Algae-derived EPA and DHA supplementation improves whole blood omega-3 status in midlife women with low fish intake: a 12-week prospective real-world pilot study

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Abstract

Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential for cardiovascular, cognitive and immune health. Suboptimal omega-3 status is common in Western populations, including the UK, where intake of oily fish is often low. This study aimed to evaluate changes in whole blood omega-3 biomarkers following supplementation with algae-derived EPA and DHA in midlife women with low baseline intake.

In this 12-week prospective, single-arm longitudinal study, 30 healthy women aged 45–68 years with low oily fish intake (<1 portion/week) consumed a daily algae-derived omega-3 supplement providing 150 mg EPA and 300 mg DHA. Whole blood fatty acid composition was assessed using dried blood spot analysis at baseline, week 6 and week 12. Primary outcome was change in Omega-3 Index; secondary outcomes included EPA%, DHA%, omega-6:omega-3 ratio, AA:EPA ratio and trans-fat index. Paired analyses assessed within-participant changes over time.

Mean Omega-3 Index increased from 5.03 ± 1.49% at baseline to 6.86 ± 1.12% at week 6 and remained elevated at week 12 (6.81 ± 1.65%; $p < 0.001$). Significant increases were observed in EPA and DHA at both timepoints ($p < 0.001$). The omega-6:omega-3 ratio and AA:EPA ratio decreased significantly over the intervention period ($p < 0.001$), alongside a modest reduction in trans-fat index ($p < 0.05$). Changes were evident by week 6 and sustained at week 12. Participant-reported outcomes indicated modest perceived improvements in wellbeing; these findings are exploratory.

Supplementation with algae-derived EPA and DHA was associated with significant increases in

whole blood omega-3 biomarkers in midlife women with low baseline intake. These findings demonstrate measurable changes in omega-3 status at guideline-aligned intake levels under real-world conditions and support the value of longitudinal, community-based approaches in nutritional research. Further controlled studies are warranted.

Keywords

Omega-3 Index, eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), vegan Omega-3, midlife women, Omega-6:3 ratio, female health data gap

Introduction

Omega-3 fatty acids are essential long-chain polyunsaturated fatty acids that must be obtained through the diet. Alpha-linolenic acid (ALA) is plant-derived, whereas eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are long-chain omega-3 fatty acids found primarily in marine sources and algae. EPA and DHA contribute to a range of physiological processes, including cardiovascular, neurological, visual and immune function (Calder, 2018; Swanson et al., 2012).

In the United Kingdom, the Scientific Advisory Committee on Nutrition recommends a daily intake of approximately 450 mg of combined EPA and DHA for adults, typically achieved through consumption of at least two portions of fish per week, including one portion of oily fish (SACN, 2004; SACN, 2020). However, national dietary surveys consistently report low oily fish consumption across the UK population (e.g. only 25% of the population regularly consumes oily fish), with many adults failing to meet the recommendations for EPA and DHA (Derbyshire, 2019; NDNS, 2021). The problem of low EPA and DHA intake and status is not restricted to the United Kingdom: suboptimal omega-3 status has been reported in many populations (Schuchardt et al., 2024).

Omega-3 status is influenced not only by dietary intake but also by sex (Lohner et al., 2013), age (De Groot et al., 2019) and life stage (De Groot et al., 2019). Midlife represents a biologically distinct phase in women characterised by endocrine transition, particularly fluctuating and declining oestrogen levels during perimenopause and menopause. Oestrogen plays regulatory roles in lipid metabolism, vascular function, inflammatory signalling and mitochondrial activity

(Mauvais-Jarvis, 2015; Tramunt et al., 2020; Calder, 2010). Declining oestrogen during menopause has been associated with increased cardiometabolic risk, changes in body fat distribution, endothelial dysfunction and alterations in immune regulation (Mauvais-Jarvis, 2015; Tramunt et al., 2020; Camon et al., 2024; Lovejoy et al., 2008; Peters et al., 2022).

Omega-3 fatty acids may play a role in improving women's health through mitigating the adverse impacts of oestrogen decline. EPA and DHA are incorporated into cell membranes where they influence membrane fluidity, lipid raft formation and intracellular signalling, eicosanoid production and the synthesis of specialised pro-resolving mediators (Calder, 2015; Calder, 2020). In women in midlife, where inflammatory signalling and cardiometabolic risk may be changing, EPA and DHA intake and status may therefore be particularly relevant. Despite this, much of the foundational omega-3 fatty acid intervention research has historically been conducted in predominantly male or mixed-sex cohorts, often without sex-stratified analyses. Women, particularly those undergoing perimenopausal transition, remain underrepresented in cardiovascular, metabolic and nutrition intervention research. This contributes to what has been described as the "female health data gap," where sex-specific physiology and interventions are insufficiently studied across the life course (Criado-Perez, 2019; Mauvais-Jarvis et al., 2020).

The Omega-3 Index, defined as EPA + DHA as a percentage of total fatty acids in whole blood, is an established biomarker associated with EPA and DHA intake, EPA and DHA levels in some tissues, including the heart, and future cardiovascular risk and mortality (Harris & von Schacky, 2004). An Omega-3 Index below 4 % has been associated with higher cardiovascular risk, while levels between 8–12 % are considered optimal (Harris & von Schacky, 2004; Harris et al., 2017). Unlike plasma fatty acids, whole blood cell measurements reflect longer-term incorporation of fatty acids into cellular membranes and therefore provide a more stable indicator of tissue omega-

3 status. Reports from the UK suggest an average population Omega-3 index of around 5.5% (Harris et al., 2023). Whole blood measurements of EPA and DHA can be used to estimate Omega-3 Index. Complementary fatty acid markers, including EPA%, DHA%, the omega-6:omega-3 ratio, the arachidonic acid to EPA (AA:EPA) ratio and the trans-fat index, provide additional information regarding fatty acid balance, inflammatory signalling and dietary fat quality.

Marine-derived EPA and DHA supplements (e.g. fish oils) has been widely studied. However, shifts away from animal-based dietary patterns have increased demand for algae-derived sources of EPA and DHA. Algal oil EPA and DHA have bioavailability comparable to fish oil-derived EPA and DHA (Ryan & Symington, 2015; Bailey et al., 2025), although few studies have examined combined EPA+DHA algal formulations, most focussing on DHA-rich formulations, and few have been conducted in real-world populations.

Given both the physiological changes occurring during midlife and the persistent insufficiency in dietary EPA and DHA intake, evaluating accessible and sustainable omega-3 intake strategies in women in midlife is clinically relevant. The present study aimed to evaluate changes in whole blood omega-3 biomarkers following supplementation with algae-derived EPA+DHA in midlife women with low baseline intake, using a real-world, community-based approach. By focusing on a defined female cohort during hormonal transition, this study contributes to addressing sex-specific evidence gaps while exploring the real-world applicability of algae-derived omega-3 fatty acid supplementation.

Methods

Study Design

This was a 12-week, prospective, single-arm longitudinal study in a community-based setting, designed to assess within-participant changes in whole blood omega-3 biomarkers over time.

Participants

Thirty healthy women aged 45–68 years were recruited from the Ancient + Brave Inner Circle community. Of the 30 participants enrolled, 23 provided paired data at week 6 and 21 at week 12. Reasons for attrition included incomplete sample return and loss to follow-up.

Eligibility criteria included low oily fish intake (<1 portion per week), no current use of omega-3 supplements (for > 3 months), no major medical conditions requiring recent medication changes, and the ability to complete an at-home dried blood spot collection. Participants provided digital informed consent prior to enrolment.

Intervention

Participants consumed two softgel capsules daily of an algae-derived omega-3 supplement (True Omegas+, Ancient + Brave, UK) for 12 weeks. Participants were instructed to consume the supplement with a meal to optimise digestion and absorption. Participants were instructed to maintain their usual dietary habits; timing relative to meals was not standardised. Each two-capsule serving provided 1000 mg algal-derived omega-3 oil (Schizochytrium sp.), delivering 300 mg DHA and 150 mg EPA. The formulation also contained 186 mg sea buckthorn oil (providing 50 mg palmitoleic acid (Omega-7). Softgel capsules were composed of modified corn starch,

glycerol and carrageenan. The daily combined EPA+DHA dose was 450 mg, equivalent to the UK dietary recommendations for combined long-chain omega-3 fatty acid intake (Calder et al., 2026). Adherence was self-reported and verified through regular email communication, community engagement touchpoints and study surveys.

Sample Collection and Laboratory Analysis

Blood samples were collected as blood spots at baseline (week 0), midpoint (week 6), and endpoint (week 12). These timepoints were selected to assess early changes and near steady-state incorporation of EPA and DHA into whole blood, given the approximately 120-day lifespan of red blood cells and established kinetics of Omega-3 Index response to supplementation (Browning et al., 2012).

Participants used SureScreen Health dried blood spot (DBS) kits to collect their samples. Samples were returned to SureScreen Health (Morley, United Kingdom) for whole blood fatty acid analysis. Fatty acid composition was analysed by gas chromatography (GC) following standardised protocols validated for dried blood spot analysis. The Omega-3 Index was calculated as EPA + DHA expressed as a percentage of total identified fatty acids.

Outcome Measures

The primary outcome of the study was the change in Omega-3 Index (%) from baseline to week 12.

Secondary biochemical outcomes included whole blood EPA (%), DHA (%), the Omega-6:Omega-3 ratio, the AA:EPA ratio, and the trans-fat index.

Participant-reported outcomes were also collected using a structured subjective perception questionnaire (SPQ) administered at weeks 6 and 12. The questionnaire included:

(i) a single-item measure of general well-being rated on a 0–10 scale (0 = very poor, 10 = excellent), framed relative to supplement initiation;
(ii) a 0–10 rating of perceived overall effectiveness of the intervention; and
(iii) a categorical item allowing participants to select areas in which they perceived positive change, including mobility, cognitive clarity/focus, skin, mood, and recovery from exercise.

The SPQ was designed to capture exploratory participant-reported experiences in this single-arm within participant study and was not intended to function as a validated psychometric instrument.

Statistical Analysis

Statistical analyses were conducted to evaluate within-participant changes over time. Paired two-tailed t-tests were used to compare outcomes between baseline and week 6, and between baseline and week 12. Statistical significance was defined as $p < 0.05$. All analyses were performed using spreadsheet based statistical calculations. Given the exploratory nature of the study, adjustments for multiple comparisons were not applied and findings should be interpreted accordingly.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Participants provided informed digital consent prior to enrolment.

The study involved a low-risk nutritional evaluation using a commercially available food supplement within established safe intake levels and involved at-home dried blood spot sampling and questionnaire-based data collection only. In accordance with local institutional guidance for low-risk service evaluation and citizen-science nutritional research activities, formal research ethics committee approval was not required.

Results

Changes in Omega-3 Index Over 12 Weeks

This 12-week pilot study demonstrated significant increases in whole blood EPA, DHA and Omega-3 Index following daily supplementation with 450 mg of algae-derived EPA+DHA in midlife women with low baseline oily fish intake. The magnitude of change observed is consistent with established incorporation kinetics of long-chain omega-3 fatty acids into whole blood and red blood cell membranes and supports effective bioavailability of the algae-derived formulation.

At baseline, the cohort mean Omega-3 Index was 5.03 ± 1.49%, falling within the intermediate range (4–8%), approaching the lower boundary associated with increased cardiovascular risk (< 4%). 4 women (14%) had an Omega-3 Index < 4% (Figure 1). Following supplementation, the mean Omega-3 Index increased to 6.86 ± 1.12% at week 6 and was sustained at 6.81 ± 1.65% at week 12 (Figure 1). No women at 6 and 12 weeks had Omega-3 Index < 4%. In paired analyses (n = 28), the Omega-3 Index increased by 1.74 ± 1.18 percentage points from baseline to week 6 ($t(27) = 7.78$, $p < 0.00001$), corresponding to a large effect size (Cohen's $d = 1.47$) (Figure 1). At week 12, 4 of 21 participants (19%) achieved an Omega-3 Index ≥ 8%, a level considered most desirable for cardioprotection (Figure 1).

Changes in whole blood EPA over 12 Weeks

Mean whole blood EPA increased over the supplementation period (Figure 2). At baseline, the cohort mean EPA was 1.25 ± 0.48%. Following supplementation, mean EPA increased to 1.91 ± 0.57% at week 6 and remained elevated at 1.86 ± 0.58% at week 12 (Figure 2). In paired analyses (n = 28), EPA increased by 0.66 percentage points from baseline to week 6 (paired two-tailed t-test, $p < 0.001$), corresponding to a large effect size (Figure 2). Among participants with paired baseline and week 12 data (n = 23), EPA remained significantly elevated compared with baseline (mean increase 0.61 percentage points; $p < 0.001$), also demonstrating a large effect size (Figure 2). These findings indicate rapid and sustained whole blood incorporation of EPA over the supplementation period.

Changes in whole blood DHA Over 12 Weeks

At baseline, the cohort mean whole blood DHA was 3.78 ± 1.11%. Following supplementation, DHA increased to 4.95 ± 0.74% at week 6 and further increased to 5.14 ± 0.92% at week 12 (Figure 3). In paired analyses (n = 28), DHA increased by 1.17 percentage points from baseline to week 6 ($t(27) = 7.78$, $p < 0.001$), corresponding to a large effect size (Cohen's $d = 1.47$) (Figure 3). Among participants with paired baseline and week 12 data (n = 23), DHA increased by 1.36 percentage points ($t(22) = 6.37$, $p < 0.001$), also demonstrating a large effect size (Cohen's $d = 1.33$) (Figure

3). The progressive increase between week 6 and week 12 suggests continued whole blood enrichment consistent with known DHA incorporation kinetics.

Changes in Omega-6:Omega-3 ratio over 12 weeks

The omega-6:omega-3 ratio decreased significantly over the course of the intervention. Mean values declined from 6.42 ± 1.83 at baseline to 4.78 ± 0.75 at week 6, representing a mean reduction of 1.46 units (paired t-test, $t(27) = -6.02$, $p < 0.001$, Cohen's $d = 1.14$) (Figure 4). At week 12, the ratio remained significantly lower than baseline (4.95 ± 1.01), corresponding to a mean reduction of 1.52 units (paired t-test, $t(22) = -6.60$, $p < 0.001$, Cohen's $d = 1.38$). These findings indicate a sustained shift toward a lower omega-6:omega-3 ratio during supplementation.

Changes in AA:EPA Ratio over 12 weeks

The AA:EPA ratio decreased significantly during the intervention. Mean values declined from 11.63 ± 5.75 at baseline to 7.43 ± 2.15 at week 6, representing a mean reduction of 3.79 units (paired t-test, $t(27) =$

−4.18, p < 0.001, Cohen's d = 0.79) (Figure 5). At week 12, the AA:EPA ratio remained significantly lower than baseline (7.39 ± 2.20), corresponding to a mean reduction of 3.71 units (paired t−test, t(22) = −4.15, p < 0.001, Cohen's d = 0.87).

These findings indicate a sustained shift toward a lower AA:EPA ratio following supplementation.

Changes in Trans-Fat Index Over 12 Weeks

The whole blood trans fat index decreased during the intervention (Figure 6). Mean values declined from 0.58 ± 0.15 at baseline to 0.45 ± 0.11 at week 6, representing a mean reduction of 0.12 units (paired t−test, t(27) = −3.47, p = 0.0018, Cohen's d = 0.66) (Figure 6).

At week 12, the trans fat index remained significantly lower than baseline (0.48 ± 0.17), corresponding to a mean reduction of 0.11 units (paired t−test, t(22) = −2.52, p = 0.019, Cohen's d = 0.53) (Figure 6).

Self-reported well-being outcomes

Self-reported general well-being was assessed using a structured questionnaire at weeks 6 and 12. On a 0–10 scale, mean general wellbeing scores were 7.36 ± 1.60 at week 6 (n = 14) and 8.31 ± 1.18 at week 12 (n = 13) (Table 1). Scores were consistently high and showed a modest increase between week 6 and week 12.

Participants also rated perceived effectiveness of the intervention for overall well-being, with mean scores of 7.86 ± 2.11 at week 6 and 8.54 ± 1.20 at week 12 (0–10 scale), suggesting sustained positive perception over time.

When asked to identify specific areas of perceived positive change, participants most frequently cited mobility (5/13), skin (4/13) and cognitive clarity/focus (2/13) as areas of perceived improvement at week 6 (Table 2). By week 12, skin (5/13) and cognitive clarity/focus (4/13) were most commonly reported, followed by mobility (3/13). These responses are descriptive and exploratory.

Discussion

This 12-week pilot study evaluated changes in whole blood fatty acid composition following daily supplementation with 450 mg of algae-derived EPA+DHA in midlife women with low baseline oily fish intake. Supplementation resulted in significant increases in whole blood EPA, DHA and Omega-3 Index, with measurable changes evident within six weeks and sustained through 12 weeks.

At baseline, the cohort mean Omega-3 Index (5.03%) fell within the intermediate range (4–8%), a level commonly observed in Western populations (Schuchardt et al., 2024) and associated with suboptimal long-chain omega-3 status. Following supplementation, the Omega-3 Index increased to 6.86% at week 6 and remained elevated at 6.81% at week 12. Although the cohort mean remained below the proposed optimal range of 8–12% (Harris WS & Von Schacky C. 2004), the observed increase represents a meaningful increase in omega-3 status, particularly given the relatively modest daily intake of EPA+DHA. Notably, 19% of participants achieved an Omega-3 Index ≥ 8% by week 12, a level associated with lower cardiovascular risk in observational studies.

The increase in Omega-3 Index was accompanied by significant rises in both EPA and DHA, indicating effective incorporation of supplemented long-chain omega-3 fatty acids into circulating lipid pools. EPA increased rapidly within the first six weeks of supplementation, whereas DHA continued to increase progressively through week 12. This temporal pattern is consistent with

previously reported kinetics of omega-3 fatty acid incorporation, where EPA tends to respond more rapidly to supplementation while DHA incorporation may continue over longer periods due to its structural role in membrane phospholipids (Browning et al., 2012). Previous studies have shown similar response dynamics: whole blood EPA and DHA concentrations typically rise within 4–8 weeks of supplementation as membrane phospholipids equilibrate with circulating fatty acid pools (Flock 2014, Walker RE et al. 2019). These findings are consistent with established incorporation of long-chain omega-3 fatty acids into circulating lipid pools and cellular membranes.

The increase in omega-3 fatty acid status were accompanied by favourable changes in several complementary fatty acid balance markers. The omega-6:omega-3 ratio decreased significantly from baseline to week 6 and remained lower at week 12, reflecting the relative increase in long-chain omega-3 fatty acids within the overall fatty acid pool. Although the clinical relevance of the omega-6:omega-3 ratio remains debated (Harris, 2006; Stanley et al., 2007; Jackson et al., 2024), lower values can be interpreted as reflecting a shift toward a more omega-3-enriched lipid profile.

A particularly notable finding was the reduction in the AA:EPA ratio. This ratio reflects the balance between the omega-6 fatty acid arachidonic acid, a precursor to pro-inflammatory eicosanoids, and EPA, which can compete for the same enzymatic pathways and give rise to less inflammatory lipid mediators (Calder, 2010; Calder, 2020a, Calder, 2020b, Calder, 2021). The significant reduction in AA:EPA ratio observed in this study suggests a shift in fatty acid balance that may influence downstream inflammatory signalling pathways. While clinical implications cannot be inferred from this pilot study, the magnitude of change observed is consistent with

known biochemical effects of increasing EPA availability.

The trans-fat index remained low throughout the study and decreased modestly over the intervention period. While trans-fatty acids primarily reflect dietary intake rather than endogenous metabolism, reductions in the index may reflect displacement effects within circulating fatty acid pools as EPA and DHA increase. However, the magnitude of change was small and should be interpreted cautiously.

The formulation also contained the omega-7 monounsaturated fatty acid palmitoleic acid from sea buckthorn oil. As the primary outcomes were specific to EPA and DHA incorporation, the observed changes are consistent with increased EPA and DHA enrichment. However, the study was not designed to isolate the independent effects of omega-7, and a contribution from other components cannot be excluded.

An important aspect of the present findings is that these fatty acid biomarker changes were achieved with a daily intake of 450 mg EPA+DHA, a level aligned with UK dietary recommendations for long-chain omega-3 intake. Many intervention studies investigating omega-3 fatty acid supplementation use substantially higher doses, often several g per day. The present results suggest that even moderate increases in EPA and DHA intake may produce a measurable increase in omega-3 status in individuals with low baseline intake. This is particularly relevant in populations where habitual oily fish consumption is limited.

The use of an algae-derived EPA + DHA formulation is also noteworthy. Increasing adoption of

plant-based dietary patterns has the potential to reduce intake of marine-derived omega-3 fatty acids in many populations, including those already consuming low amounts. Also, sustainability concerns surrounding global fisheries continue to grow (Lewis et al., 2025). Algal oils provide a direct source of long-chain omega-3 fatty acids (EPA and DHA) without reliance on marine animal harvesting. Demonstrating effective increases in whole blood EPA and DHA following algae-derived supplementation therefore has relevance both nutritionally and from a sustainability perspective.

The current study focused specifically on midlife women, a population frequently underrepresented in cardiovascular, metabolic and nutrition research. Hormonal transition during perimenopause and menopause is associated with shifts in lipid metabolism, vascular function and inflammatory signalling. Ensuring adequate EPA and DHA status during this life stage may therefore be of particular physiological relevance. By focusing on a defined female cohort during hormonal transition, the present study contributes to addressing persistent sex-specific gaps in nutrition research.

Participant-reported wellbeing scores were generally high and increased modestly over the course of the study, with mobility, skin, and cognitive clarity most frequently reported as areas of perceived increase. However, given the open-label design and absence of a control group, these findings should be interpreted cautiously. Subjective outcomes were exploratory and intended to generate hypotheses rather than establish causal relationships.

The community-based framework used in this study represents a real-world evidence approach that may complement traditional randomised controlled trials (RCTs). While RCTs remain essential for establishing causal effects under controlled conditions, real-world studies can provide

insight into feasibility, adherence and biomarker responses in community-based populations. Such approaches may be particularly useful in populations that are motivated to engage in proactive health behaviours but are often underrepresented in large clinical trials.

Several limitations should be acknowledged. The study employed a prospective, single-arm, within-participant design without a comparator group. which limits the ability to attribute observed changes solely to the intervention. It is worth noting that in the study of Browning et al. (2012), no changes in EPA and DHA levels in blood pools, including plasma lipids, mononuclear cells, red blood cells and platelets, occurred over 12 months in a placebo group who did not change their intake of EPA+DHA, suggesting long-term stability of blood EPA and DHA in the absence of altered intake. The sample size was modest, and participants were recruited from a health-engaged community, which may limit generalisability. Dietary intake during the intervention period was not tightly controlled and may have contributed to variability in response. Subjective well-being outcomes were based on self-report and not assessed using validated psychometric instruments.

Despite these limitations, the magnitude and consistency of biomarker changes across multiple fatty acid indicators strengthen confidence in the observed biological response to supplementation. The convergence of increases in EPA, DHA and Omega-3 Index alongside reductions in omega-6:omega-3 and AA:EPA ratios suggests meaningful shifts in whole blood fatty acid composition over the 12-week period.

Future studies should incorporate randomised controlled designs, larger and more diverse populations, and validated patient-reported outcome measures. Further research specifically examining omega-3 status and supplementation responses in women during perimenopause and menopause would also help address important life-stage-specific evidence gaps.

Conclusions

In this 12-week longitudinal study, supplementation with algae-derived EPA and DHA was associated with significant increases in whole blood omega-3 biomarkers, including the Omega-3 Index, in midlife women with low baseline intake. These findings demonstrate measurable changes in omega-3 status at guideline-aligned intake levels under real-world conditions. Further controlled studies are warranted to confirm clinical relevance.

Contributions of the authors

J. Macciochi designed the study. Jenna Macciochi and the Ancient + Brave team were responsible for participant recruitment and study conduct. Data analysis was performed by J. Macciochi and SureScreen Diagnostics. Jenna Macciochi and Faye Murton drafted the manuscript with input from Uta Boellinger, Izzy Hartnoll, Jenni Kiddle, Jo Woodhurst and Jordan Musselle-Sexton. The manuscript was reviewed and critically revised by Professor Philip Calder.

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Conflicts of Interest

Jenna Macciochi, Faye Murton, Izzy Hartnoll, Jenni Kiddle, Jo Woodhurst and Uta Boellinger are affiliated with Ancient + Brave, the manufacturer of the intervention product.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Author Biographies

Dr Jenna Macciochi is an immunologist, author and Director of Science and Innovation at Ancient + Brave. Faye Murton is an MSc Registered Associate Nutritionist (ANutr). Izzy Hartnoll is an MSc Registered Associate Nutritionist (ANutr). Jo Woodhurst and Uta Bollinger are BANT-registered nutritionists.

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Figures

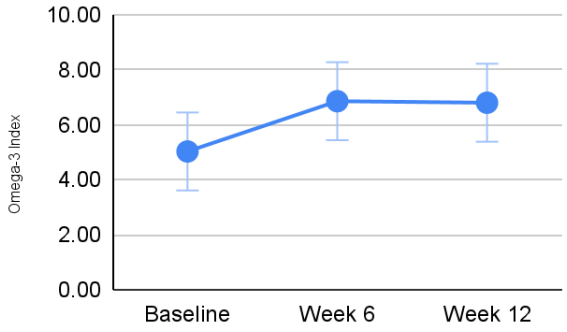


Figure 1. Mean Omega-3 Index at Baseline and 6 and 12 weeks of supplementation. Values represent mean ± SD (baseline n = 28; week 6 n = 28; week 12 n = 23 for paired analysis). Paired two-tailed t-tests demonstrated significant increases from baseline to week 6 ($t(27) = 7.78$, $p < 0.001$) and from baseline to week 12 ($t(22) = 6.37$, $p < 0.001$).

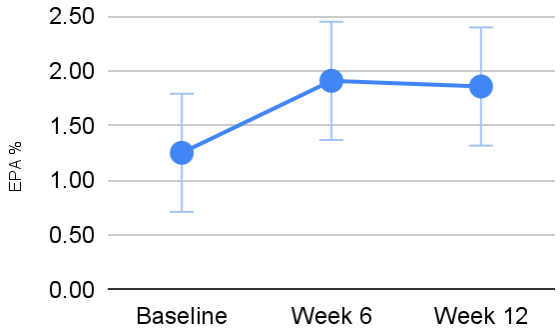


Figure 2. Mean whole blood EPA (% of total whole blood fatty acids) at Baseline and 6 and 12 weeks of supplementation. Values represent mean ± SD (baseline n = 28; week 6 n = 28; week 12 n = 23 for paired analysis). Paired two-tailed t-tests demonstrated significant increases from baseline to week 6 and baseline to week 12 ($p < 0.001$ for both comparisons).

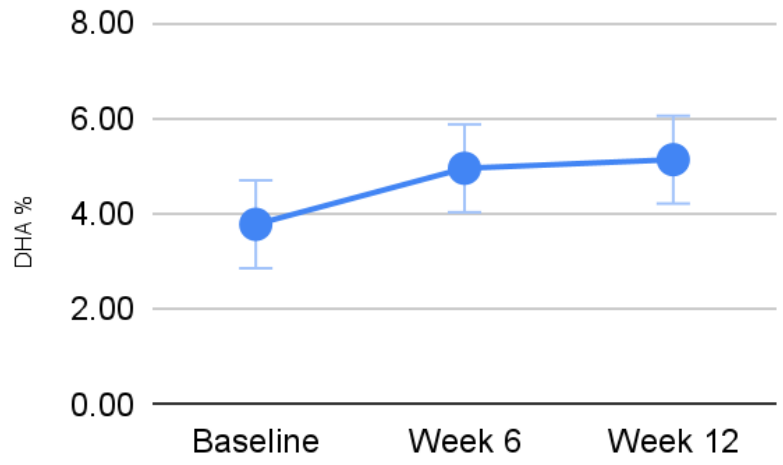


Figure 3. Whole blood DHA (%) at Baseline and 6 and 12 weeks of supplementation. Values represent mean ± SD (baseline n = 28; week 6 n = 28; week 12 n = 23 for paired analysis). Paired two-tailed t-tests demonstrated significant increases from baseline to both week 6 and week 12 ($p < 0.001$).

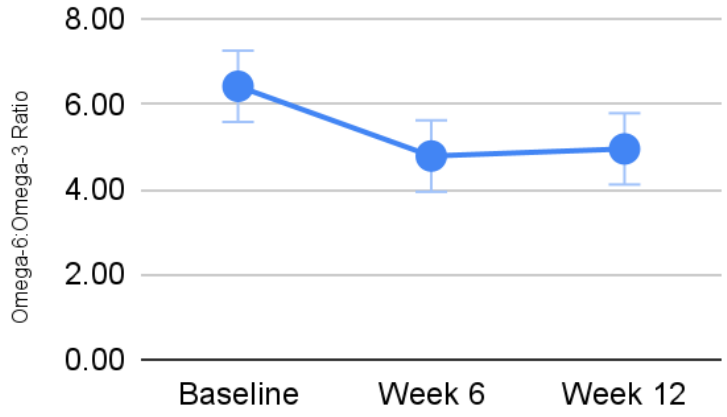


Figure 4. Whole blood Omega-6:3 ratio at Baseline and 6 and 12 weeks of supplementation. MValues represent mean ± SD. The ratio decreased significantly from baseline to week 6 and remained significantly lower at week 12 (paired t-test, $p < 0.001$).

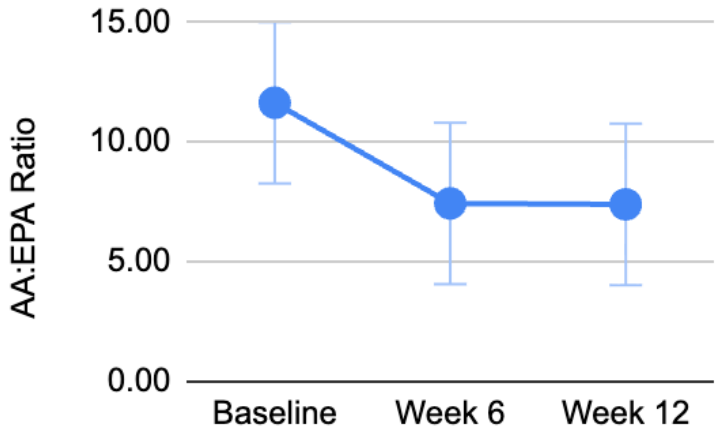


Figure 5. Whole blood AA:EPA ratio at Baseline and 6 and 12 weeks of supplementation. Values represent mean ± SD. The AA:EPA ratio decreased significantly from baseline to week 6 and remained significantly lower at week 12 (paired t-test, $p < 0.001$).

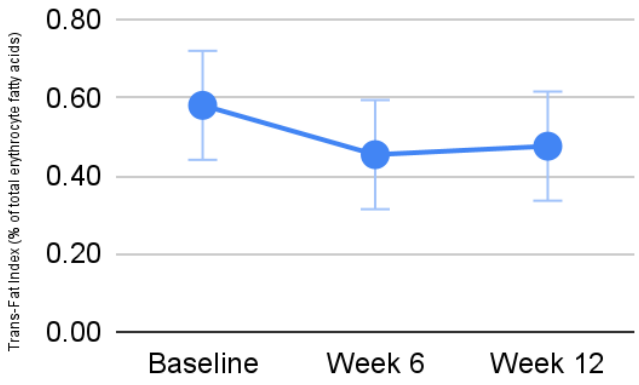


Figure 6. Whole blood trans fat index at Baseline and 6 and 12 weeks of supplementation. MValues represent mean ± SD. The trans fat index decreased significantly from baseline to week 6 and remained significantly lower at week 12 (paired t-test, $p < 0.05$).

Timepoint	Mean	SD	n
General well-being (0–10 scale)			
Week 6	7.36	1.60	14
Week 12	8.31	1.18	13
Perceived effectiveness (0-10 scale)			
Week 6	7.86	2.11	14
Week 12	8.54	1.20	13

Table 1. Self-reported well-being outcomes at week 6 and 12 of supplementation.

	Week 6 (n=14)	Week 12 (n=13)
Mobility	5	3
Skin	4	5
Cognitive clarity/focus	2	4
Mood	1	1
Recovery from exercise	1	0

Table 2. Most Frequently Reported Areas of Perceived Positive Change at Weeks 6 and 12 of Supplementation.

References

+ Alexander, D.D., Bialkowski, W., van der Veen, S., Herson, J., Bye, T., Birnbaum, Z., Harris, W.S., Ahnen, D.J. and Miller, P.E. (2017) 'A Meta-Analysis of Randomized Controlled Trials and Prospective Cohort Studies of Eicosapentaenoic and Docosahexaenoic Long-Chain Omega-3 Fatty Acids and Coronary Heart Disease Risk', *Mayo Clinic Proceedings*, 92(1), pp. 15–29. Available at: https://doi.org/10.1016/j.mayocp.2016.10.018.
+ Allam-Ndoul, B., Guénard, F., Barbier, O. and Vohl, M.-C. (2017) 'Effect of different concentrations of omega-3 fatty acids on stimulated THP-1 macrophages', *Genes & Nutrition*, 12(1), p. 7. Available at: https://doi.org/10.1186/s12263-017-0554-6(Accessed: 4 March 2026).
+ Bailey, E., Wojcik, J., Rahn, M., Roos, F., Spooren, A. and Koshibu, K., 2025. Comparative Bioavailability of DHA and EPA from Microalgal and Fish Oil in Adults. *Nutrients*, 17(19), p.4109. https://doi.org/10.3390/nu17194109
+ Bernstein, A.M., Ding, E.L., Willett, W.C. and Rimm, E.B. (2012) 'A meta-analysis shows that docosahexaenoic acid from algal oil reduces serum triglycerides and increases HDL-cholesterol and LDL-cholesterol in persons without coronary heart disease', *Journal of Nutrition*, 142(1), pp. 99–104. doi:10.3945/jn.111.148973.
+ Browning, L.M., Walker, C.G., Mander, A.P., West, A.L., Madden, J., Gambell, J.M., Young, S., Wang, L., Jebb, S.A. and Calder, P.C., 2012. Incorporation of eicosapentaenoic and docosahexaenoic acids into lipid pools when given as supplements

providing doses equivalent to typical intakes of oily fish. *The American Journal of Clinical Nutrition*, 96(4), pp.748–758. https://doi.org/10.3945/ajcn.112.041343

+ Calder, P.C., 2010. Omega-3 fatty acids and inflammatory processes. *Nutrients*, 2(3), pp. 355–374. doi: 10.3390/nu2030355

+ Calder, P. C. (2015) 'Functional roles of fatty acids and their effects on human health', *Journal of Parenteral and Enteral Nutrition*, 39(1_suppl), 18S–32S. https://doi.org/10.1177/0148607115585912.

+ Calder, P.C., 2018. Very long-chain n-3 fatty acids and human health: fact, fiction and the future. *Proceedings of the Nutrition Society*, 77(1), pp.52–72. https://doi.org/10.1017/S0029665117003950

+ Calder, P. C. (2020) 'Omega-3 fatty acids and inflammatory processes: from molecules to man', *Biochemical Society Transactions*, 48(3), 1109–1127. https://doi.org/10.1042/BST20191317.

+ Calder PC. n-3 PUFA and inflammation: from membrane to nucleus and from bench to bedside. Proceedings of the Nutrition Society. 2020b;79:404–416.

+ Calder PC. Eicosanoids. *Essays in Biochemistry*. 2020a;64(3):423–441.

+ Calder, P.C., 2021. n-3 PUFA and inflammation: from membrane to nucleus and from bench to bedside. *Proceedings of the Nutrition Society*, 80(1), pp.68–81. https://doi.org/10.1017/S0029665120007077

+ Calder, P.C., Cawood, A.L., James, C., Page, F., Putnam, S. and Minihane, A.M., 2026. An overview of national and international long chain omega-3 polyunsaturated fatty acid intake recommendations for healthy populations. *Nutrition Research Reviews*, pp.1–28. https://doi.org/10.1017/S0954422425000179

+ Camon, C., Garratt, M. and Correa, S.M. (2024) ‘Exploring the effects of estrogen deficiency and aging on organismal homeostasis during menopause’, *Nature Aging*, 4(12), pp. 1731–1744. https://doi.org/10.1038/s43587-024-00767-0

+ Craddock, J. C., E. P. Neale, Y. C. Probst, and G. E. Peoples. 2017. Algal supplementation of vegetarian eating patterns improves plasma and serum docosahexaenoic acid concentrations and Omega-3 indices: A systematic literature review. *Journal of Human Nutrition and Dietetics: The Official Journal of the British Dietetic Association* 30 (6):693–9. doi: 10.1111/jhn.12474.

+ Criado Perez, C. (2019) Invisible Women: Exposing Data Bias in a World Designed for Men. Chatto & Windus. Available at: https://carolinecriadoperez.com/book/invisible-women/ (Accessed: 27 March 2026).

+ De Groot, R.H.M., Emmett, R. and Meyer, B.J., 2019. Non-dietary factors associated with n-3 long-chain PUFA levels in humans - a systematic literature review. *British Journal of Nutrition*, 121(7), pp.793–808. https://doi.org/10.1017/S0007114519000138

+ Derbyshire, E. (2019) 'Oily Fish and Omega-3s Across the Life Stages: A Focus on Intakes and Future Directions', *Frontiers in Nutrition*, 6, p. 165. Available at: https://pubmed.ncbi.nlm.nih.gov/31781570/ (Accessed: 12 December 2025).

+ Fekete, K., Marosvölgyi, T., Jakobik, V. and Decsi, T. (2009) ‘Methods of assessment of n-3 long-chain polyunsaturated fatty acid status in humans: a systematic review’, *American Journal of Clinical Nutrition*, 89(6), pp. 2070S–2074S.

+ Flock MR, Skulas-Ray AC, Harris WS, Etherton TD, Fleming JA, Kris-Etherton PM. Determinants of erythrocyte omega-3 fatty acid content in response to fish oil supplementation: a dose-response randomized controlled trial. J Am Heart Assoc. 2013

Nov 19;2(6):e000513. doi: 10.1161/JAHA.113.000513. PMID: 24252845; PMCID: PMC3886744.

+ Fu, Y., Wang, Y., Gao, H., Li, D., Jiang, R., Ge, L., Tong, C., & Xu, K. (2021). Associations among dietary omega-3 polyunsaturated fatty acids, the gut microbiota, and intestinal immunity. *Mediators of Inflammation, 2021*, 8879227. https://doi.org/10.1155/2021/8879227

+ Harris, William & Polreis, Jason. (2016). Measurement of the Omega-3 Index in Dried Blood Spots. Annals of Clinical and Laboratory Research. 04. 10.21767/2386-5180.1000137.

+ Harris WS, Von Schacky C. (2004). The Omega-3 Index: a new risk factor for death from coronary heart disease?', Preventive Medicine, 39(1), pp. 212–220. doi:10.1016/j.ypmed.2004.02.030.

+ Harris WS. Omega-3 fatty acids and cardiovascular disease: a case for omega-3 index as a new risk factor. Pharmacol Res. 2007 Mar;55(3):217-23. doi: 10.1016/j.phrs.2007.01.013. Epub 2007 Jan 25. PMID: 17324586; PMCID: PMC1899522.

+ Harris, W.S., 2006. The omega-6/omega-3 ratio and cardiovascular disease risk: uses and abuses. *Current Atherosclerosis Reports*, 8(6), pp.453–459. https://doi.org/10.1007/s11883-006-0019-7

+ Harris WS, Tintle NL, Etherton MR, Vasan RS. (2023) Estimation and predictors of the Omega-3 Index in the UK Biobank. *British Journal of Nutrition*, 130(2), pp. 223–232. https://doi.org/10.1017/S0007114522003117

+ Jackson, K.H., Harris, W.S., Belury, M.A., Kris-Etherton, P.M. and Calder, P.C., 2024. Beneficial effects of linoleic acid on cardiometabolic health: an update. *Current Opinion in Clinical Nutrition & Metabolic Care*, 27(6), pp.447–455. https://doi.org/10.1097/MCO.0000000000001023

+ Lane, K.E., Derbyshire, E., Medina, A., Loughrill, E., Holmes, M. and Wall, C. (2022) 'Bioavailability and conversion of plant-based sources of Omega-3 fatty acids – a scoping review of human studies', Critical Reviews in Food Science and Nutrition, 62(13), pp. 3493–3521. doi:10.1080/10408398.2021.1880364.

+ Lewis, E., Steenson, S., Haslam, R. P., McDonald, E., Sharman, M., Traka, M., Stanton, A., Napier, J. A., Sweeting, A., Saleh, R. N. M., Hornberger, M., Givens, I., Calder, P. C., & Minihane, A. M. (2025). Sustainable and available sources of omega-3 fatty acids for health: Are the current dietary recommendations, food sources and legislation fit for purpose? *Nutrition Research Reviews*, 1–16. https://doi.org/10.1017/S0954422425100127

+ Lohner, S., Fekete, K., Marosvölgyi, T. and Decsi, T., 2013. Gender differences in the long-chain polyunsaturated fatty acid status: systematic review of 51 publications. *Annals of Nutrition and Metabolism*, 62(2), pp.98–112. https://doi.org/10.1159/000345599

+ Lovejoy, J.C., Champagne, C.M., de Jonge, L., Xie, H. and Smith, S.R. (2008) 'Increased visceral fat and decreased energy expenditure during the menopausal transition', *Obesity (Silver Spring)*, 16(6), pp. 1364–1370. doi: 10.1038/oby.2008.187.

+ Mauvais-Jarvis, F. (2015). Sex differences in metabolic homeostasis, diabetes, and obesity. *Endocrinology*, 156(10), 3232–3241. https://doi.org/10.1210/en.2015-1556

+ National Diet and Nutrition Survey (2021) *National Diet and Nutrition Survey: results from years 11–14 (2019–2022)*. London: Department of Health and Social Care / Food Standards Agency / NatCen Social Research / MRC Epidemiology Unit. Available at: https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-2019-to-2023(accessed 27 March 2026).

+ National Institutes of Health, Office of Dietary Supplements (2025) *Omega-3 Fatty Acids: Health Professional Fact Sheet*. Available at: https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/ (Accessed: 12 December 2025).disease? Prev Med. 2004 Jul;39(1):212-20. doi:10.1016/j.ypmed.2004.02.030. PMID: 15208005

+ Peters, B.A., Lin, J., Qi, Q., Usyk, M., Isasi, C.R., Mossavar-Rahmani, Y., Derby, C.A., Santoro, N., Perreira, K.M., Daviglus, M.L., Kominiarek, M.A., Cai, J., Knight, R., Burk, R.D. and Kaplan, R.C. (2022) 'Menopause is associated with an altered gut microbiome and estrobolome, with implications for adverse cardiometabolic risk in the Hispanic Community Health Study/Study of Latinos', *mSystems*, 7(3), p.e0027322. doi: 10.1128/msystems.00273-22.

+ Pizzini, A., Lunger, L., Sahanic, S., Nemec, A., Egger, A., Hoermann, G., Kurz, K., Widmann, G., Bellmann-Weiler, R., Weiss, G., Sonnweber, T., & Tancevski, I. (2019). Effects of omega-3 fatty acids on immune cells. *International Journal of Molecular Sciences, 20*(21), 5028. https://doi.org/10.3390/ijms20205028

+ Russell, F.D. and Meital, L.T. (2022) 'Health impacts of Omega-3 fatty acid deficiency', Nutrients, 14(12), 2554. doi:10.3390/nu14122554

+ Ryan, L. & Symington, A. M. (2015) ‘Algal-oil omega-3 fatty acids: bioavailability and implications for human health’, *Nutrition Research Reviews*, 28(2), 239–251. https://doi.org/10.1017/S0954422415000017.[web

+ Schuchardt, J.P., Beinhorn, P., Hu, X.F., Chan, H.M., Roke, K., Bernasconi, A., Hahn, A., Sala-Vila, A., Stark, K.D. and Harris, W.S., 2024. Omega-3 world map: 2024 update. *Progress in Lipid Research*, 95, p.101286. https://doi.org/10.1016/j.plipres.2024.101286

+ Scientific Advisory Committee on Nutrition (SACN) (2004) *Advice on fish consumption: benefits and risks*. London: Food Standards Agency. Available at: https://www.gov.uk/government/publications/sacn-advice-on-fish-consumptio (accessed 27 March 2026)

+ Scientific Advisory Committee on Nutrition (SACN) (2020) *Dietary recommendations for long-chain n-3 polyunsaturated fatty acids (EPA and DHA)* (statement updating 2004 fish-intake advice). London: Department of Health and Social Care. Available at: https://www.gov.uk/government/publications/sacn-statement-on-expressing-fat-and-carbohydrate-recommendations (accessed 27 March 2026)

+ Stanley, J.C., Elsom, R.L., Calder, P.C., Griffin, B.A., Harris, W.S., Jebb, S.A., Lovegrove, J.A., Moore, C.S., Riemersma, R.A. and Sanders, T.A.B., 2007. UK Food Standards Agency Workshop Report: the effects of the dietary n-6:n-3 fatty acid ratio on cardiovascular health. *British Journal of Nutrition*, 98(6), pp.1305–1310. https://doi.org/10.1017/S000711450784284X

+ Swanson, D., Block, R. and Mousa, S.A. (2012) 'Omega-3 Fatty Acids EPA and DHA: Health Benefits Throughout Life', *Advances in Nutrition*, 3(1), pp. 1–7. Available at: https://doi.org/10.3945/an.111.000893

+ Tramunt, B., Smati, S., Grandgeorge, N., Lenfant, F., Arnal, J.-F., Montagner, A., & Gourdy, P. (2020). Sex differences in metabolic regulation and diabetes susceptibility. *Diabetologia*, 63(3), 420–431. https://doi.org/10.1007/s00125-019-05046-4

+ Walker RE, Jackson KH, Tintle NL, Shearer GC, Bernasconi A, Masson S, Latini R, Heydari B, Kwong RY, Flock M, Kris-Etherton PM, Hedengran A, Carney RM, Skulas-Ray A, Gidding SS, Dewell A, Gardner CD, Grenon SM, Sarter B, Newman JW, Pedersen TL, Larson MK, Harris WS. Predicting the effects of supplemental EPA and DHA on the omega-3 index. Am J Clin Nutr. 2019 Oct 1;110(4):1034-1040. doi: 10.1093/ajcn/nqz161. PMID: 31396625.

+ Yurko-Mauro, K., McCarthy, D., Rajamanickam, D., Nelson, E.B., Van Dyck, C., Gray, R., Nelson, B., Jack, C., Jr., Quinn, J.F., McAnulty, P. and Raman, R. (2010) 'Beneficial effects of docosahexaenoic acid on cognition in age-related cognitive decline', *Alzheimer's & Dementia*, 6(6), pp. 456–464. Available at: https://doi.org/10.1016/j.jalz.2010.01.013.