

Targeting The Omega-6/Omega-3 Fatty Acid Ratio In Dementia Prevention: Results From A Randomized Controlled Ten-week Feasibility Trial

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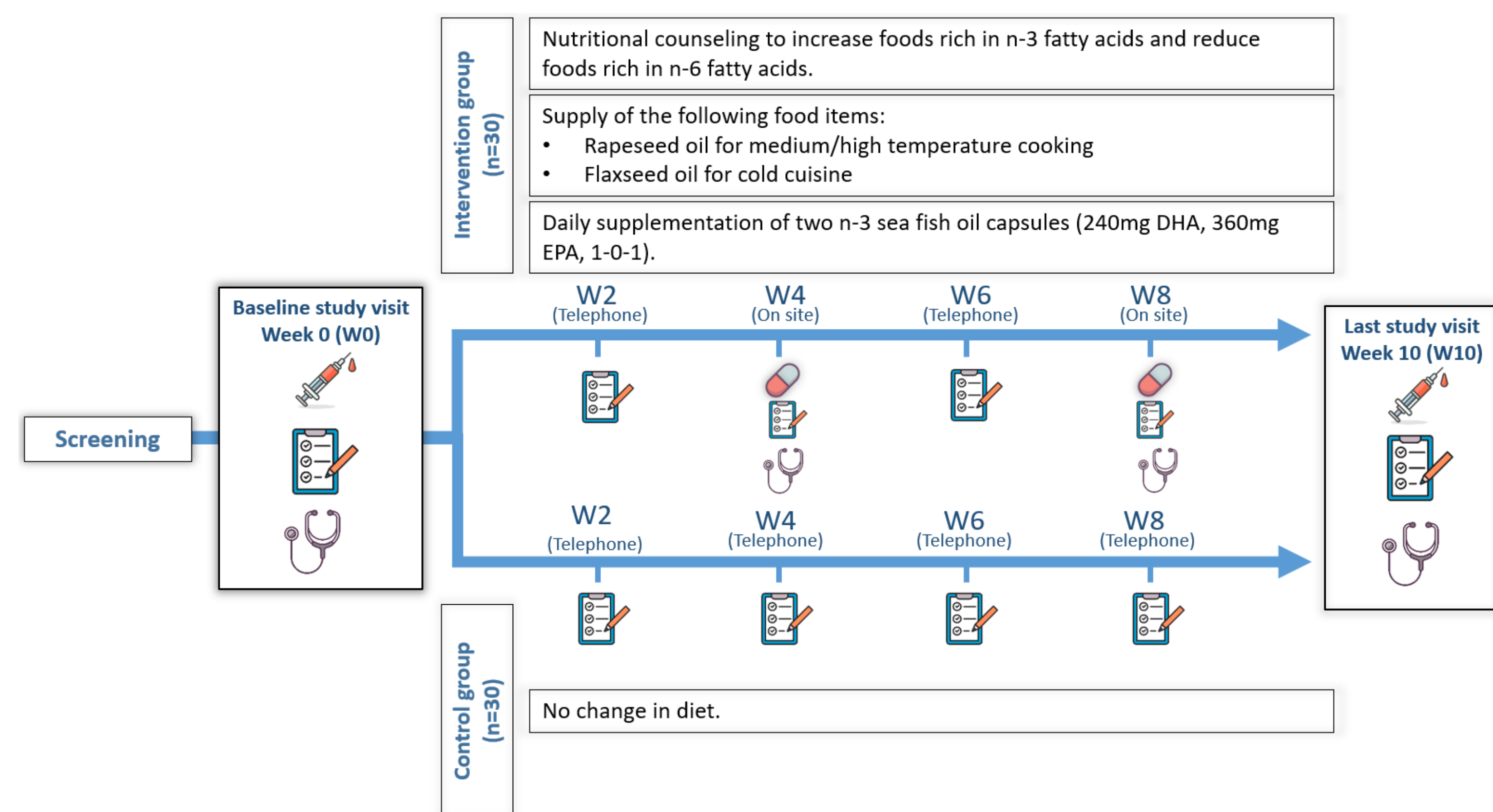
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BACKGROUND

- Modifiable lifestyle factors play an important role in promoting healthy brain aging, and diet is frequently discussed as a potential dementia prevention target.
- A Western diet high in saturated fats and n-6 polyunsaturated fatty acids (PUFAs) is associated with inflammation and chronic diseases, including Alzheimer's disease.
- An elevated n-6/n-3 fatty acid (FA) ratio may disrupt the balance between pro- and anti-inflammatory processes in the brain and potentially accelerate neurodegenerative processes.
- We report results from a ten-week dietary intervention in cognitively healthy older individuals to reduce the n-6/n-3 FA ratio.

METHOD

Fig. 1 Study Flow Chart



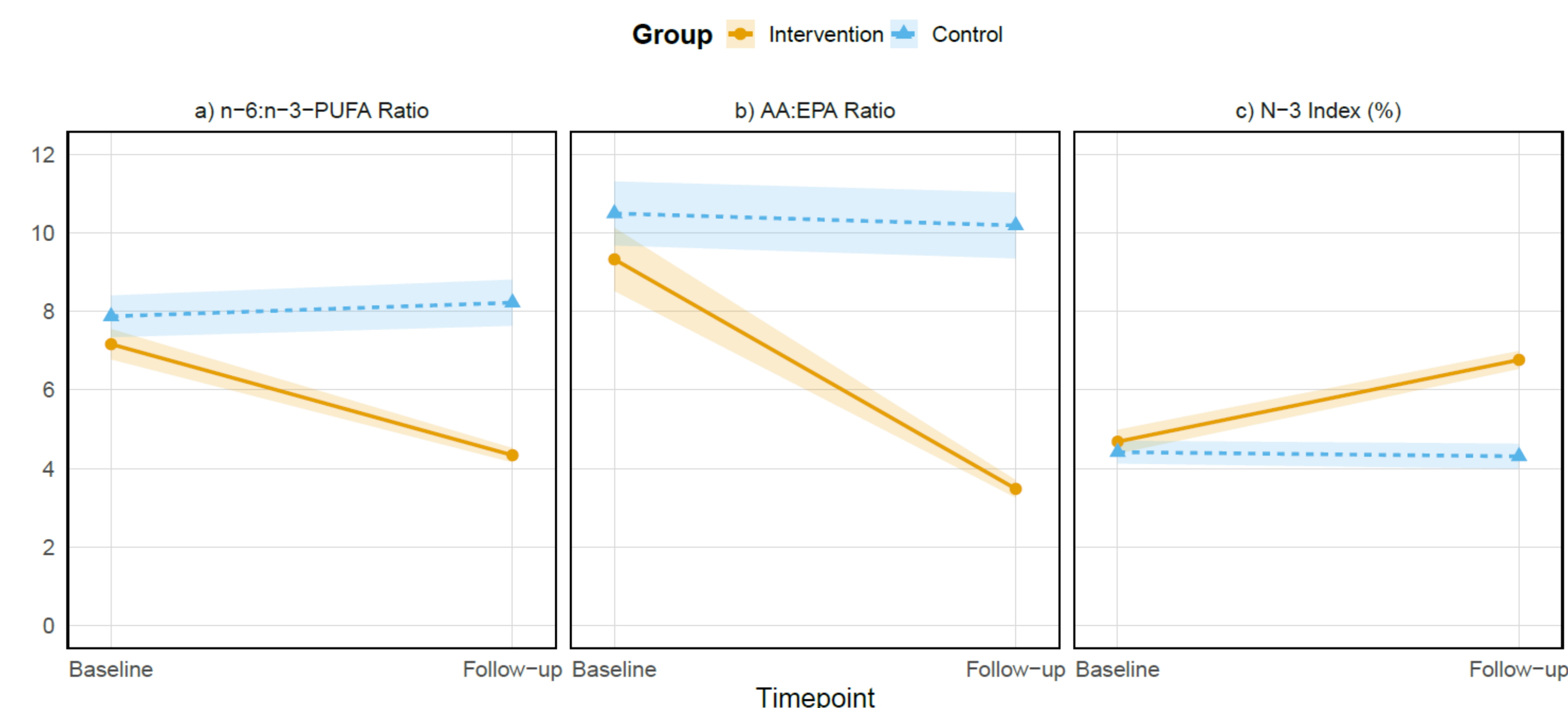
- 60 cognitively healthy participants from the Cologne Alzheimer's Prevention Register were randomly allocated into an intervention and a control group.
- Intervention: dietary advice to optimize the ratio of foods containing n-6 and n-3 FAs, supplementation of cooking oils and omega-3 fish oil capsules.
- Control: no change to eating habits.
- Primary endpoint: Reduction in the n-6/n-3 ratio.
- PUFAs were considered as absolute concentrations and percentage distributions in serum phospholipids: ALA (C18:3 n-3), EPA (C20:5 n-3), DHA (C22:6 n-3), LA (C18:2 n-6), DGLA (C20:3 n-6), and AA (C20:4 n-6).
- The n-6:n-3 FA ratio calculation was based on 1) $\Sigma(n-6 \text{ FAs})/\Sigma(n-3 \text{ FA})$ ratio and 2) the AA:EPA ratio.
- Two-way mixed ANCOVA models were carried out to analyze group differences in the n-6:n-3 FA ratio over time, adjusted for age, sex, and recruitment wave.

RESULTS

Table 1. Sample characteristics at Baseline

	Intervention (n=30)	Control (n=30)	p
Age, M(SD)	66.7 (9.7)	69.1 (7.6)	.289
Gender female, n(%)	18 (60)	17 (56.7)	.793
Education years, M(SD)	17 (2.9)	16.1 (2.6)	.224
BMI, M(SD)	26.7 (4.1)	26.4 (3.9)	.761
MMSE, M(SD)	29.6 (0.9)	29.6 (0.7)	.807
Family history of dementia, n(%)	20 (67.0)	14 (47.0)	.118
SCD in memory domain, n(%)	22 (73.3)	21 (70)	.774
ApoE-4 carrier, n(%)	14 (46.7)	7 (23.3)	.058

Fig. 2. Changes in PUFA ratios and n-3-index over the 10-week study period between groups.



Mean concentrations ($\pm$ SE) of a) n-6:n-3 ratio, b) AA:EPA ratio and c) n-3 index across the 10-week study duration for the intervention and control group. AA arachidonic acid, EPA eicosapentaenoic acid, n-3 index EPA + DHA as % of total identified serum phospholipid FAs.

- A two-factor mixed ANCOVA revealed a significant *group x time* interaction effect ($F(1)=47.88$, $p<.0001$, $\eta^2=0.465$). The n-6:n-3 FA ratio decreased over time in the intervention group ($\beta=-2.82$, 95% CI [-3.47, -2.18], $p<.0001$), but not the control group ($\beta=0.34$, 95% CI [-0.30, 0.99], $p=0.294$), whilst controlling for recruitment wave, gender, and age. The same pattern was observed for the AA:EPA ratio and the n-3 index.
- The concentration of n-3 FAs ALA and EPA as well as the DHA percentage of total FAs increased significantly in the intervention group, but not the control group. Concurrently, the concentration of all n-6 FAs (LA, AA, DGLA) decreased significantly only in the intervention group.
- Out of all participants in the intervention group, 28 (93.3%) reported that the nutritional counseling enabled them to change their diet. Barriers to implementing the nutritional intervention were reported by 8 participants (26.7%), among them vacations and shift work.

CONCLUSION

- The findings of the study demonstrate the feasibility of achieving a targeted alteration in the FA profile within 10 weeks, through a combined intervention strategy encompassing dietary counseling and omega-3 supplementation.
- While an increase of EPA and DHA was expected as a result of the fish oil supplementation, the changes in other PUFAs can be attributed to participants' dietary changes, likely as a result of the nutritional counseling.
- Our study contributes evidence on the feasibility and effect of a nutritional intervention in a key target group for brain health services.
- Upcoming analyses will focus on the influence of the intervention on AD plasma biomarkers as well as other outcomes, such as cognition and lifestyle changes.

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