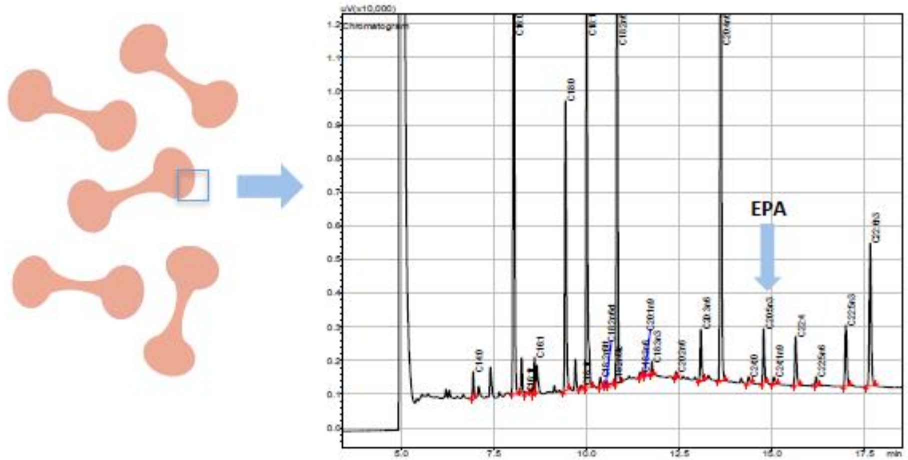
[*] $P < .05$; [†] $P < .01$; [‡] $P < .001$.

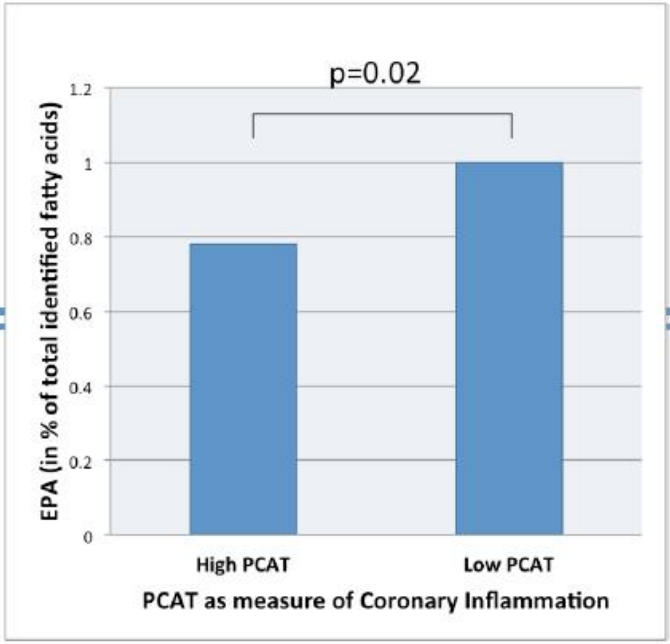
§Hazard ratios presented here were adjusted for all variables in Table 1 with the addition of grouped total cholesterol (and removing total cholesterol to high-density lipoprotein cholesterol ratio) and the grouped Omega-3 Index.

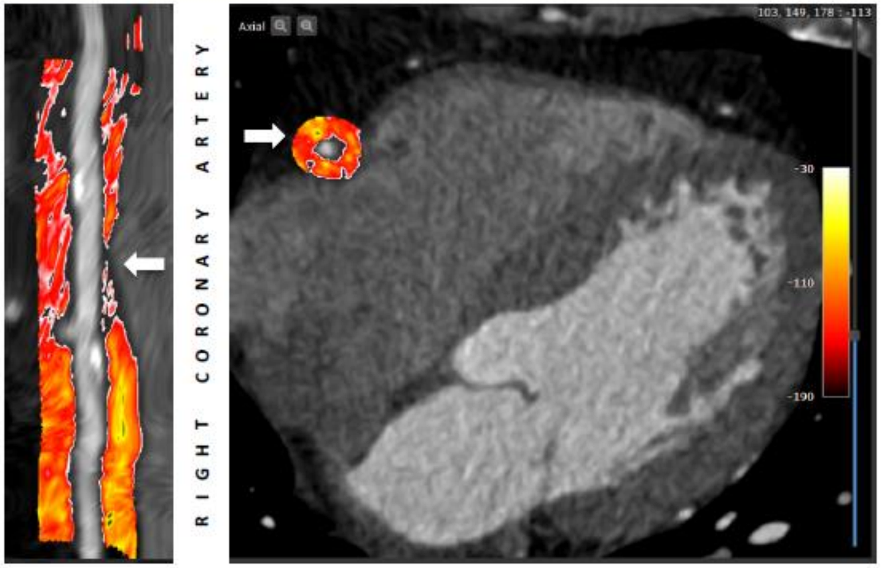
‖Linear trend test models were fit for both the Omega-3 Index and TC simultaneously, after adjusting for variables as described in footnote "§".

Harris et al, J Clin Lipidol. 2018;12:718

Erythrocyte Membrane - Fatty Acid Analysis







Pericoronary Adipose Tissue (PCAT) Attenuation Analysis

Bittner et al, Atherosclerosis. 2020;12:71

Den Omega-3 Index erhöhen –

Effekte auf Surrogatparameter

Herzfrequenz	▼	(Harris et al Am J Cardiol 2006; 98:1393-5)
Herzfrequenz-Variabilität	▲	(Carney et al Psychosom Med 2010;72:748)
Blutdruck	▼	(Dewell et al J Nutr Res 2011;141:2166; Skulas-Ray et al Ann Behav Med 2012;44:301
Plättchenfunktion	▼	(Larsson et al, Thromb Haemost 2008;100: 634 Harris et al, Lipids 2008;43:805)
Inflammator. Biomarker	▼	(Duda et al Cardiovasc Res 2009;81:319 Dewell et al J Nutrition 2011;141:2166 Blocket al World J Cardiovasc Dis2012;2:14
Triglyceride	▼	(Skulas-Ray Am J Clin Nutr 2011;93:243, Schuchardt et al PLEFA 2011;85:381 Shearer et al J Lipid Res. 2012;53:2429)
„Small dense“ LDL	▼	(Maki et al J Clin Lipidol 2011;5:483)
„Large bouyant“ LDL	▲	(Maki et al J Clin Lipidol 2011;5:483)

Meta-Analyse Interventionsstudien mit CV Risikofaktoren

Table 2 Pooled effects of eicosapentaenoic acid and/or docosahexaenoic acid supplementation on risk factors associated with cardiovascular disease

Outcome	Number of studies	Effect size (95% CI)	*P*-value*	Test of heterogeneity† *Q*-value	*P*-value	I^2
Total cholesterol (mmol L^{-1})	108	−0.051 (−0.166, 0.064)	0.387	1440.211	0.0001	92.57
LDL-cholesterol (mmol L^{-1})	100	0.150 (0.058, 0.243)	0.001	1270.903	0.0001	92.21
HDL-cholesterol (mmol L^{-1})	110	0.039 (0.024, 0.054)	0.0001	204.740	0.0001	46.76
Triglycerides (mmol L^{-1})	110	−0.368 (−0.427, −0.309)	0.0001	508.295	0.0001	80.34
Systolic blood pressure (mmHg)	50	−2.195 (−3.172, −1.217)	0.0001	109.009	0.0001	56.88
Diastolic blood pressure (mmHg)	50	−1.08 (−1.716, −0.444)	0.0001	123.045	0.0001	61.80
Heart rate (bpm)	26	−1.37 (−2.415, −0.325)	0.01	68.661	0.0001	63.58
C-reactive protein (mg L^{-1})	20	−0.343 (−0.454, −0.232)	0.0001	926.382	0.0001	97.95
Tumor necrosis factor α (pg mL^{-1})	11	−0.277 (−0.661, 0.108)	0.159	21.771	0.016	54.07
Fibrinogen (g L^{-1})	14	−0.032 (−0.146, 0.082)	0.584	21.229	0.069	38.76
Platelet count (× 10^3)	9	−1.110 (−11.367, 9.146)	0.832	13.865	0.085	42.30
Soluble intercellular adhesion molecule-1 (ng mL^{-1})	9	−0.054 (−0.219, 0.108)	0.515	20.084	0.010	60.16
Soluble vascular cell adhesion molecule-1 (ng mL^{-1})	9	−8.112 (−23.507, 7.283)	0.302	10.449	0.235	23.44
Flow-mediated dilation (%)	6	1.460 (−0.475, 3.395)	0.139	28.657	0.0001	82.55

*For meta-analysis: $P < 0.05$ was considered statistically significant.

†For heterogeneity assessment: $P < 0.1$ for *Q* test or I^2 >50% was considered to indicate significant heterogeneity across the studies.

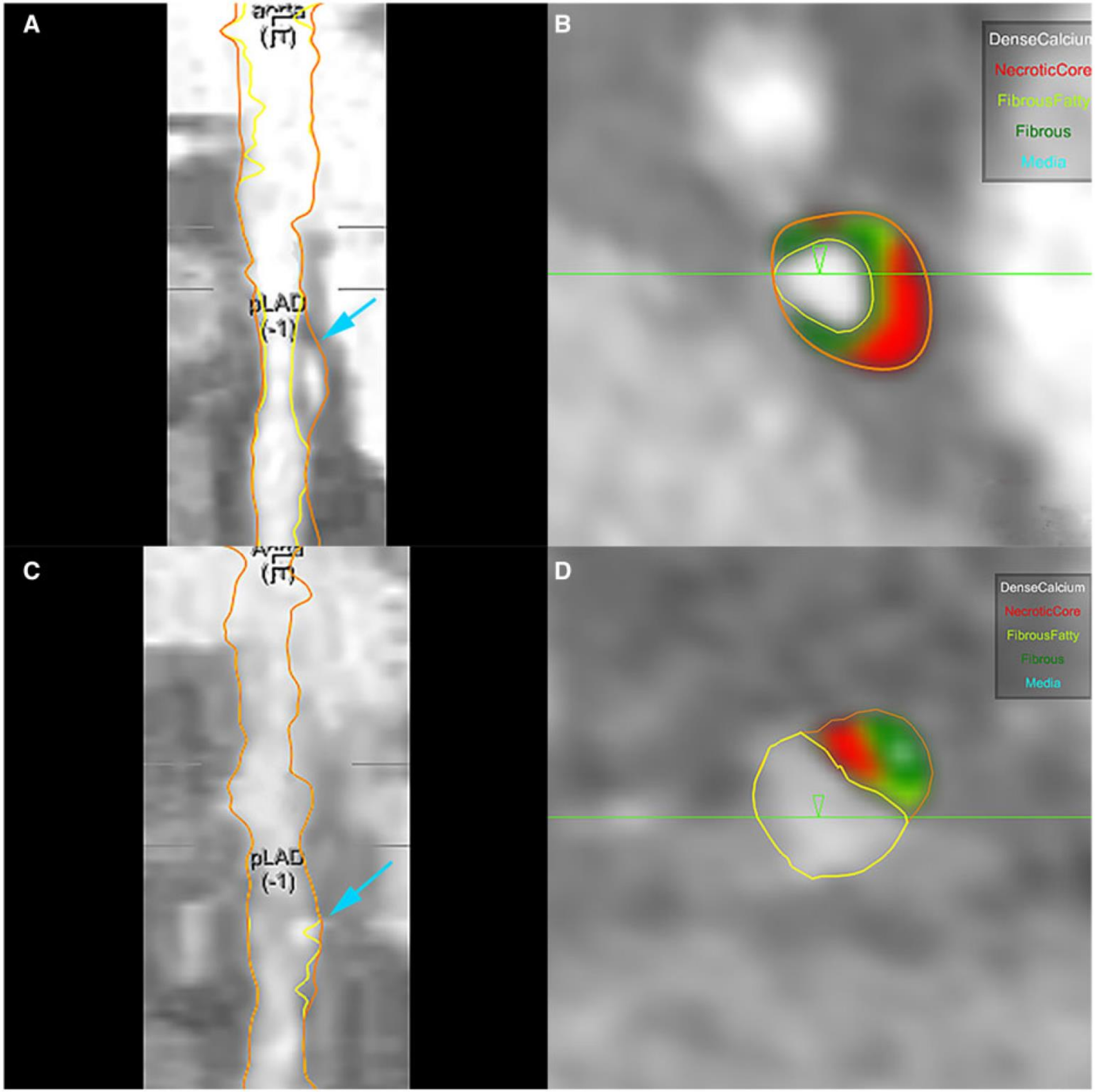
CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Abumweis et al J Human Nutr Diet 2018;31:67

Den Omega-3 Index erhöhen –

Effekte auf Intermediärparameter

Koronarläsionen	▼	(von Schacky, Ann Int Med 1999;130:554)
LV-Remodeling	▲	(Heydari et al Circulation 2016;134:378)



Budoff et al, Eur Heart J. 2020;e-pub Aug 29

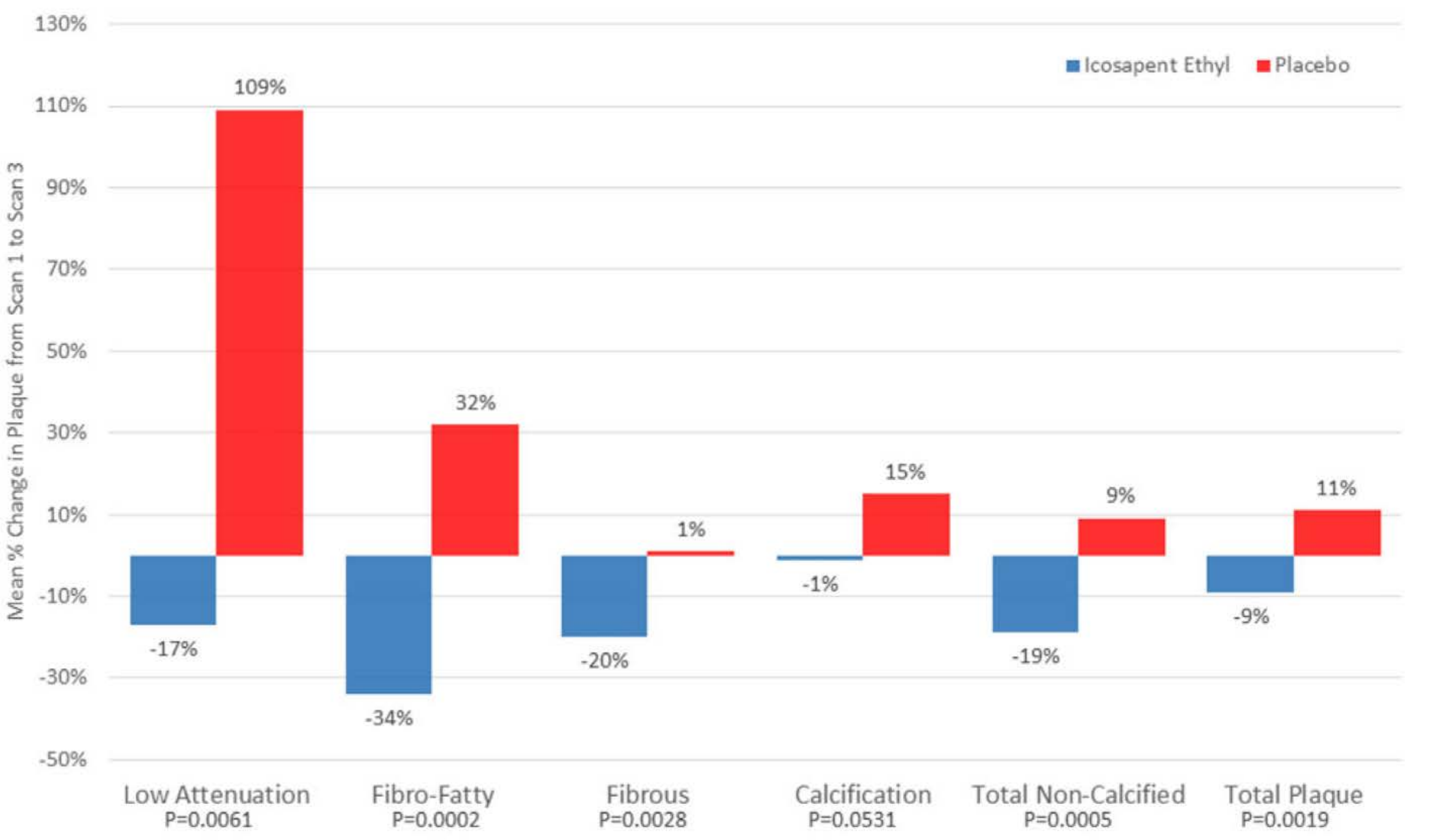
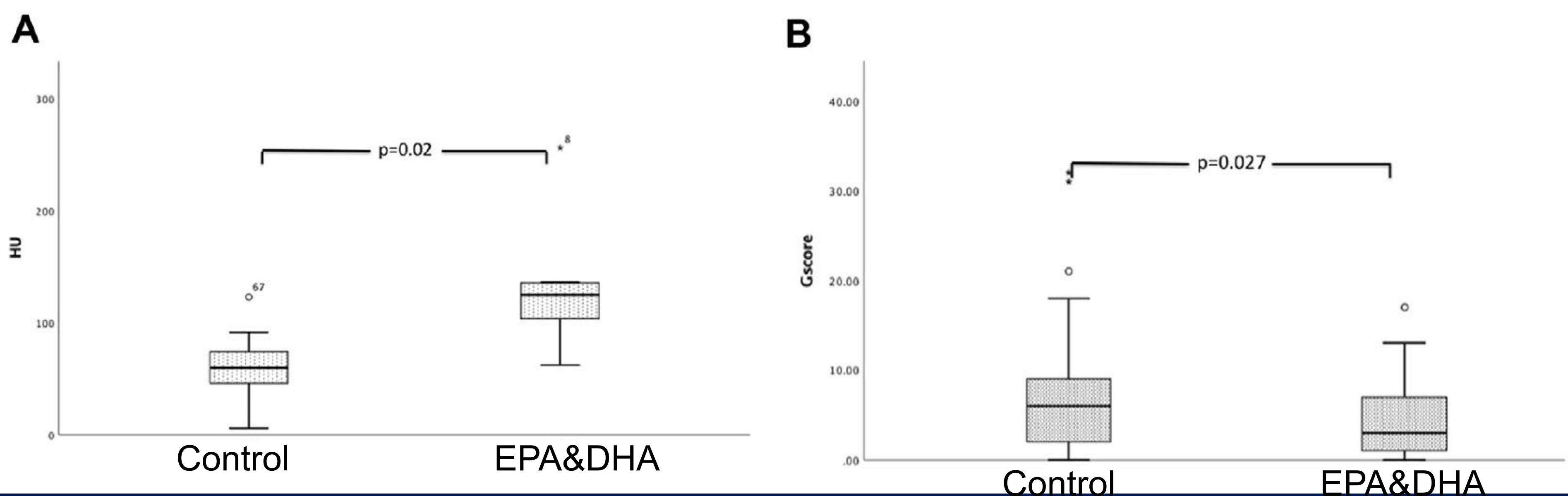


Figure 1 Mean plaque progression for each type of plaque composition measured on cardiovascular CT for the icosapent ethyl and placebo groups (icosapent ethyl group, *n* = 31 and placebo group, *n* = 37) after multivariable adjustment. Univariable analysis and multiple linear regression were used to examine the change in plaque levels between the cohorts. Multivariable models were adjusted by baseline plaque, age, sex, diabetes status, hypertension, and baseline triglyceride levels. All statistical analyses report two-sided *P*-values for the outcomes. A *P*-value <0.048 was considered significant for the outcomes.

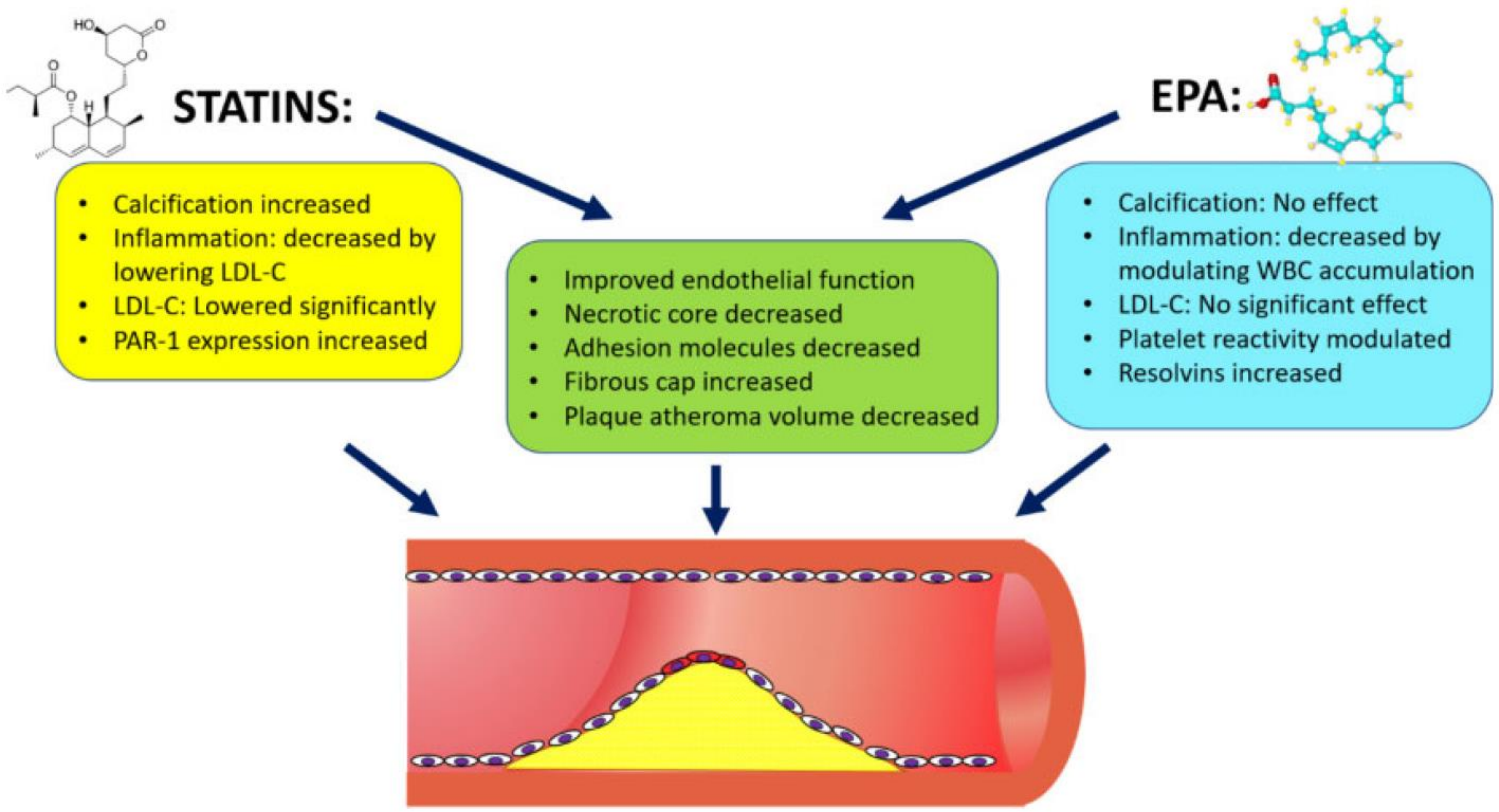
Budoff et al, Eur Heart J. 2020;e-pub Aug 29

1 g EPA&DHA in 53 Patienten, 53 Kontrollen, retrospektiv 3 Jahre Coronar-CT zu Kalk (Houndsfield Units, HU) und G-Score (weiche Läsionen)



Feuchtner et al, Clin Nutr 2020; Jul 22;S0261-5614(20)30381-2

Statine, EPA&DHA und Koronarläsionen



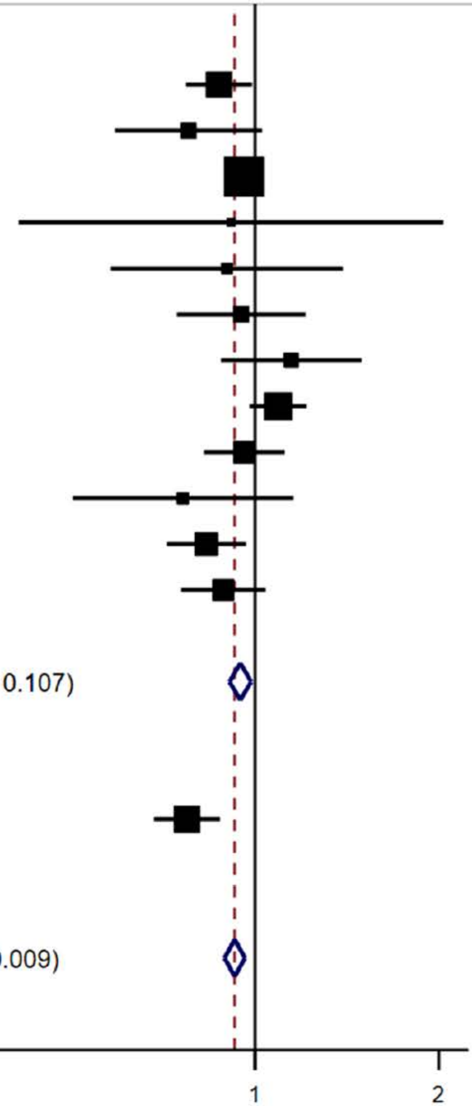
Tokgozoglu & Catapano Eur Heart J 2020; e-pub Nov 3

Klinische Endpunkte

c

Total CHD

Study ID	RR (95% CI)	Events, Treatment	Events, Control	% Weight
Excluding REDUCE-IT				
GISSI-P	0.87 (0.77, 0.99)	424/5666	485/5658	11.08
JELIS	0.78 (0.59, 1.03)	88/9326	113/9319	2.58
GISSI-HF	0.96 (0.90, 1.02)	1309/3494	1360/3481	31.11
DOIT	0.91 (0.41, 2.04)	11/282	12/281	0.27
SU.FOL.OM3	0.90 (0.58, 1.39)	37/1253	41/1248	0.94
Alpha Omega	0.95 (0.74, 1.21)	120/2404	128/2433	2.91
OMEGA	1.15 (0.88, 1.49)	112/1919	96/1885	2.21
ORIGIN	1.09 (0.98, 1.21)	635/6281	580/6255	13.27
R&P	0.96 (0.83, 1.12)	310/6239	324/6266	7.38
AREDS-2	0.76 (0.50, 1.16)	39/2147	49/2056	1.14
VITAL	0.83 (0.72, 0.97)	308/12933	370/12938	8.45
ASCEND	0.89 (0.76, 1.04)	275/7740	310/7740	7.08
Subtotal (I-squared = 35.4%, p = 0.107)	**0.95 (0.91, 0.99) p=0.008**	**3668/59684**	**3868/59560**	**88.42**
REDUCE-IT	0.77 (0.68, 0.88) p<0.001	392/4089	507/4090	11.58
Overall (I-squared = 54.7%, p = 0.009)	**0.93 (0.89, 0.96) p<0.001**	**4060/63773**	**4375/63650**	**100.00**



Hu et al, JAHA 2019;8:e013543

Warum gibt es positive Studien?

DART, Diet and Reinfarction Trial, Zweijährige Ernährungsstudie, randomisiert, Monozentrisch, faktorielles Design in 2033 Pat kurz nach erstem MI

2 x fetter Fisch pro Woche

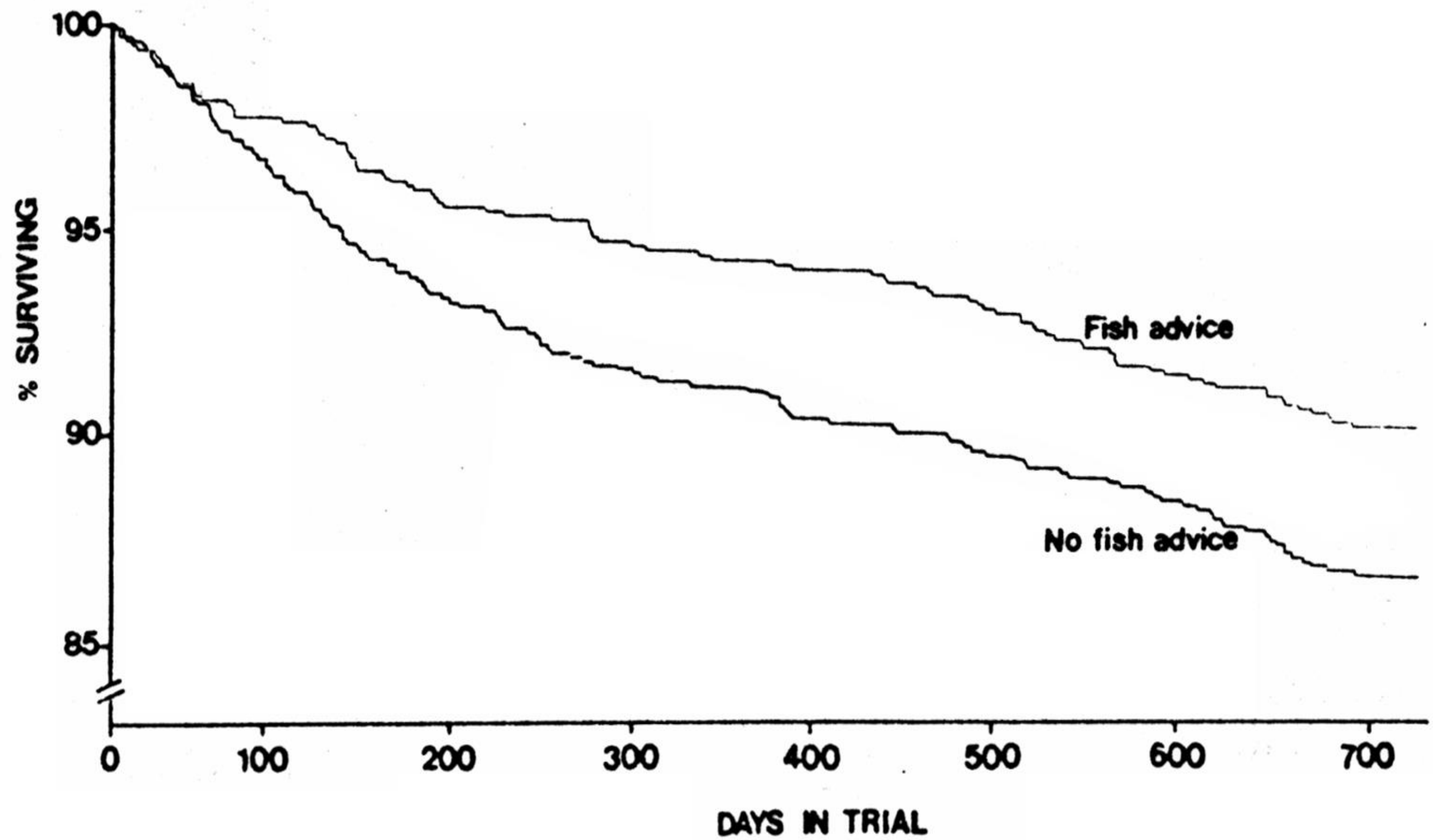
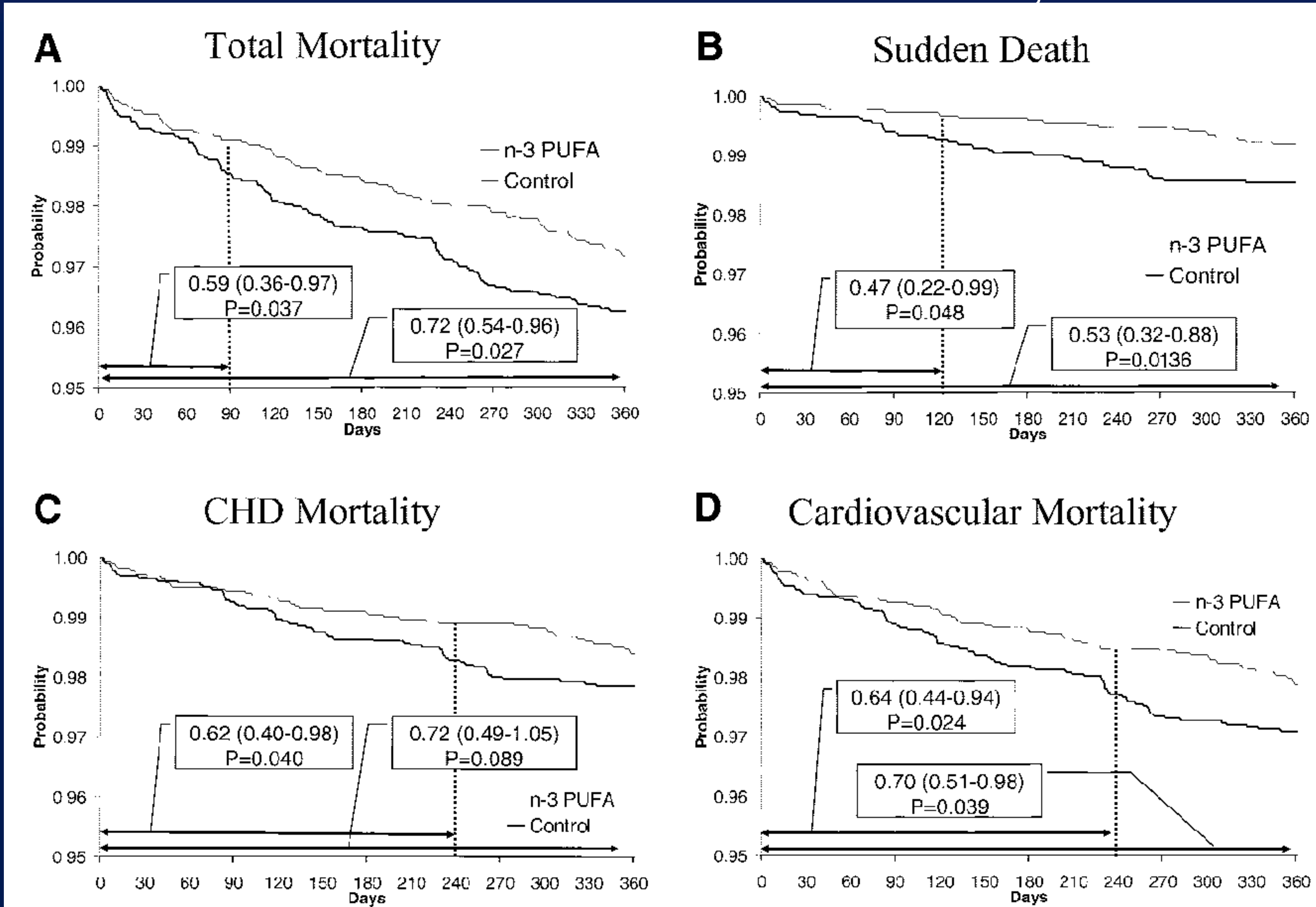


Fig 2—Survival: fish advice.

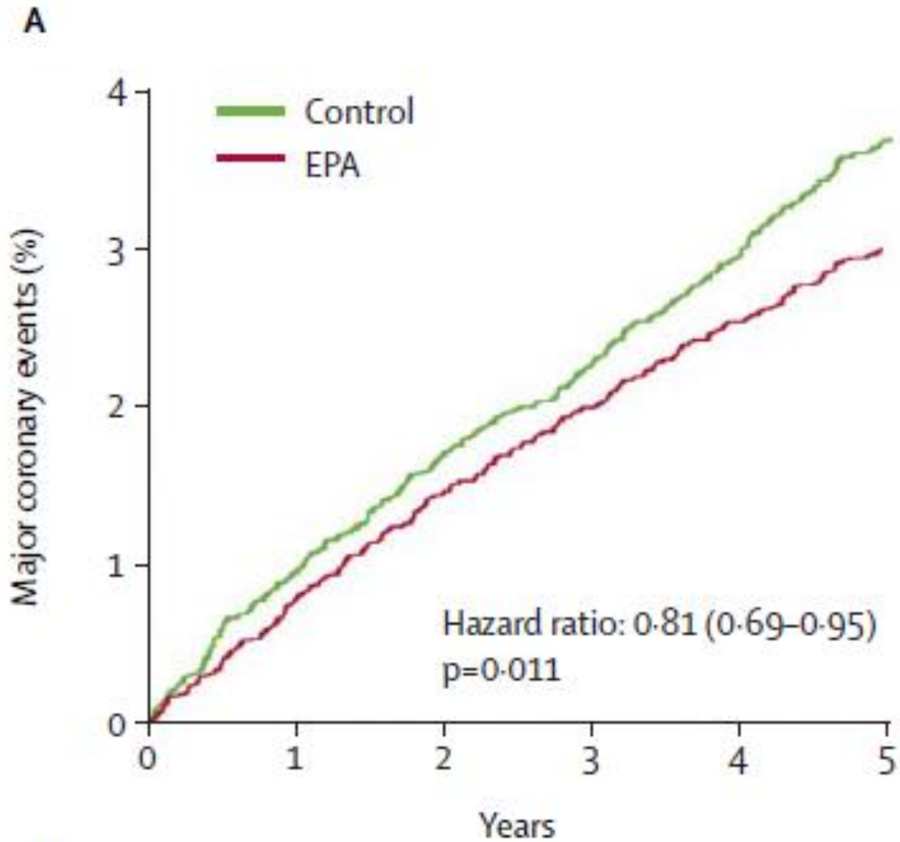
Burr et al, Lancet 1989; II:554:757

Total C 154, n-3 111



Marchioli et al Circulation 2002;105:1897-1903

JELIS: RCT in 19 466 Hyperlipidämiker, ± kardiovask. Erkrankung, davon 9326 1,8 g / Tag EPA
9319 Kontrollen, Mittlerer Follow-up 4,6 Jahre.



Numbers at risk

	0	1	2	3	4	5
Control group	9319	8931	8671	8433	8192	7958
Treatment group	9326	8929	8658	8389	8153	7924

Primärer Endpunkt: koronares Ereignis, tödlicher und nicht-tödlicher Herzinfarkt, andere wie Revaskularisation

Yokoyama et al, Lancet 2007;369:1090

REDUCE-IT

RCT mit 8179 Teilnehmer mit CV Risiko, alle Statin

4 g EPA-Ethylester vs. Placebo

4.9 Jahre mittlere Studiendauer

Primärer Endpunkt: MACE

CV Tod, nicht-tödlicher Myokardinfarkt,

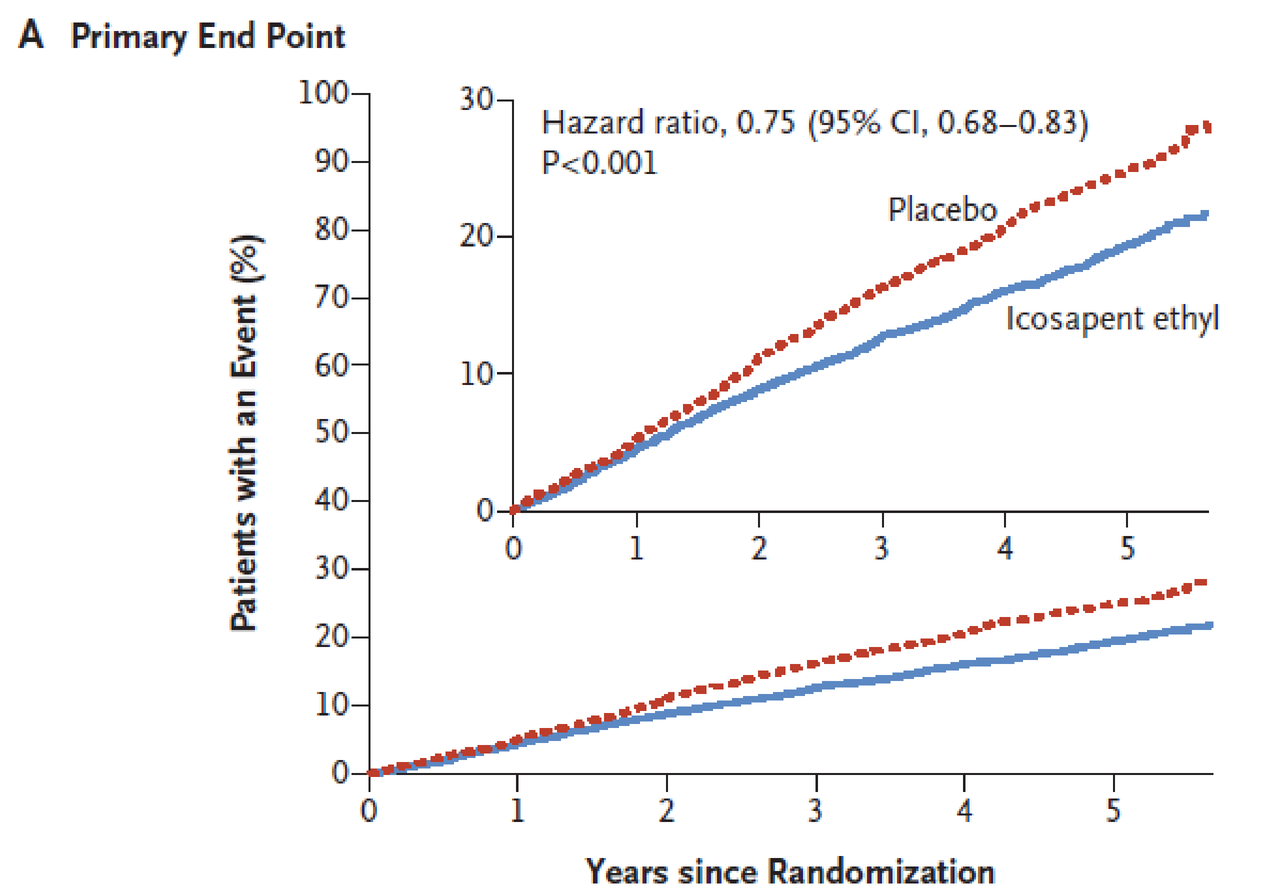
nicht-tödlicher Schlaganfall

koronare Revask, instabile AP mit KH-Aufnahme

Serumspiegel knapp versechsfacht!

Bhatt et al, N Engl J Med 2018, e-pub Nov 10

REDUCE-IT



No. at Risk	0	1	2	3	4	5
Placebo	4090	3743	3327	2807	2347	1358
Icosapent ethyl	4089	3787	3431	2951	2503	1430

25% relative Risikoreduktion, p<0.001

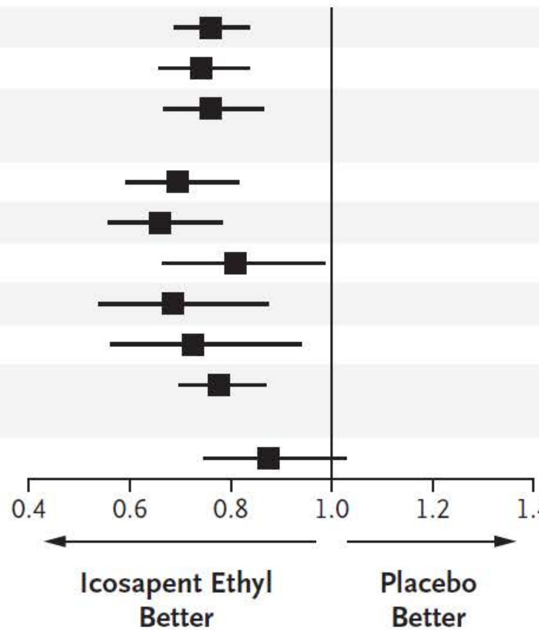
Bhatt et al, N Engl J Med 2018, e-pub Nov 10

REDUCE-IT

RCT mit 8179 Teilnehmer mit CV Risiko, alle Statin

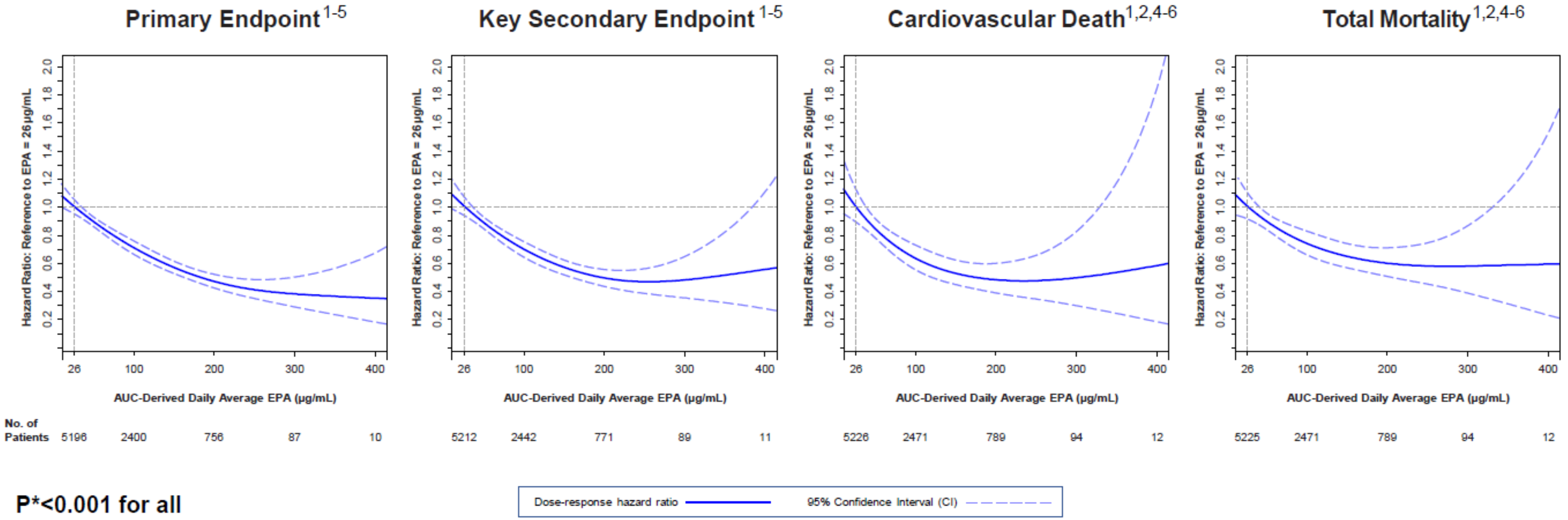
4 g EPA-Ethylester vs. Placebo, 4.9 Jahre mittlere Studiendauer

End Point	Icosapent Ethyl (N=4089)	Placebo (N=4090)	Hazard Ratio (95% CI)	P Value for Interaction
	no. of patients with event (%)			
Primary composite	705 (17.2)	901 (22.0)	0.75 (0.68–0.83)	<0.001
Key secondary composite	459 (11.2)	606 (14.8)	0.74 (0.65–0.83)	<0.001
Cardiovascular death or nonfatal myocardial infarction	392 (9.6)	507 (12.4)	0.75 (0.66–0.86)	<0.001
Fatal or nonfatal myocardial infarction	250 (6.1)	355 (8.7)	0.69 (0.58–0.81)	<0.001
Urgent or emergency revascularization	216 (5.3)	321 (7.8)	0.65 (0.55–0.78)	<0.001
Cardiovascular death	174 (4.3)	213 (5.2)	0.80 (0.66–0.98)	0.03
Hospitalization for unstable angina	108 (2.6)	157 (3.8)	0.68 (0.53–0.87)	0.002
Fatal or nonfatal stroke	98 (2.4)	134 (3.3)	0.72 (0.55–0.93)	0.01
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	549 (13.4)	690 (16.9)	0.77 (0.69–0.86)	<0.001
Death from any cause	274 (6.7)	310 (7.6)	0.87 (0.74–1.02)	—



Bhatt et al, N Engl J Med 2018, e-pub Nov 10

Primary and Key Secondary Composite Endpoints, Cardiovascular Death, and Total Mortality by On-Treatment Serum EPA



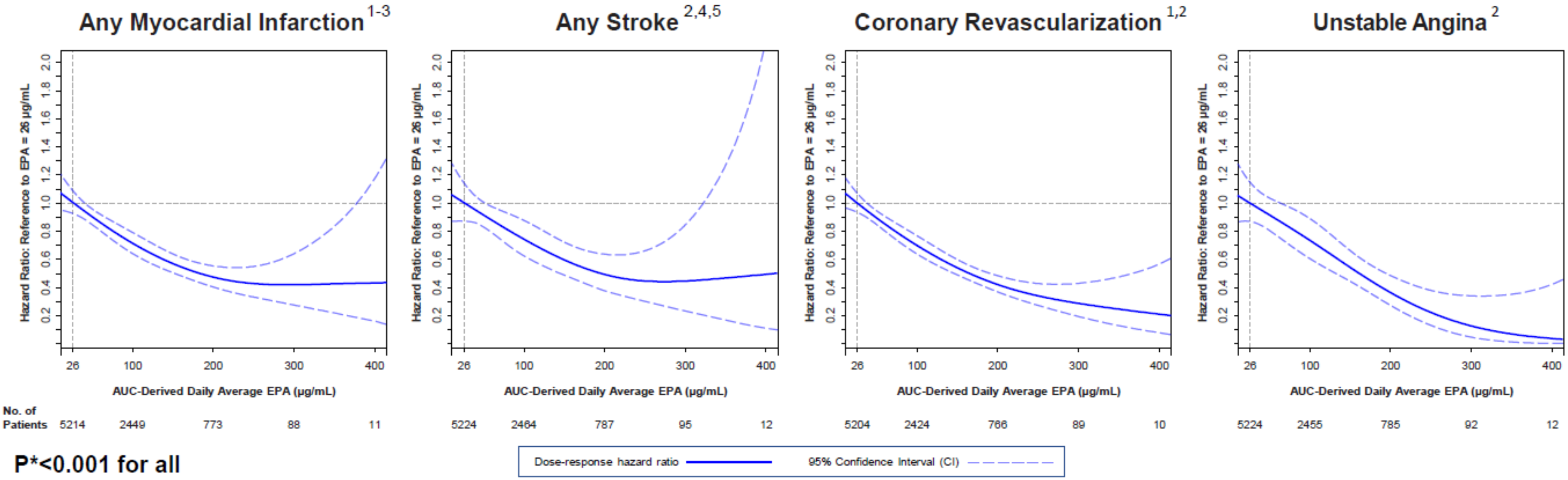
P*<0.001 for all

Note: Area under the curve (AUC)-derived daily average serum EPA (µg/mL) is the daily average of all available post baseline EPA measurements prior to the event. Dose-response hazard ratio (solid line) and 95% CI (dotted lines) are estimated from the Cox proportional hazard model with a spline term for EPA and adjustment for randomization factors and statin compliance[1], age[2], sex[3], baseline diabetes[4], hsCRP[5], treatment compliance[6].

*P value is <0.001 for both non-linear trend and for regression slope.

Bhatt DL. ACC/WCC 2020, Chicago (virtual).

Dose-Response of Hazard Ratio (95% CI) Any Myocardial Infarction, Any Stroke, Coronary Revascularization, Unstable Angina by On-Treatment Serum EPA



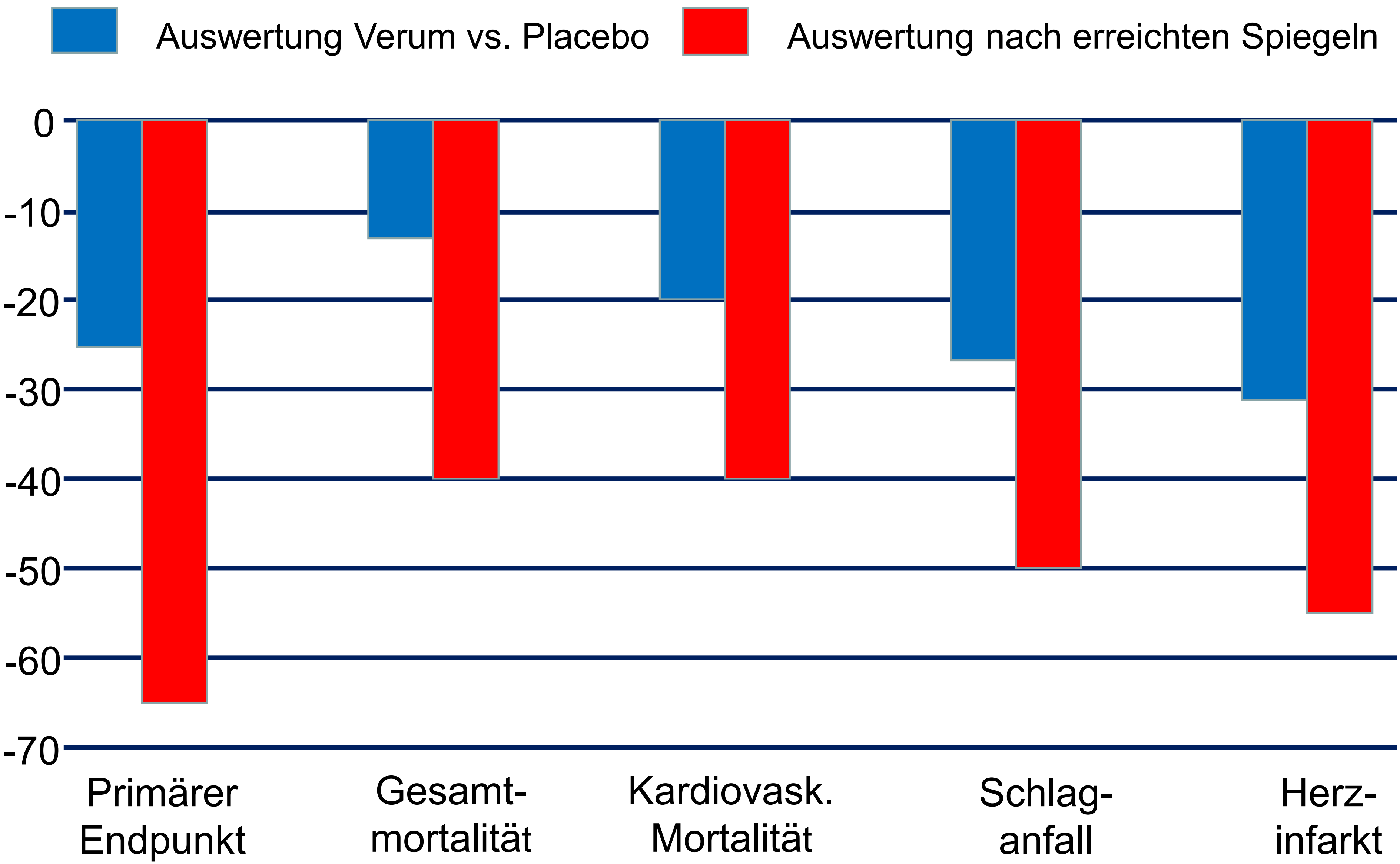
P*<0.001 for all

Note: Area under the curve (AUC) -derived daily average serum EPA (µg/mL) is the daily average of all available post baseline EPA measurements prior to the event. Dose-response hazard ratio (solid line) and 95% CI (dotted lines) are estimated from the Cox proportional hazard model with a spline term for EPA and adjustment for randomization factors and sex[1], baseline diabetes[2], hsCRP[3], statin compliance[4], age[5].

***P value is <0.001 for both non-linear trend and for regression slope.**

Bhatt DL. ACC/WCC 2020, Chicago (virtual).

REDUCE-IT: Spiegel entscheiden über Ereignisse



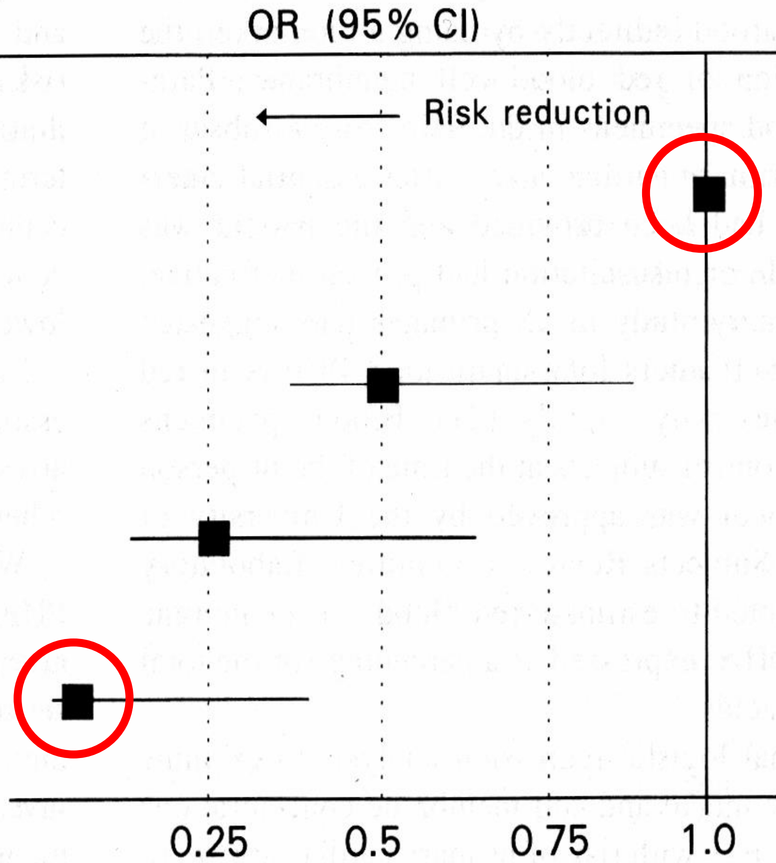
Was bedeutet das für die Studienmethoden?

Interventionsstudien ohne Messung von Ausgangsspiegeln
und ohne Messungen von Spiegeln die während der Studie erreicht werden, sind nicht sonderlich aussagekräftig.
Sind aber immer in allen Cochrane-Analysen zu allen Themen
Positive Ergebnisse von Interventionsstudien,
die keine Spiegel gemessen haben, beruhen auf:
Guter Bioverfügbarkeit (Fisch: DART, oder Emulsion)
Hoher Dosis (REDUCE-It, JELIS)
Kollektiv mit niedrigen Ausgangsspiegeln regional / Grunderkrankung
(GISSI-P, GISSI-HF), Ernährungsform usw.

Meta-Analysen können nicht besser sein als die Interventionsstudien
auf denen sie beruhen.

Plötzlicher Herztod

n-3 PUFA quartile	Percentage of total fatty acids	Case subjects (*n*=82)	Control subjects (*n*=108)
1	3.3	36	25
2	4.3	21	24
3	5.0	15	26
4	6.5	10	33



Siscovick D et al, Am J Clin Nutr 2000; 71:208S

Gruppo Italiano per lo Studio della Sopravvivenza nell´Infarto miocardico

3.5 Jahre randomisiert, offen, multi-zentrisch, faktorielles Design, 11324 Pat kurz nach erstem MI

0.85 g ω-3 Fettsäuren / Tag

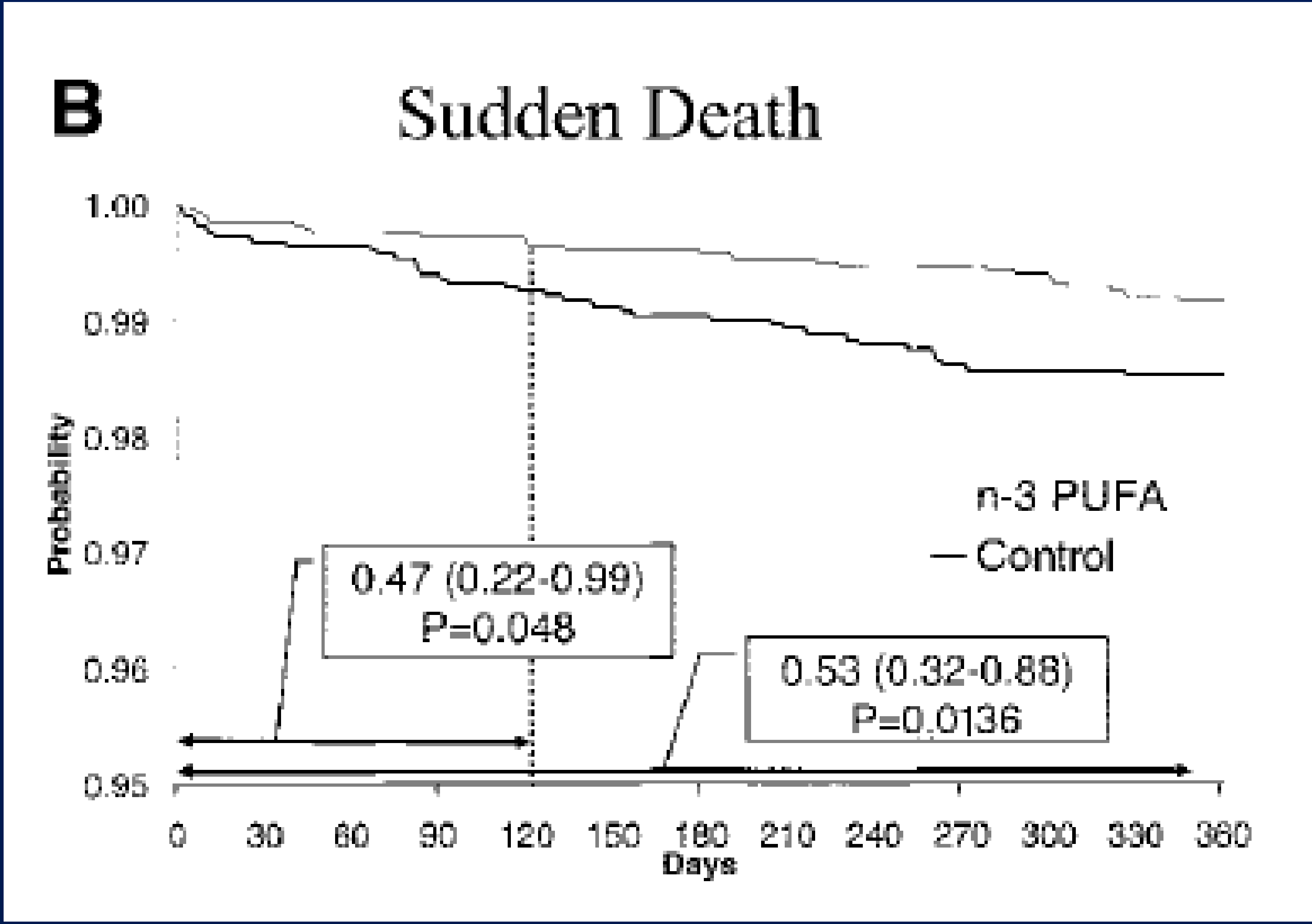
300 mg Vitamin E / Tag

Kombination

weder noch

GISSI-P, Lancet 1999; 354:447

Ca. 50 % Reduktion plötzlicher Herztod in GISSI-P

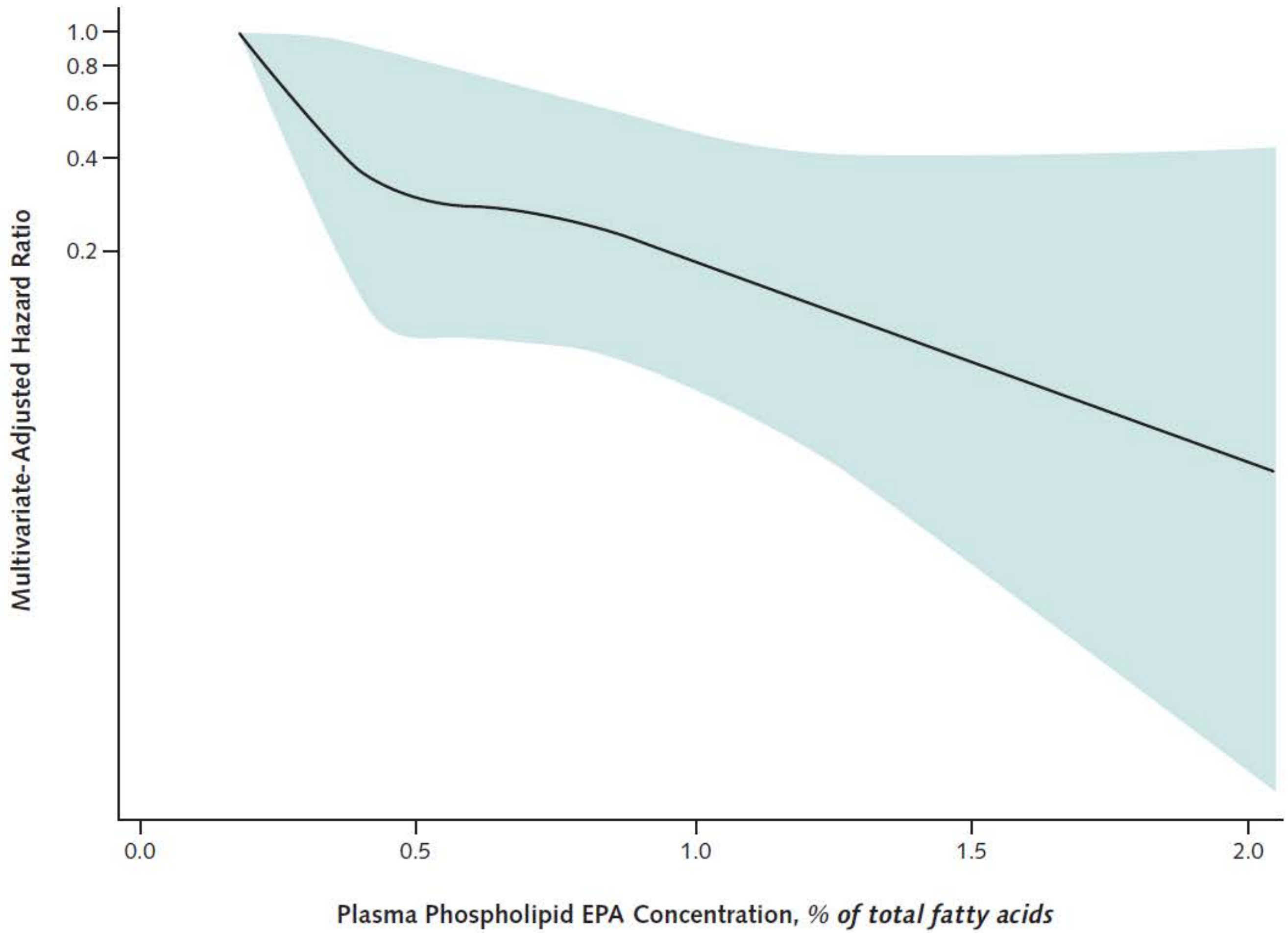


Marchioli et al Circulation 2002;105:1897

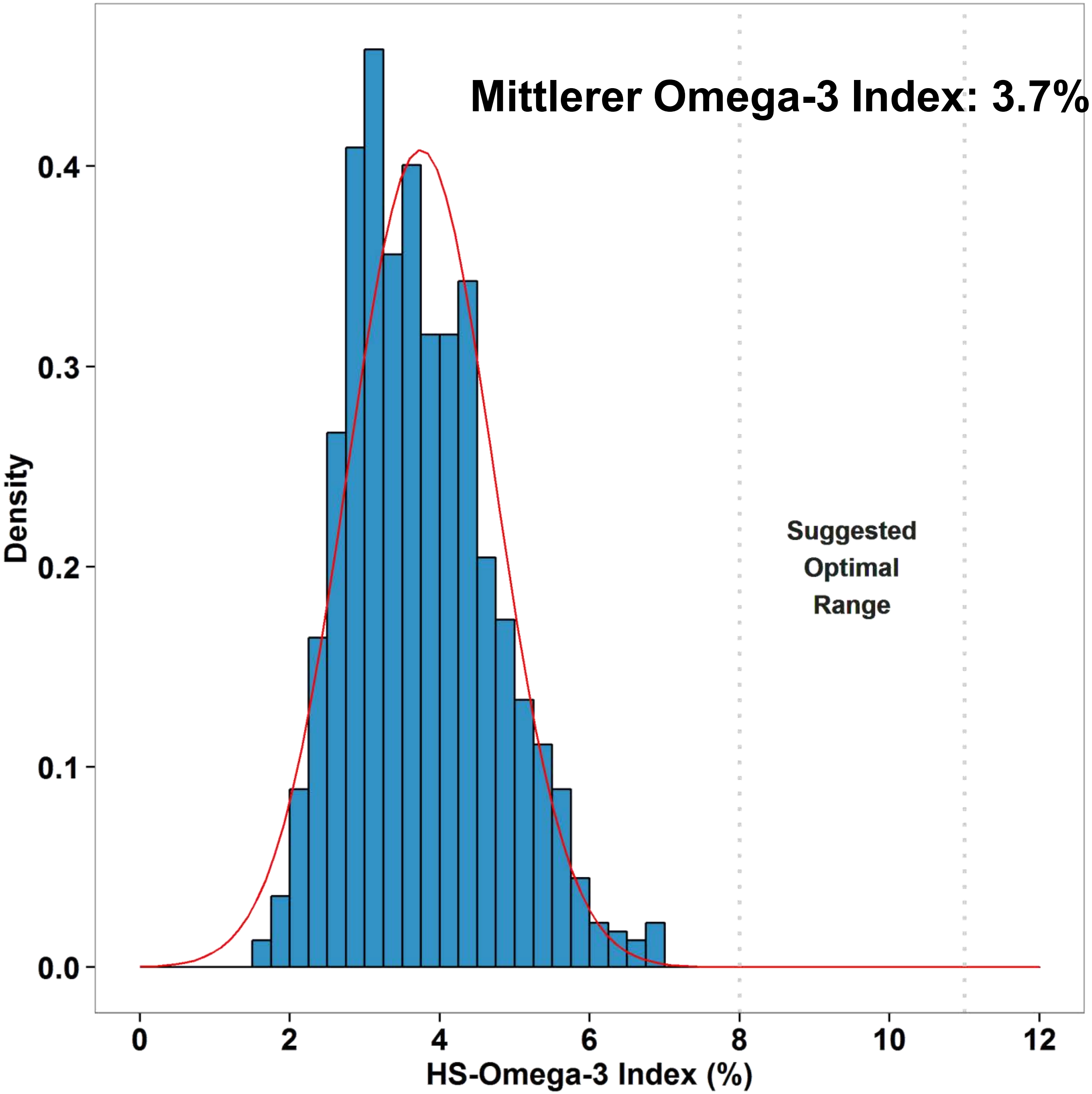
Herzinsuffizienz

Cardiovasc Health Study: Spätere Entwicklung Herzinsuffizienz
2763 kardial Gesunde, 10 Jahre Beobachtung, 555 Fälle von CHF

Figure. **Nonparametric multivariate-adjusted relationship between plasma phospholipid EPA concentrations and incidence of CHF.**



Mozaffarian et al Ann Int Med 2011;155:160



Mittlerer Omega-3 Index: 3.7%
Density
0.4
0.3
0.2
0.1
0.0
Suggested
Optimal
Range
0
2
4
6
8
10
12
HS-Omega-3 Index (%)

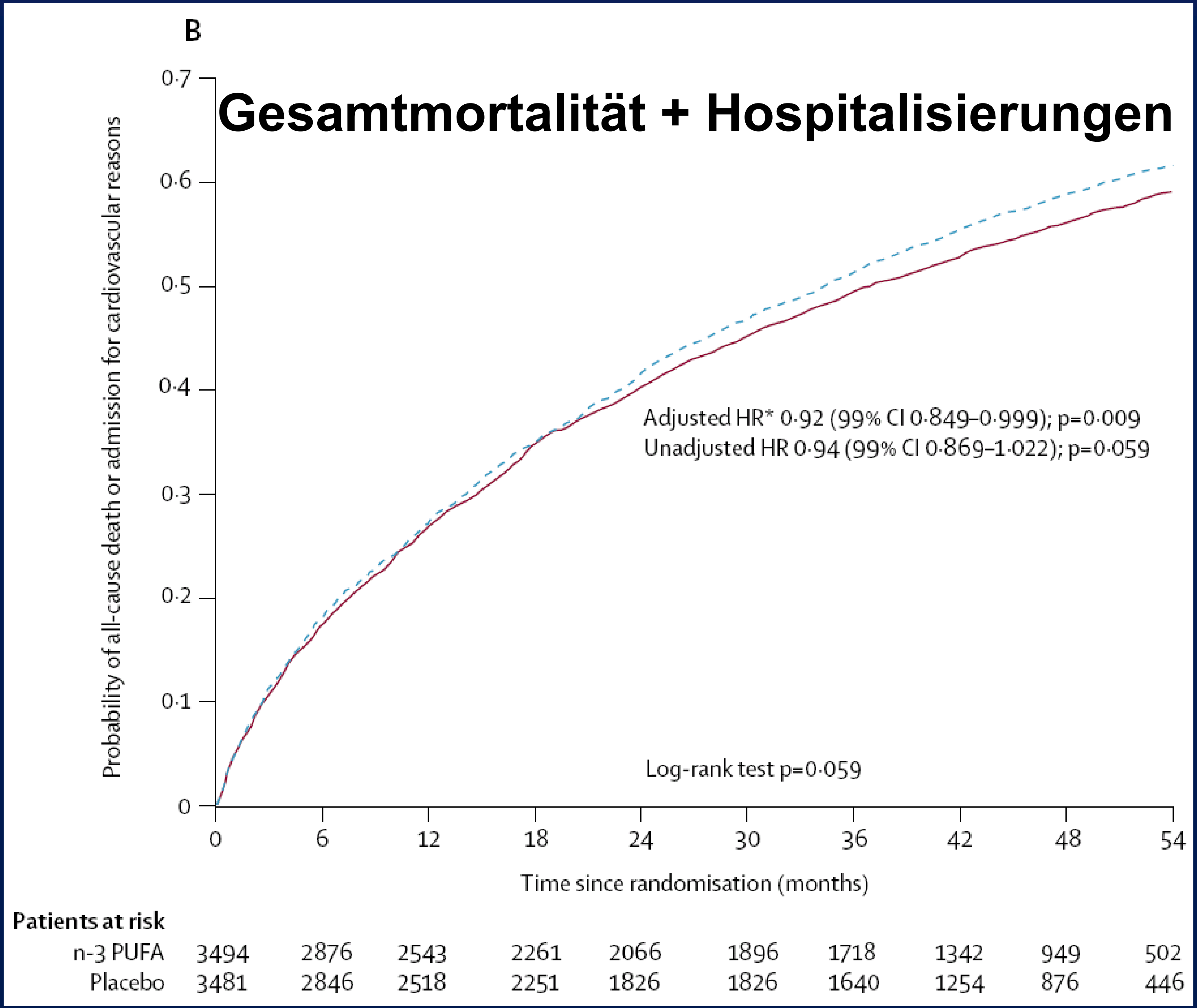
GISSI-HF: Omega-3 Index

	Baseline	3 Monate	
Placebo	4,73±1,70	4,81±1,49	
Verum	4,75±1,68	6,73±1,93	p<0.0001

Noch deutlich unter Zielbereich 8 – 11%

Harris et al, Nutr Res 2016;36:989

GISSI-HF: Primärer Endpunkt



GISSI-HF, Lancet 2008,372:1231

Zusammenfassung Kardiologie

Ein niedriger HS-Omega-3 Index korreliert mit

- erhöhter Mortalität
- Myokardinfarkten
- plötzlichem Herztod
- Schlaganfällen
- Herzinsuffizienz

Erhöhen des HS-Omega-3 Index reduziert

- Mortalität und Morbidität an den genannten Erkrankungen

Optimal: Zielbereich HS-Omega-3 Index: 8 – 11%

Sicherheit und Verträglichkeit

JELIS: RCT in 19 466 Hyperlipidämiker, ± kardiovask. Erkrankung, davon 9326 1,8 g / Tag EPA in Japan
9319 Kontrollen, Mittlerer Follow-up 4,6 Jahre.

	Control (n=9319)	EPA (n=9326)	p value
Common adverse experiences			
Pain (joint pain, lumbar pain, muscle pain)	180 (2·0%)	144 (1·6%)	0·04
Gastrointestinal disturbance (nausea, diarrhoea, epigastric discomfort)	155 (1·7%)	352 (3·8%)	<0·0001
Skin abnormality (eruption, itching, exanthema, eczema)	65 (0·7%)	160 (1·7%)	<0·0001
Haemorrhage (cerebral, fundal, epistaxis, subcutaneous)	60 (0·6%)	105 (1·1%)	0·0006
REDUCE-IT Blutungen (mittl. FU 4,6 Jahre) :	2,1%	2,7%	

JELIS, Yokoyama et al 2007;369:1090, Bhatt et al, N Engl J Med 2018, e-pub Nov 10

HS-Omega-3 Index erhöhbar durch erhöhte Zufuhr.

EPA+DHA bis 5 g / Tag (EFSA)

bzw. 3 g / Tag (FDA)

Sicher.

Verträglichkeit und Bioverfügbarkeit maximal,

wenn mit Hauptmahlzeit aufgenommen.

HS-Omega-3 Index >16% vermeiden

Defizit?

Health Reports

Omega-3 Index of Canadian adults

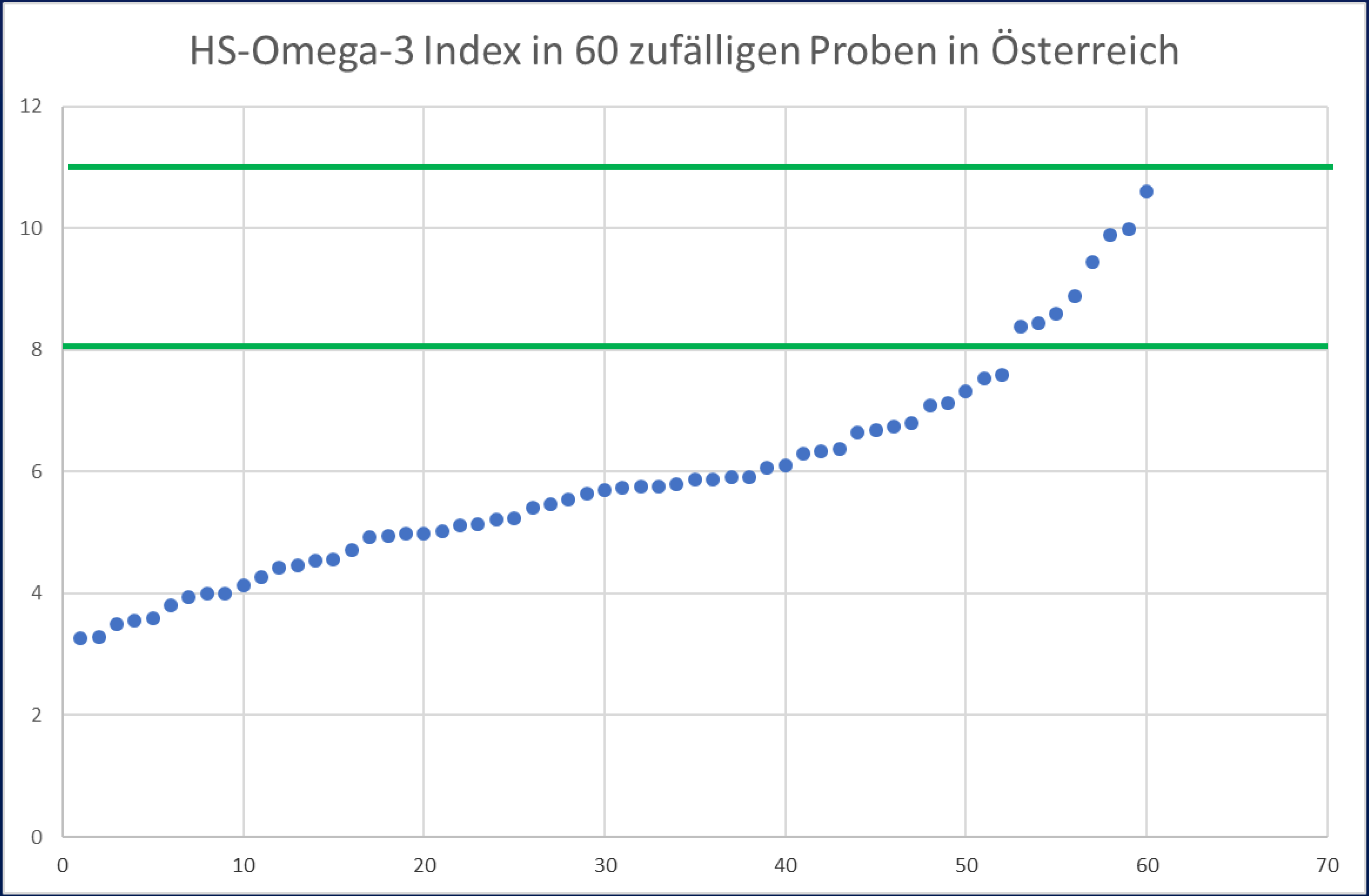
4.5%

by Kellie Langlois and Walisundera M. N. Ratnayake

Release date: November 18, 2015

Statistics Canada Statistique Canada

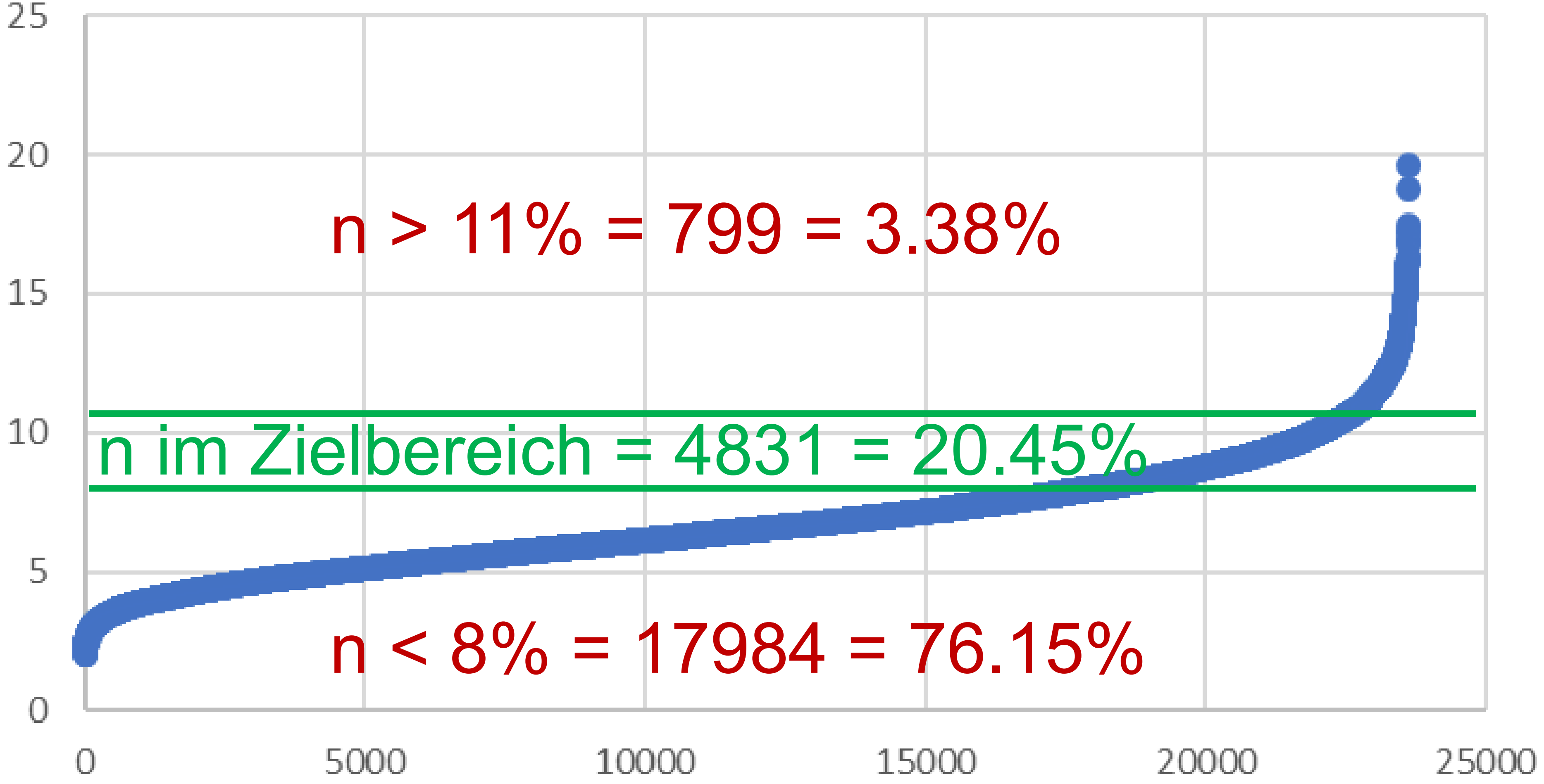
Canada



Mittelwert 5,88±1,74%, 8 (13%) im Zielbereich

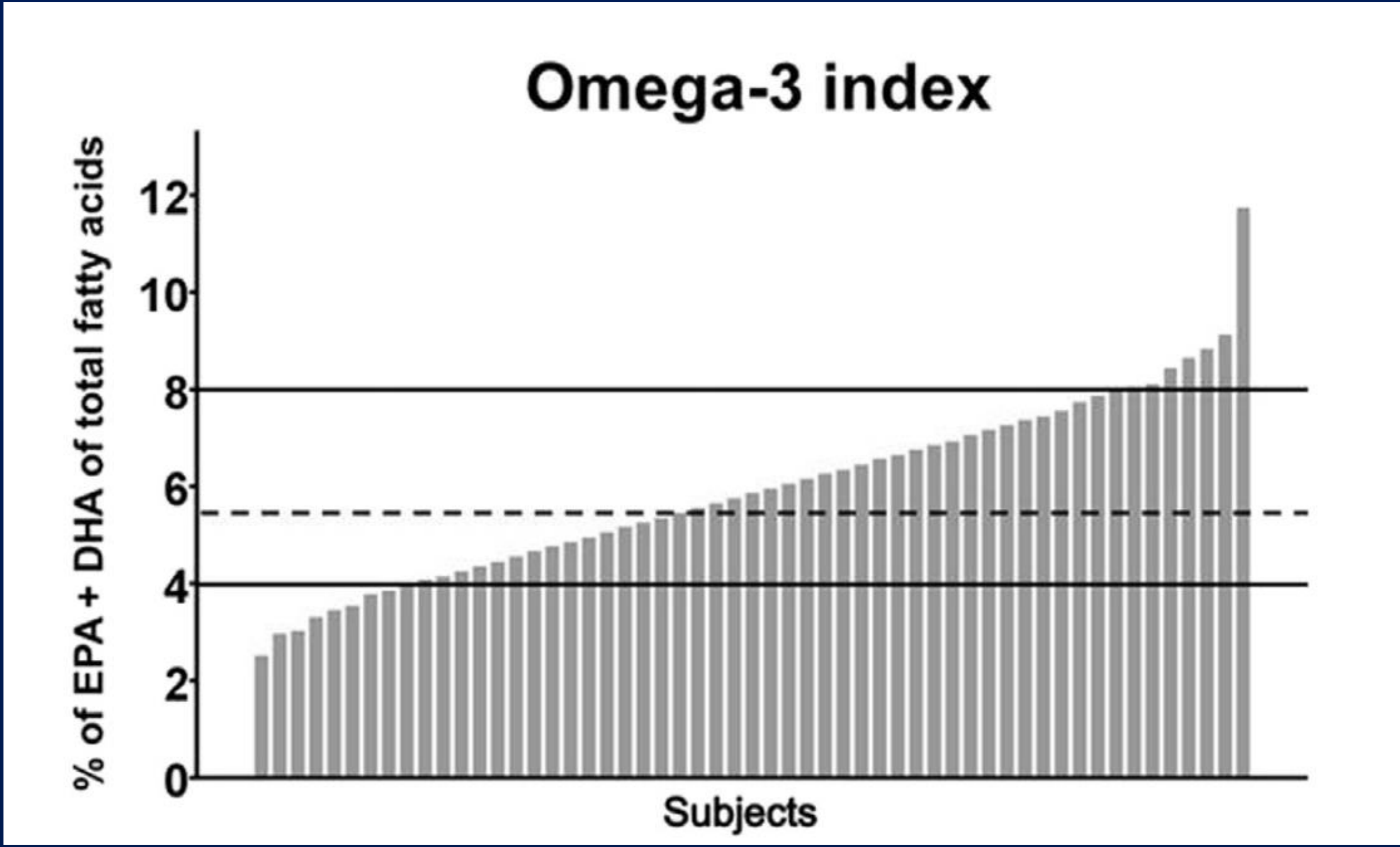
Rivelles, von Schacky, unpubliziert

Omega-3 Index in 23 615 Erythrozyten-Proben aus Europa



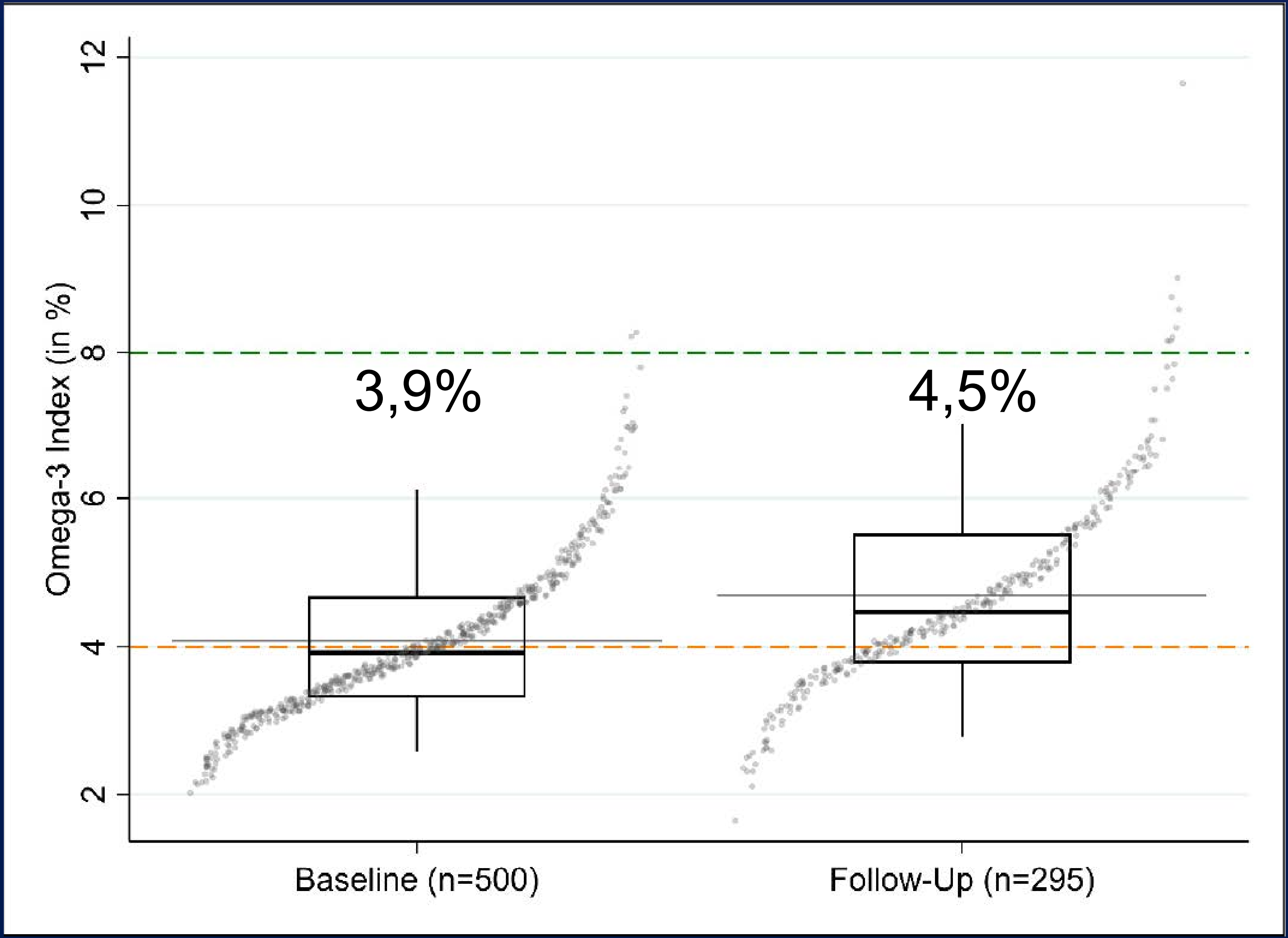
n < 2% = 0, n > 20% = 0

446 deutsche Frauen zwischen 40 und 60 Jahre alt
Semi-repräsentativ
Mittel 5.49±1.17%, <8%: 97.3% aller Frauen



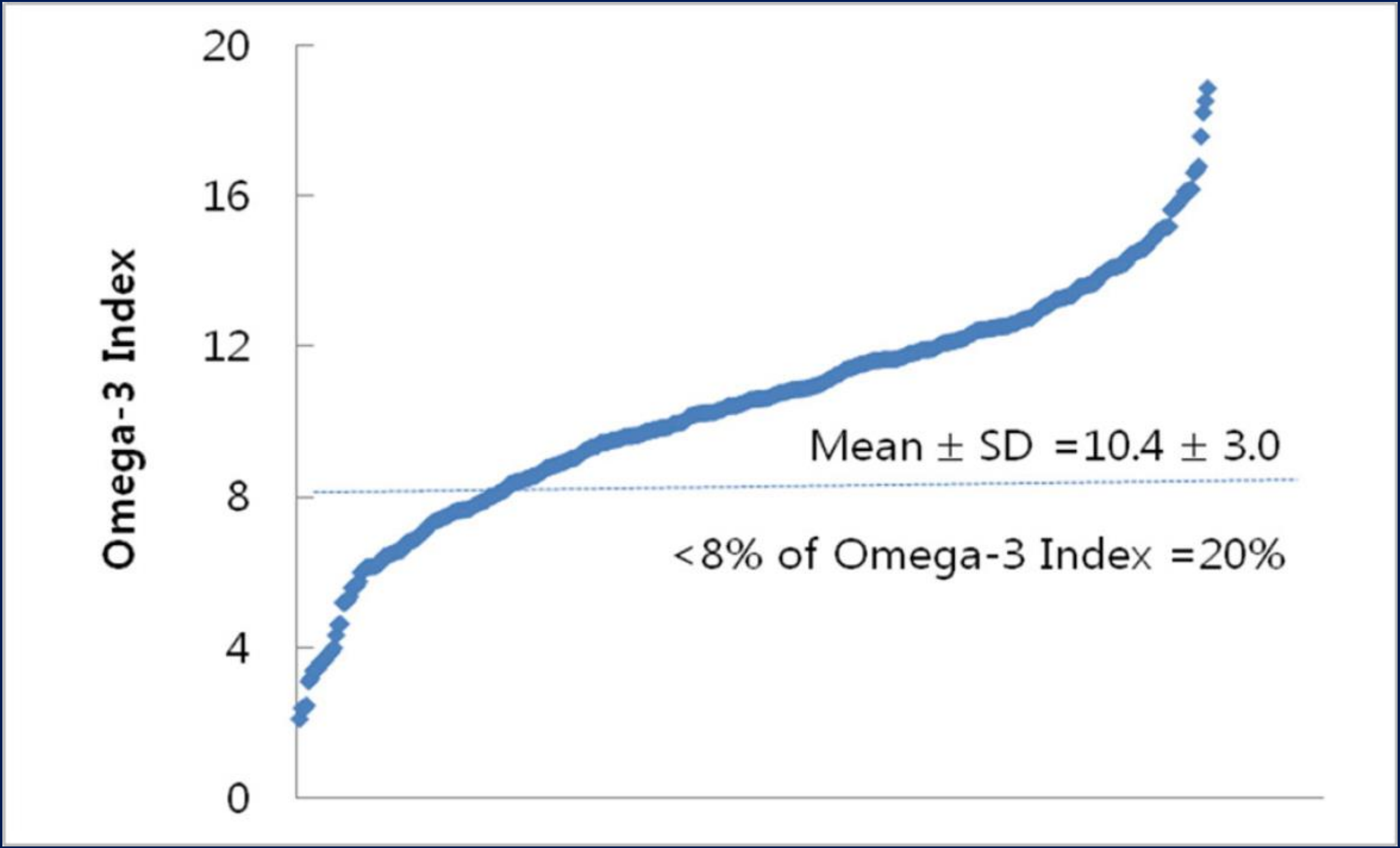
Gellert et al, PLEFA 2017;117:54

HS-Omega-3 Index vor und nach 4 Monaten mehr Fisch in der Kantine



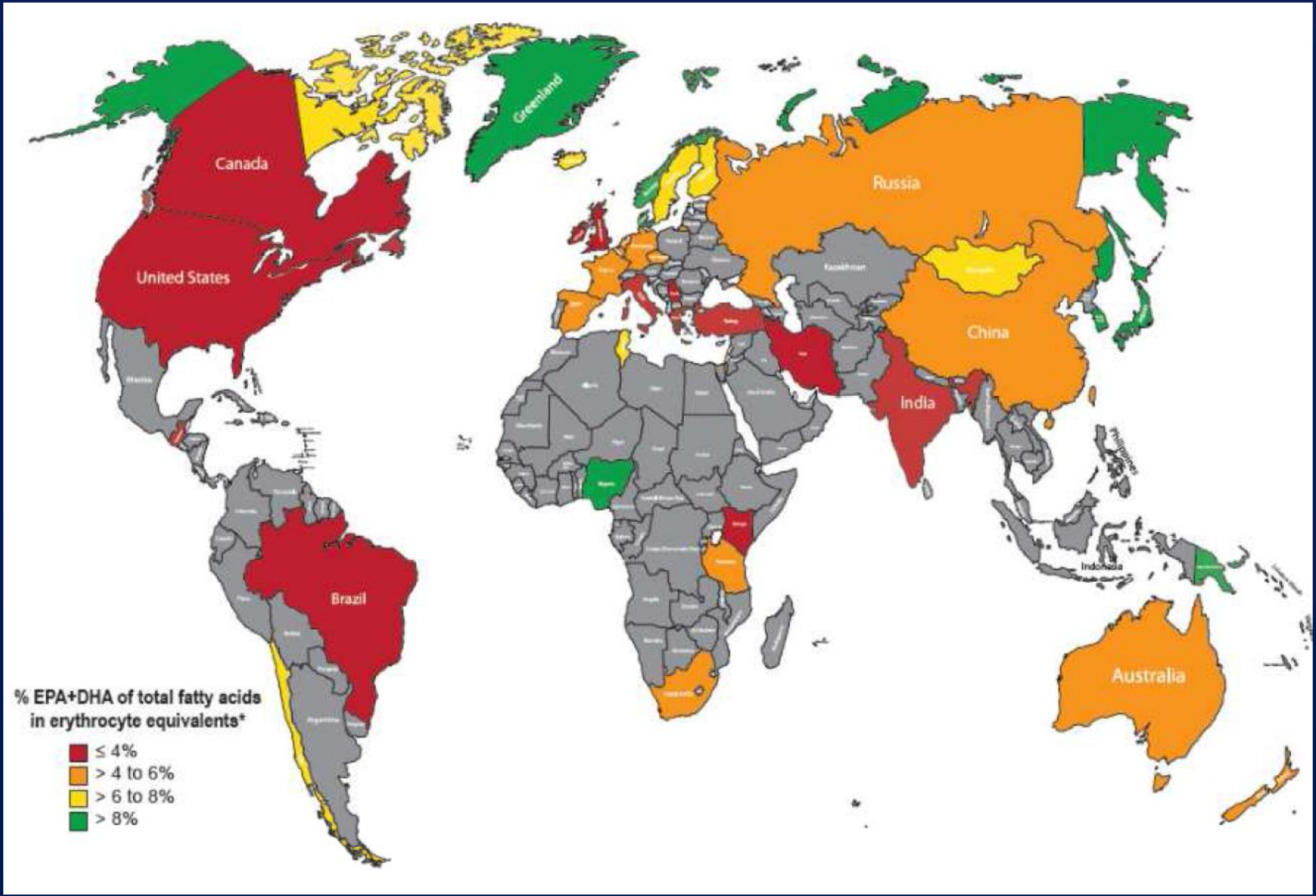
Rein at al, Nutrients 2020;12:3267

HS-Omega-3 Index in 1000 Süd-Koreanern Keine Supplementation, Mittel 10,4 ± 3,0 %



Park et al, unpublished

Omega-3 Index rund um die Welt



Stark K et al, Prog Lipid Res 2016, e-pub May 20

Mythos

Nahrungsergänzungsmittel sind für gesunde Personen, die sich normal ernähren, in der Regel überflüssig. Bei ausgewogener Ernährung bekommt der Körper alle Nährstoffe, die er braucht.

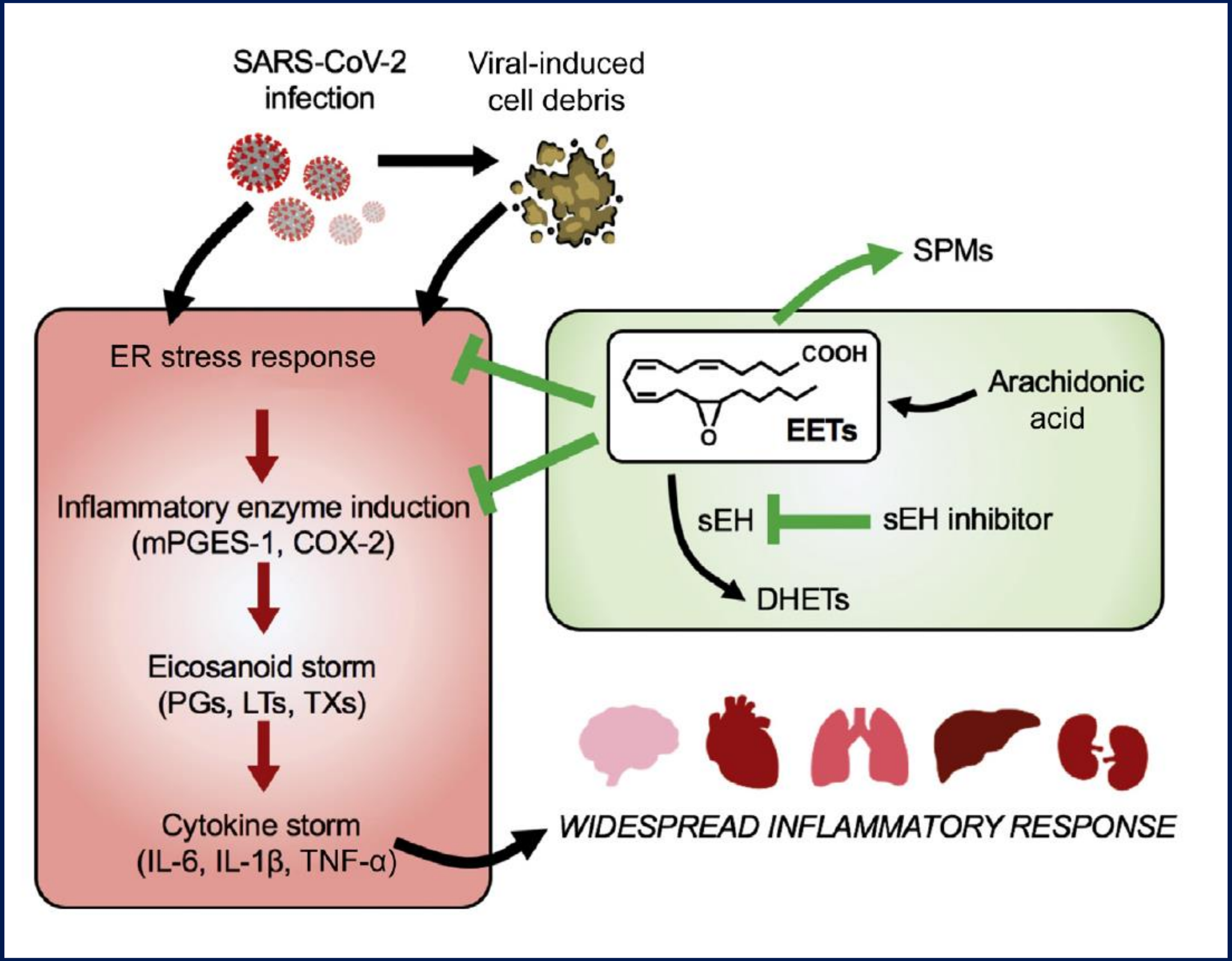
Realität: Falsch bei Omega-3 Defizit

http://www.bfr.bund.de/de/gesundheitliche_bewertung_von_nahrungsergaenzungsmitteln-945.html

Defizit gefunden - Positive Effekte auch bei

- Schwangerschaft
- Wochenbett
- Babies & Kinder
- ASD, ADHS
- Blutdruck
- Einigen chronisch entzündlichen Erkrankungen
- Muskel
- „altersbedingtem“ Muskelverlust
- Gelenke
- Schmerz
- Athleten
- Rotatorenmanschettenruptur
- u.v.a.m.

COVID-19



Hammock et al, Am J Path 2020;190:1782

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ELSEVIER

May omega-3 fatty acid dietary supplementation help reduce severe complications in Covid-19 patients?

Pierre Weill [a], Claire Plissonneau [b, c], Philippe Legrand [d, e], Vincent Rioux [d, e], Ronan Thibault [e, f, *]

Letzter Satz Abstract:
Ein optimaler omega-3 PUFA Status
könnte helfen Infektionen vorzubeugen, inklusive Covid-19.

Weill et al, Biochimie 2020;S0300-9084(20)30209-1

HS-Omega-3 Index and Death from Covid-19

Table 4
Associations of the omega-3 index with death adjusted for age and sex.

Risk factor	Adjusted Models OR (95% CI)[a]	Firth's test P-value[a]	F-test P-value[b]
Comparing O3I Q4 vs Q1–3			
Q1–3: O3I<5.7%	1.00		
Q4: O3I≥5.7%	0.25 (0.03, 1.11)	0.071	0.099

Asher et al, Prostaglandins Leukot Essent Fatty Acids. 2021 Jan 20;166:102250.

Laufende Studien zu Covid	n Teilnehmer
NCT04335032	284
NCT04460651	1500
NCT04505098	16500
NCT04495816	126
NCT04323228	40
NCT04435223	62
NCT04335032	240
NCT04507867	240
NCT04553705	200
NCT04483271	100
NCT04609423	80 000

Ernährung: ein paar Mythen zerstört durch Fakten?

Online, 23. Februar 2021

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