

# Effect of 1 year krill oil supplementation on depression and self-esteem in typically developing Dutch adolescents

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Effect of 1 year krill oil supplementation on depression and self-esteem in typically developing Dutch adolescents:  
Preliminary results

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MP Zeegers, PA Kirschner, RHM de Groot



# Research Question

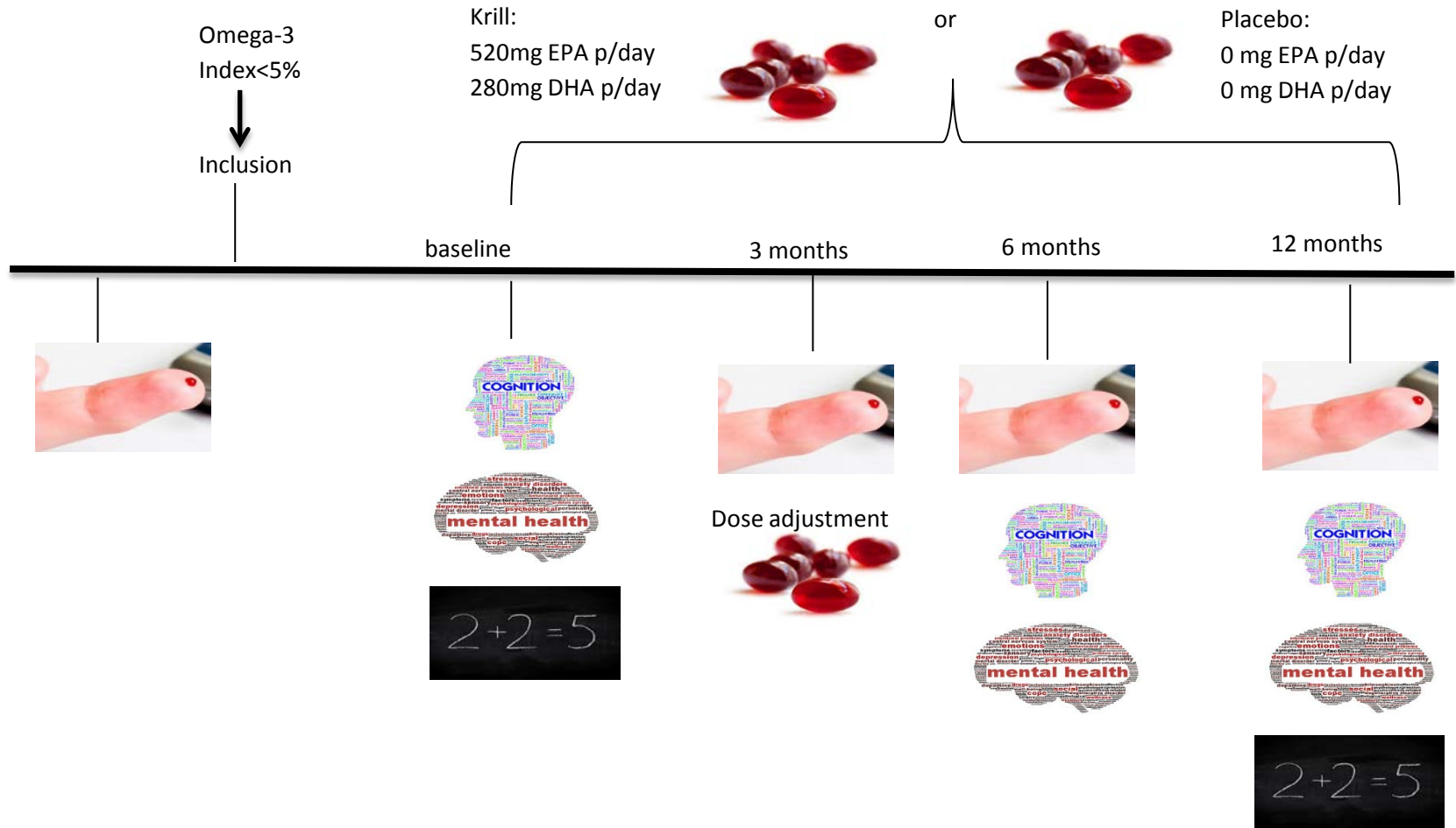
What is the influence of 1 year of krill oil supplementation in 13-15 year old adolescents attending lower general secondary education on:

**Cognitive functioning and academic achievement?**

**Mood and self-esteem?**

**Sleep quality and quantity and visual processing?**

# Study design



# Unique characteristics

Adolescents

Lower general secondary education  
(TL/MAVO)

Selection <5% Omega-3 Index

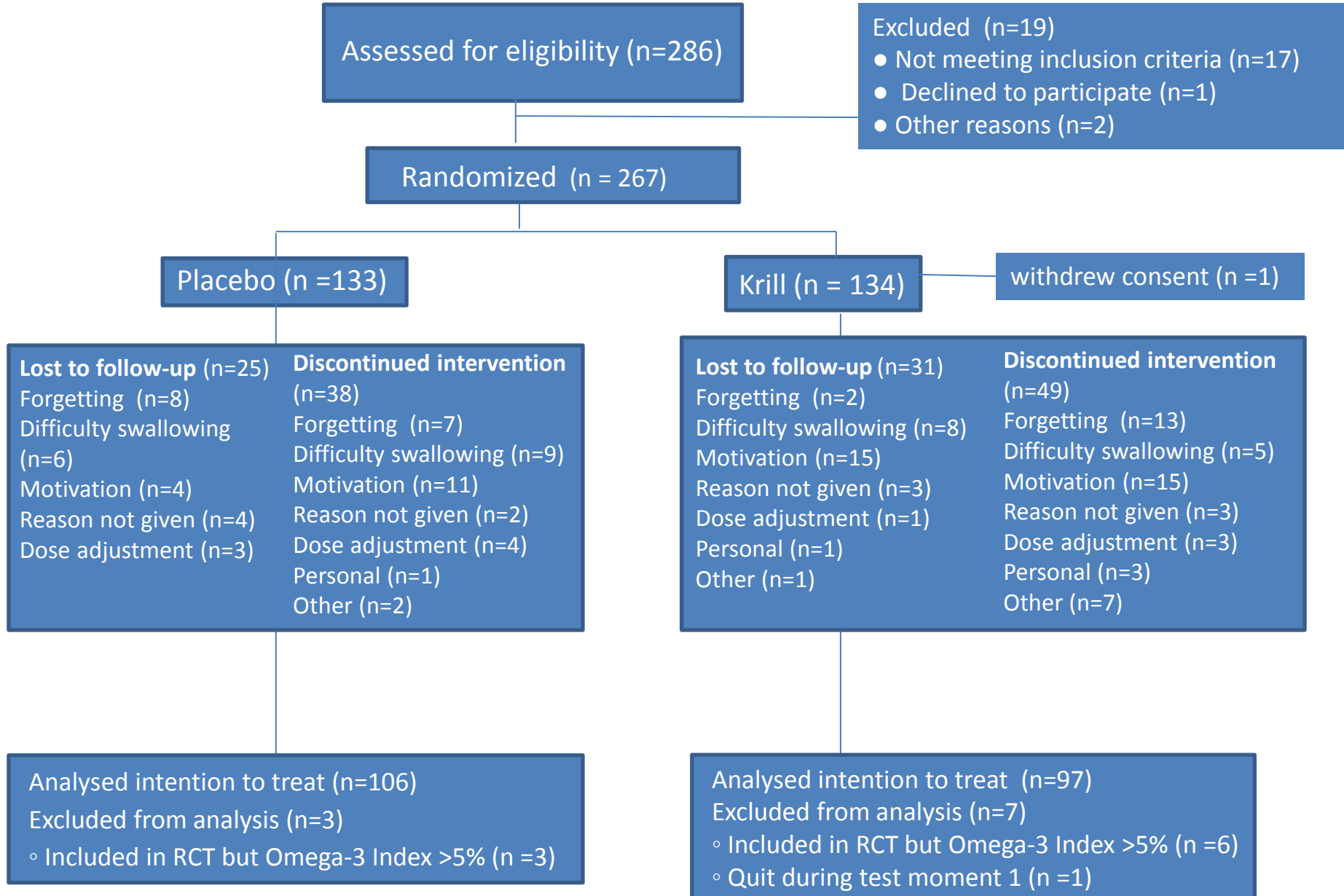
Personalised dose-adjustment after 3  
months

Supplement consumed at dinner time

# Mood and Self-esteem

Test	Measures
Center of Epidemiology Studies Depression Scale – Dutch version	Depression
Rosenberg Self-esteem questionnaire	Self-esteem

# Flow chart



# Statistics baseline

- Bayesian analyses
- Baseline data corrected for:
  - CESD: smoking, sex and BMI
  - RSE: smoking, diagnosis and sex
- CESD used as a continuous variable, for descriptive purposes CESD > 16 as depressed.



# Frequentist vs Bayesian

- Frequentist analyses non-significant result:
  - There is evidence for the  $H_0$  (i.e. there is no association) or
  - The data are insensitive in distinguishing the  $H_1$  from the  $H_0$  (i.e. nothing follows from the data)
- Bayesian analyses, Bayes Factor
  - There is evidence for  $H_0$  ( $BF > 3$ )
  - There is evidence for  $H_1$  ( $BF < 0.33$ )
  - Data is not sensitive (i.e. nothing follows from the data;  $BF = 0.33-1$ )

# Baseline characteristics

	N	Mean	SD	Fatty acid (%wt/wt of total FA, except for O3I)	N	Mean	SD
Age (years)	257	14.11	0.50	Omega-3 Index	257	3.78	0.56
Male/Female	257	124/133 [48.2/51.8%]	-	DHA 22:6n-3	257	2.55	0.46
Smoking no/yes <sup>1</sup>	255	231/24 [89.9/9.3%]	-	EPA 20:5n-3	257	0.38	0.15
BMI	240	19.98	3.00	DPA 22:5n-3	257	1.22	0.19
Alcohol units per week <sup>2</sup>	256	0.47	1.80	AA 20:4n-6	257	11.15	1.27
LPE	240	5.05	1.5	ObA 22:5n-6	257	0.44	0.10

<sup>1</sup> Smoking 'yes' was defined as anybody who indicated to smoke more than 0 cigarettes per week.

<sup>2</sup> Diagnosis was indicated by students themselves and included (but not limited to) dyslexia, dyscalculia, depression, autism and ADHD.

<sup>3</sup> Alcohol consumption was asked as how many times per week and units per consumption moment, alcohol per week is defined as these factors multiplied.

# Depression

- 29.4% scored CESD  $\geq 16$ 
  - Girls: 42.3%  $\geq 16$
  - Boys: 15.6%  $\geq 16$
- 17.1% scored CESD  $\geq 22$
- Those with depression: more girls, higher BMI, further in puberty, lower self-esteem.

# Baseline results

	One fatty acid				All fatty acids in 1 model		
Predictor fatty acid	Regression coefficient	95% credibility interval <sup>1</sup>	BF <sub>10</sub> <sup>2</sup>		Regression coefficient	95% credibility interval	BF <sub>omit</sub> <sup>3</sup>
Omega-3 Index	-0.016	-0.14;0.11	0.14				
DHA	-0.04	-0.16;0.08	0.15	DHA	-0.02	-0.15;0.11	3.12
EPA	0.06	-0.06;0.18	0.34	EPA	0.09	-0.05;0.22	1.42
AA	-0.13	-0.25;-0.02	2.65	AA	-0.03	-0.18;0.11	2.79
DPA	-0.13	-0.24;-0.02	1.01	DPA	-0.11	-0.25;0.03	0.84
ObA	-0.16	-0.28;-0.04	251.95	ObA	-0.09	-0.22;0.03	1.20

O3I = Omega-3 Index

One fatty acid model, is a model in which only one predictor of interest is entered (Omega-3 Index, DHA, EPA, AA, DPA, or ObA). All fatty acids model is a model in which all fatty acids (DHA, EPA, AA, DPA, and ObA) are entered, i.e. for example the association between DHA and self-esteem is corrected for the other fatty acids (EPA, AA, DPA, ObA).

All analyses were adjusted for BMI, smoking (yes/no), and sex.

<sup>1</sup> Credibility intervals are analogous to confidence intervals in traditional statistics.

<sup>2</sup> BF<sub>10</sub> refers to the evidence for the model with the specific fatty acid compared to a model with only covariates.

<sup>3</sup> BF<sub>omit</sub> indicates whether the model improves with the omission of that specific fatty acid. BF<sub>omit</sub> numbers above 3 indicate that keeping the variable in the model is not preferable.

# Self-esteem

	One fatty acid				All fatty acids in one model		
Predictor fatty acid	Regression coefficient	95% credibility interval <sup>1</sup>	BF <sub>10</sub> <sup>2</sup>		Regression coefficient	95% credibility interval	BF <sub>omit</sub> <sup>3</sup>
Omega-3 Index	-0.05	-0.18;0.08	0.18				
DHA	-0.03	-0.15;0.10	0.15	DHA	0.001	-0.13;0.13	3.12
EPA	-0.09	-0.20;0.03	0.32	EPA	-0.08	-0.21;0.05	1.59
AA	0.008	-0.12;0.10	0.14	AA	-0.06	-0.20;0.08	2.04
DPA	-0.02	-0.09;0.14	0.16	DPA	0.07	-0.07;0.20	1.76
ObA	0.09	-0.03;0.20	4.15	ObA	0.07	-0.05;0.20	1.63

O3I = Omega-3 Index

One fatty acid model, is a model in which only one predictor of interest is entered (Omega-3 Index, DHA, EPA, AA, DPA, or ObA). All fatty acids model is a model in which all fatty acids (DHA, EPA, AA, DPA, and ObA) are entered, i.e. for example the association between DHA and self-esteem is corrected for the other fatty acids (EPA, AA, DPA, ObA).

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<sup>1</sup> Credibility intervals are analogous to confidence intervals in traditional statistics.

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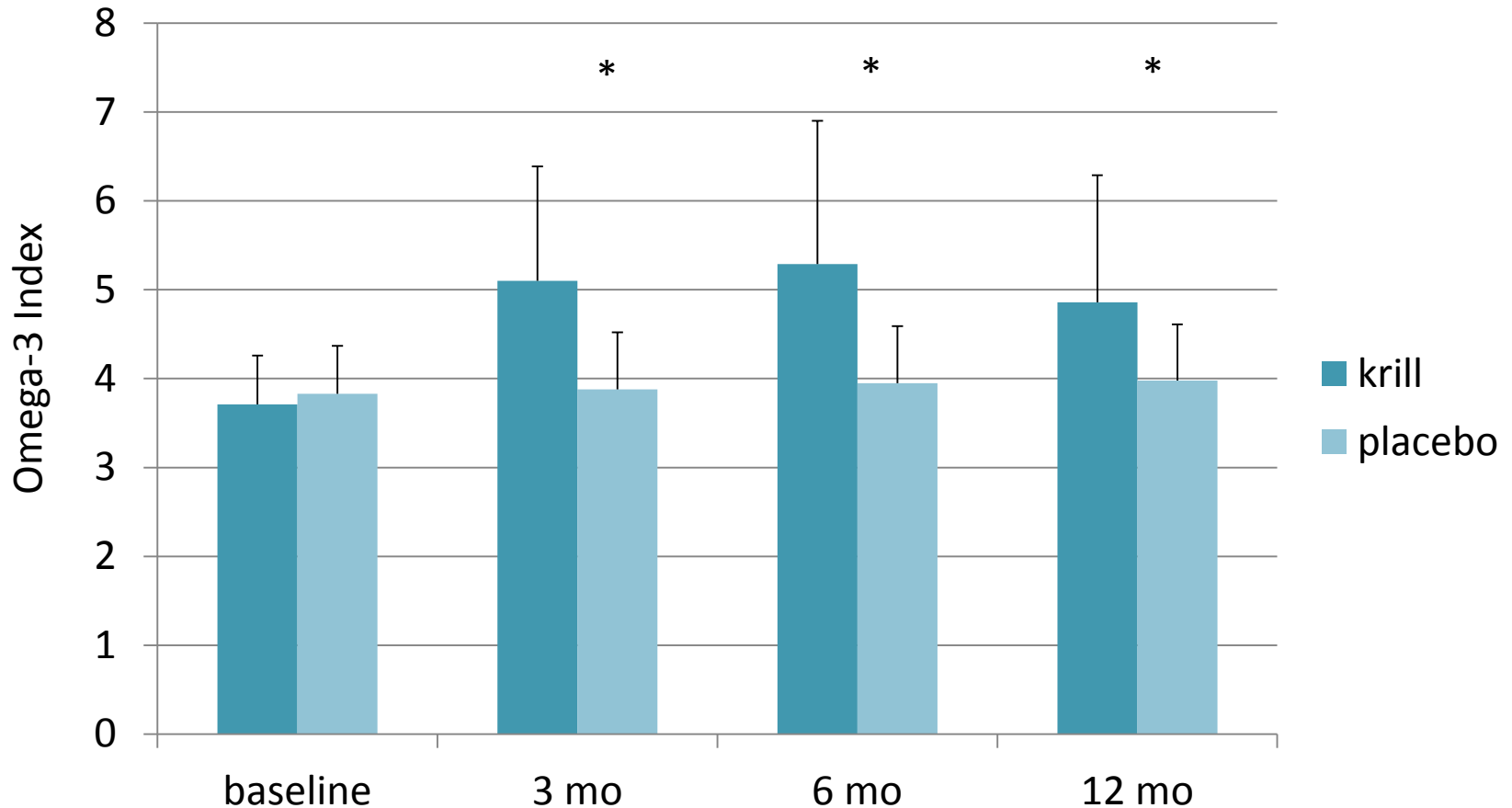
# Intervention

# Change in fatty acids (ITT)

fatty acid (%wt/wt of total FA)	condition	baseline	3 months	6 months	12 months
AA 20:4n-6	Placebo	11.19 ± 1.36	10.97 ± 1.18	11.02 ± 1.49	11.15 ± 1.30
	Krill	11.12 ± 1.18	10.26 ± 1.13*	10.28 ± 1.41 *	10.702 ± 1.49*
EPA 20:5n-3	Placebo	0.38 ± 0.14	0.43 ± 0.15	0.41 ± 0.14	0.40 ± 0.12
	Krill	0.38 ± 0.15	0.93 ± 0.58*	0.95 ± 0.69*	0.75 ± 0.58*
ObA 22:5n-6	Placebo	0.43 ± 0.11	0.41 ± 0.17	0.42 ± 0.09	0.38 ± 0.12
	Krill	0.45 ± 0.10	0.32 ± 0.12*	0.32 ± 0.11*	0.34 ± 0.13*
DPA 22:5n-3	Placebo	1.22 ± 0.20	1.29 ± 0.23	1.30 ± 0.20	1.30 ± 0.19
	Krill	1.22 ± 0.17	1.58 ± 0.34*	1.54 ± 0.35*	1.47 ± 0.31 *
DHA 22:6n-3	Placebo	2.60 ± 0.44	2.61 ± 0.52	2.69 ± 0.53	2.72 ± 0.54
	Krill	2.49 ± 0.46	3.25 ± 0.73*	3.40 ± 0.90*	3.20 ± 0.84*

\* Krill oil and placebo condition are significantly different  $p < 0.05$

# Change in Omega-3 Index over time



\* Krill oil and placebo condition are significantly different  $p < 0.05$



# In comparison

Target group	Omega-3 index
Unselected Japanese men (n 262)	9.58
Unselected Germans (n 5000)	7.15 ± 2.19
Unselected Europeans (n 10000)	6.96 ± 2.15
Framingham-Offspring (n 3196)	4.90 ± 2.10
American adolescents with major depression (n 150)	3.46
Americans with major depression (n 118)	2.90 ± 1.50

Adapted from: Von Schacky , C. Omega-3 index and cardiovascular health. *Nutrients* 2014;6:799–814.  
doi:10.3390/nu6020799

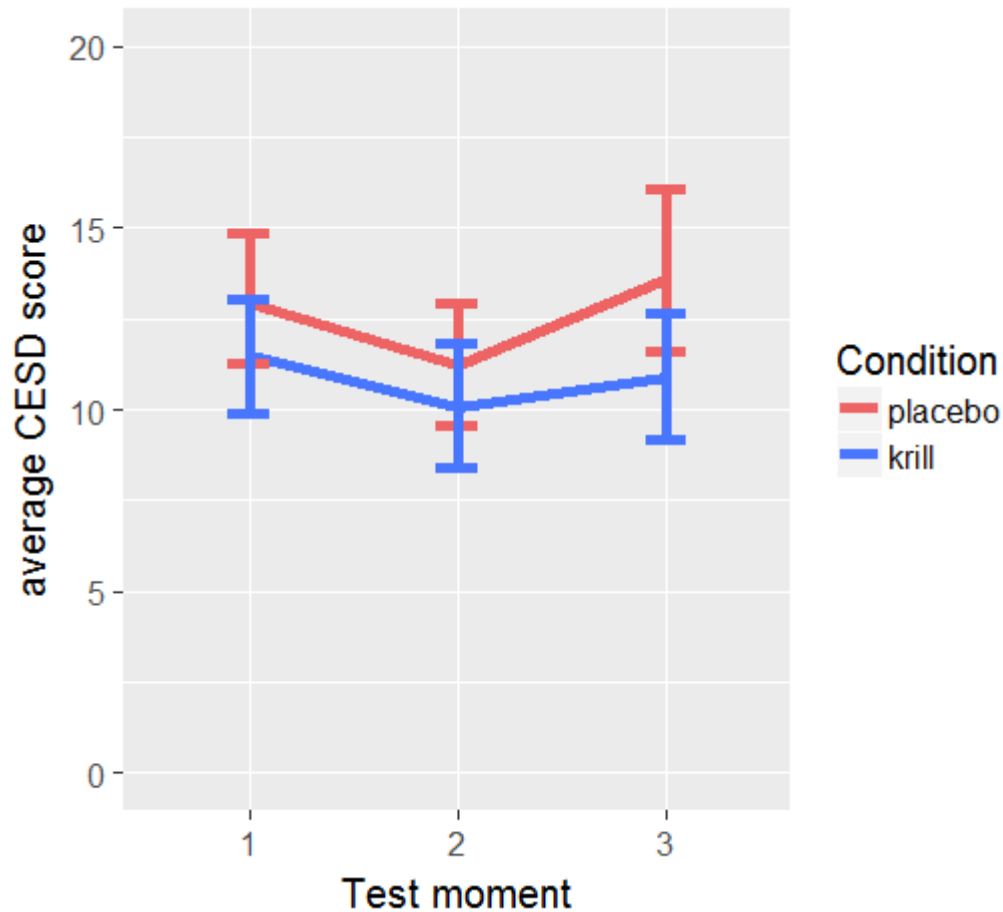
# Depression

Depression >15	Baseline	6 months	12 months
No	70.6%	78.7%	73.5%
Yes	29.4%	21.3%	26.5%
Depression >21			
No	82.9%	88%	81.4%
Yes	17.1%	12%	18.6%

# Analyses

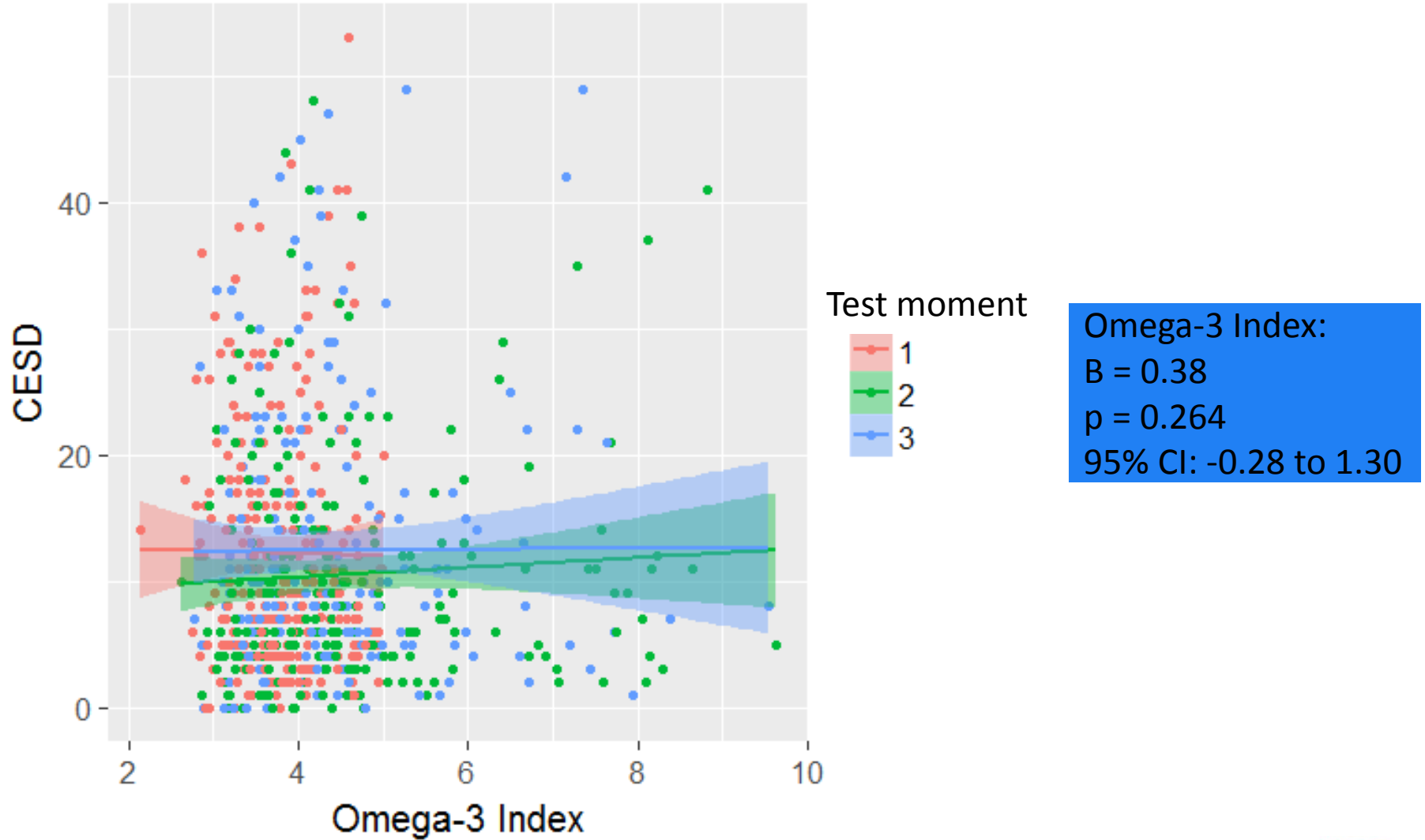
- Multilevel analyses – with person as unit
- Intention to treat and according to blood Omega-3 Index
- Correction for covariates
  - Drinking (units per week)
  - Smoking (yes/no)
  - Age at baseline
  - BMI (self-reported at baseline)
  - Sex
  - Cohort number
  - Diagnosis which can influence learning (yes/no)
  - Test moment
  - Level of parental education (low/high)
  - In condition analyses: condition\*test moment

# Results depression



ITT analyses:  
B = -0.64  
p = 0.624  
95% CI: -3.19 to 1.90

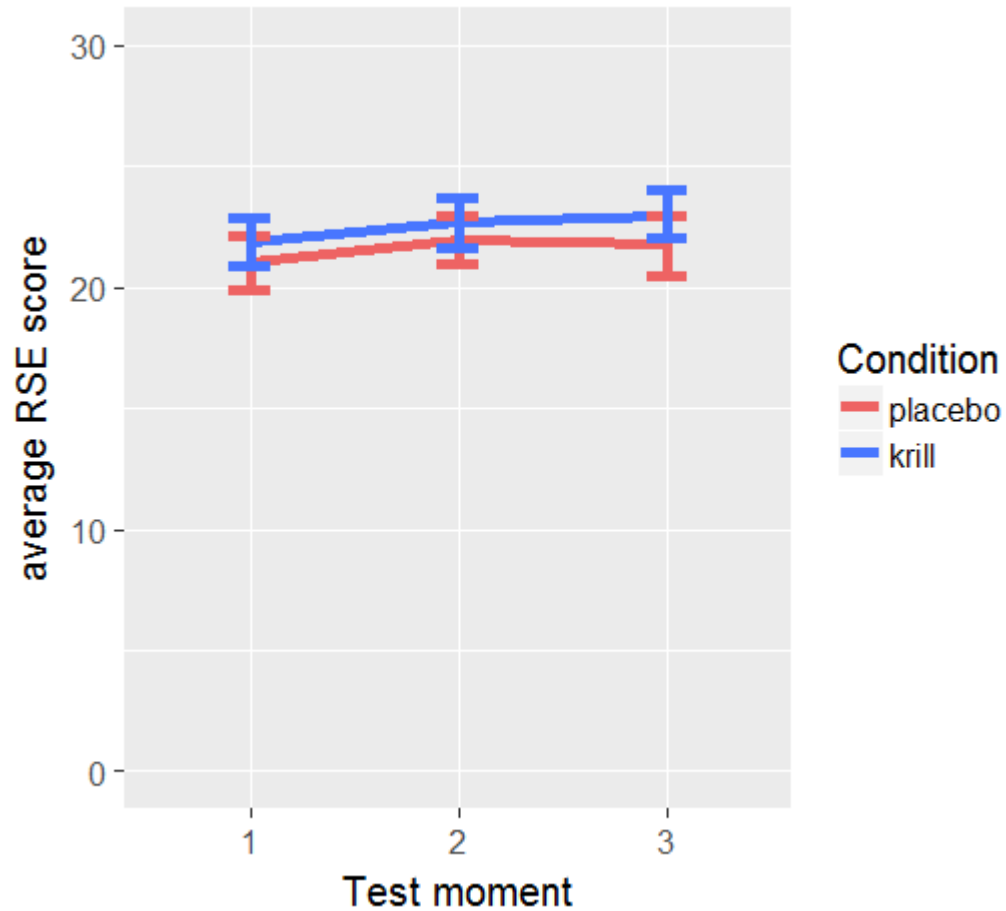
# Results depression



# Other fatty acids

CES-D	Beta	P	95% CI
DHA	-0.17	0.749	[-1.17; 0.84]
EPA	0.68	0.399	[-0.88; 2.23]
DPA	-0.71	0.604	[-3.36; 1.94]
AA	-0.36	0.165	[-0.86; 0.14]
OBA	-4.07	0.198	[-10.19; 2.06]

# Results: self-esteem



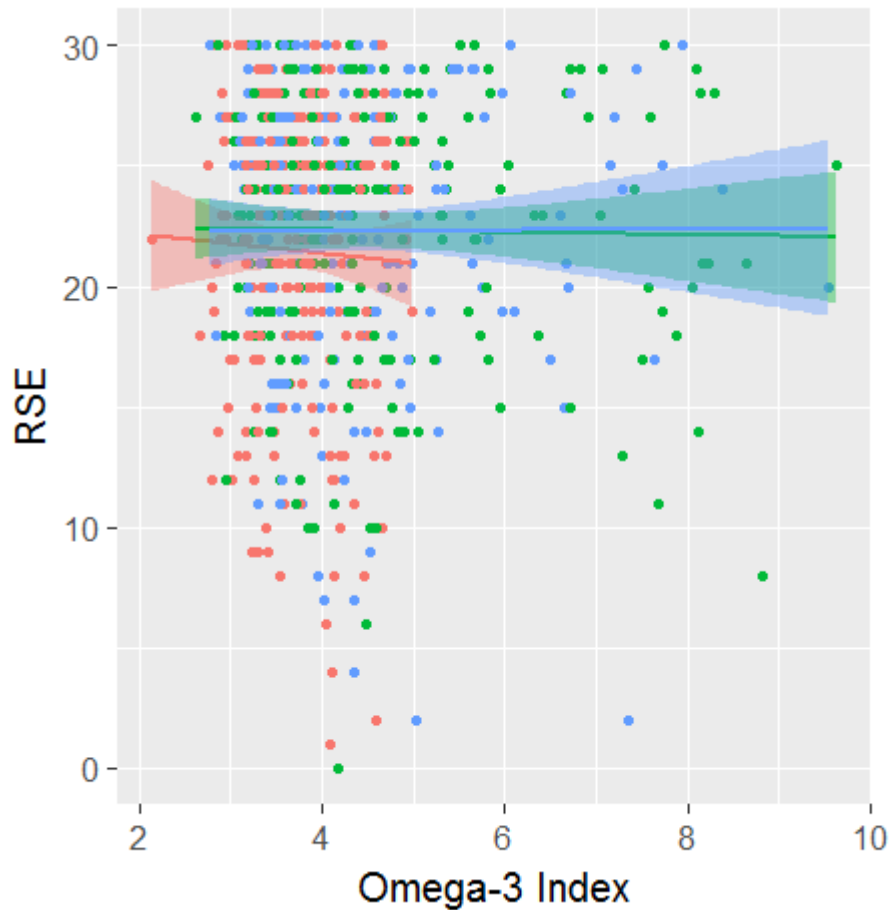
ITT analyses:

$B = 0.28$

$p = 0.721$

95% CI: -1,22; 1,77

# Results: self-esteem



Test moment

- 1
- 2
- 3

Omega-3 Index:  
B = -0.03  
p = 0.866  
95% CI: -0.38 to 0.32



# Other fatty acids

RSE	Beta	P	95% CI
DHA	0.08	0.761	[-0.45; 0.61]
EPA	-0.14	0.736	[-0.96; 0.68]
DPA	-0.41	0.573	[-1.83; 1.00]
AA	-0.13	0.367	[-0.39; 0.14]
OBA	-1.61	0.333	[-4.85; 1.62]

# Discussion (1)

- Depression is very common in adolescents.
- No significant effects of supplementation on depression and self-esteem.
- Even analyses according to omega-3 fatty acid status did not show effects
- 1 year of krill oil, still low Omega-3 Index
  - Did not take capsules – compliance
  - Factors associated with metabolism
  - Krill oil

# Discussion (2)

- Important to take blood values!

# Funding

- Study was funded by:
  - Grant of Dutch Scientific Organisation
  - Aker Biomarine
  - Omegametrix

# Publications

- van der Wurff, I., Von Schacky, C., Berge, K., Zeegers, M., Kirschner, P. A., & de Groot, R. (2016). Association between Blood Omega-3 Index and Cognition in Typically Developing Dutch Adolescents. *Nutrients*, 8(1), 13.
- van der Wurff, I. S. M., von Schacky, C., Berge, K., Kirschner, P. A., & de Groot, R. H. M. (2016). A protocol for a randomised controlled trial investigating the effect of increasing Omega-3 index with krill oil supplementation on learning, cognition, behaviour and visual processing in typically developing adolescents. *BMJ open*, 6(7), e011790. doi:10.1136/bmjopen-2016-011790.
- van der Wurff, I.S.M.; Meyer, B.J.; de Groot, R.H.M. (2017). A Review of Recruitment, Adherence and Drop-Out Rates in Omega-3 Polyunsaturated Fatty Acid Supplementation Trials in Children and Adolescents. *Nutrients*, 9 (5), 474. doi:10.3390/nu9050474



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