Etiology and Pathophysiology/Metabolism

Fish or n3-PUFA intake and body composition: a systematic review and meta-analysis

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Summary

Obesity is a major public health issue and an important contributor to the global burden of chronic disease and disability. Studies indicate that fish and omega-3 polyunsaturated fatty acids (n3-PUFA) supplements may help prevent cardiovascular and metabolic diseases. However, the effect of fish oil on body composition is still uncertain, so we performed a systematic review of randomized controlled trials and the first meta-analysis on the association between fish or fish oil intake and body composition measures. We found evidence that participants taking fish or fish oil lost 0.59 kg more body weight than controls (95% confidence interval [CI]: −0.96 to −0.21). Treatment groups lost 0.24 kg m⁻² (body mass index) more than controls (−0.40 to −0.08), and 0.49 % more body fat than controls (−0.97 to −0.01). Fish or fish oil reduced waist circumference by 0.81 cm (−1.34 to −0.28) compared with control. There was no difference for fat mass and lean body mass. Further research is needed to confirm or refute our findings and to reveal possible mechanisms by which n3-PUFAs might reduce weight.

Keywords: Body composition, fish, n3-PUFA.

Introduction

Obesity is a major public health issue and an important contributor to the global burden of chronic disease and disability (1). For more than two decades, the prevalence and incidence of obesity worldwide has reached pandemic proportions (1,2). Its association with deleterious outcomes, such as type 2 diabetes, heart disease and depression, and its direct relation to increased all-cause mortality and reduced life expectancy (1,3,4) make it a pressing global health problem.

Attempts to control the epidemic of obesity usually target behaviour and environmental aspects of the problem. The World Health Organization strategy consists of a range of long-term measures, including primary prevention, weight maintenance, management of complications and weight loss (5). However, the global obesity epidemic continues despite these measures, indicating that new approaches are needed.

A much-debated approach is consumption of omega-3 polyunsaturated fatty acids (n3-PUFA, including eicosapentaenoic acid [EPA] and docosahexanoic acid [DHA]), either through eating fish (which contain n3-PUFA) or taking supplements in the form of fish oil capsules. There is a growing evidence that n3-PUFAs have beneficial effects on health, including prevention of cardiovascular diseases, such as stroke and coronary heart disease (6,7), and metabolic diseases, such as dyslipidaemia (8,9). However, the influence of n3-PUFA on body composition is unclear.

Ecological studies in several countries indicate that a diet rich in fish is associated with low body weight (10). Several clinical studies suggest that fish oils and n3-supplements support weight-loss diets (11,12), but the benefit was not evident in other studies (13,14). A narrative review of these studies supported the argument that n3-PUFA may reduce obesity (15), whereas a systematic review of clinical trials that assessed the effects of dietary n3-PUFA on body weight in adults reported that four out of five studies did not show...
any important change (16). Only few randomized controlled trials (RCTs) assessed the influence of whole fish, and therefore a combination of fish oil and fish protein, on weight loss. These studies showed a similar effect of whole fish compared to fish oil, even when lean fish was used, suggesting a potential role of fish protein in weight loss (17–19). To date, no meta-analysis on this subject has been carried out.

We undertook a systematic review and meta-analysis of RCTs to assess the evidence for an effect of fish or fish oil on body composition.

Methods

Databases and search strategy

We conducted and reported the present meta-analysis according to the Cochrane Handbook of Systematic Reviews on Interventions (20) and the PRISMA guideline (21). We searched the electronic databases Medline, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL) (search last updated on 1 May 2013). The search strategy was combined for all exposures and outcomes of interest. Search terms included Fish, seafood, salmon, tuna, cod, anchovy, bass, bream, dogfish, eel, haddock, hake, herring, huss, mackerel, monkfish, mullet, plaice, red snapper, rock, sardines, pilchards, skate, sole, swordfish, trout, turbot, n3 fatty acid, n3 supplement*, n3 pufa, n3 polyunsaturated fatty acid, omega-3, eicosapentaenoic acid, EPA, docosahexanoic acid, DHA, and were combined with terms related to body composition: obesity, adiposity, body mass index, BMI, weight, waist, waist-to-hip ratio, WHR, fat, adipose, overweight, Quetelet index, diet, body composition. Where possible, we used MeSH headings (or other standardized indexing terms). The search was restricted to humans, but unrestricted for publication date or language (see Supporting Information Appendix S1 for Medline search strategy. Search strategies for Embase and CENTRAL were similar).

The reference lists of all included studies were examined to identify studies not found by the search of electronic databases. The references of all studies found were entered into an electronic database (Reference Manager, version 12, Thomson Reuters, New York, NY, USA) and duplicates were removed.

Eligibility criteria

The titles and abstracts of retrieved references were checked for inclusion or exclusion, according to the following pre-established criteria. We included RCTs in men or women and individuals of any ethnicity that reported body composition measures as primary or secondary outcomes. The exposures were fish or n3-PUFA derived exclusively from fish. Outcome measures were body mass index (BMI), body fat percentage, body weight, waist circumference, hip circumference, waist-to-hip ratio, lean body mass or other measures of body composition. We excluded studies that used n3-PUFA from vegetal sources, and RCTs with a crossover design that did not report results at cross-over. We also excluded studies that aimed to increase body weight for cachectic patients (22,23) or newborns (24,25). See flowchart in Fig. 1 for details on the identification of eligible studies. Two independent reviewers (NB, MP) assessed eligibility and reached consensus by discussion.

Data extraction

Two independent reviewers (NB, MP, ZH or KH) extracted data from the full-text papers on all studies included. The reviewers used a standard data extraction sheet, entered in duplicate into an electronic database (EpiData, version 3.1, Copenhagen, Denmark). Discrepancies were resolved by discussion. Bibliographic details (author, publication year), details of the population (e.g. gender, age, setting), sample size per comparison group and number of people lost to follow-up, exposure (fish or n-3 capsules) and daily dosage, obesity-related phenotypes (e.g. BMI, waist circumference) before and after the intervention were all extracted. Furthermore, potential confounders were accounted for and quality criteria such as type of randomization or blinding of participants and outcome assessors were extracted.

Study quality

To assess the internal validity of the studies and the accuracy of reporting, we followed published guidelines to a priori identify criteria that may be related to the risk of bias (26,27): sequence generation, concealment of allocation, blinding of participants, blinding of clinicians, blinding of outcome assessor and intention-to-treat analyses. For each included study, we noted whether or not the quality criteria were met, or if they were not described.

Data analysis

We combined data using fixed-effects meta-analyses. We calculated mean differences in changes from baseline between the two comparison groups, with 95% confidence intervals. Standard deviations of changes from baseline were consistently reported only in three studies (18,28,29). Where standard deviations of changes from baseline were missing, we used the formula provided in the Cochrane Handbook of Systematic Reviews (20) to calculate standard errors and then converted them into standard deviations. In this formula, we used a correlation coefficient of 0.8 for the outcome lean body mass, and 0.9 for the other outcomes, as reported in the studies.
Statistical evidence for heterogeneity between studies was assessed by the $I^2$ statistic (30). Funnel plots were used to examine possible small study bias; we used a regression test to test for funnel plot asymmetry (31). We also performed stratified analyses and random-effects meta-regressions to assess the effect of study quality criteria, patient characteristics and intervention characteristics on the results. The statistical package Stata (version 11.2, Stata Corp., College Station, TX, USA) was used for all analyses.

### Results

#### Study selection

We found 988 unique studies. After exclusions according to our criteria, we retrieved 38 studies as full text. Of these, 17 studies met the inclusion criteria, and we used 15 in the meta-analyses. We excluded two studies that reported results not in a format suited for meta-analysis. One (17) reported the outcomes as percentage of changes from baseline. This study showed no difference in body weight, waist circumference, fat mass and lean body mass between the fish group and the control group after an 8-week diet. The other study (32) reported outcome data (BMI and waist circumference) as median and interquartile ranges. It showed no difference between intervention and control groups after 3 years of follow-up.

#### Study characteristics of included studies

Most studies were conducted in European countries (eight studies). Three were carried out in Australia, two in North...
We did not find evidence for publication bias (see Supporting Information Appendix S2). The regression test (body weight: $P = 0.31$; BMI: $P = 0.63$) did not indicate publication bias.

### Results of meta-analyses

We gathered data suitable for meta-analyses for six different outcomes (body weight, BMI, body fat percentage, fat mass, waist circumference and lean body mass). In general, meta-analyses showed a more pronounced change in body composition in the intervention groups than in the control groups (Fig. 2 and Supporting Information Appendix S3). The heterogeneity between studies assessed by $I^2$ statistics was 0% for all meta-analyses performed.

The meta-analysis of outcome body weight (12 studies) showed more weight loss in the intervention groups than in the control groups ($-0.59$ kg, 95% confidence interval [CI]: $-0.96$ to $-0.21$, $P = 0.002$). For the outcome BMI (13 studies), the meta-analysis showed a greater decrease in BMI in the intervention groups than in the control groups ($-0.24$ kg m$^{-2}$, 95% CI: $-0.40$ to $-0.08$, $P = 0.003$). Similarly, for the outcome body fat percentage (seven studies),

### Table 1: Characteristics of studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Setting or population</th>
<th>Intervention group (n, % male)</th>
<th>Control group (n, % male)</th>
<th>Exposure, per day (mg): EPA/DHA</th>
<th>Duration of study (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abete et al. (17)*</td>
<td>Spain</td>
<td>General population</td>
<td>8 (100%)</td>
<td>10 (100%)</td>
<td>3 meals with fatty fish weekly</td>
<td>56</td>
</tr>
<tr>
<td>Bays et al. (29)</td>
<td>USA</td>
<td>Unclear</td>
<td>84 (71%)</td>
<td>83 (76%)</td>
<td>1,600/1,500</td>
<td>56</td>
</tr>
<tr>
<td>Crochemore et al.</td>
<td>Brazil</td>
<td>Hospital, high blood pressure and diabetes program</td>
<td>28 (0%)</td>
<td>13 (0%)</td>
<td>A: 357.5/352.5</td>
<td>30</td>
</tr>
<tr>
<td>DeFina et al. (68)</td>
<td>USA</td>
<td>General population</td>
<td>64 (31%)</td>
<td>64 (31%)</td>
<td>2,500/500</td>
<td>168</td>
</tr>
<tr>
<td>Ebrahim et al. (6)</td>
<td>Iran</td>
<td>General population</td>
<td>47 (15%)</td>
<td>43 (9%)</td>
<td>180/120</td>
<td>180</td>
</tr>
<tr>
<td>Emsley et al. (69)</td>
<td>South Africa</td>
<td>Community psychiatric services and university hospital</td>
<td>39 (69%)</td>
<td>33 (70%)</td>
<td>2,000</td>
<td>84</td>
</tr>
<tr>
<td>Hill et al. (70)</td>
<td>Australia</td>
<td>Unclear</td>
<td>33 (33%)</td>
<td>32 (41%)</td>
<td>Total 6,000</td>
<td>84</td>
</tr>
<tr>
<td>Itariu et al. (71)</td>
<td>Austria</td>
<td>Bariatric surgery clinic</td>
<td>27 (15%)</td>
<td>28 (18%)</td>
<td>1,840/1,520</td>
<td>56</td>
</tr>
<tr>
<td>Kabir et al. (11)</td>
<td>France</td>
<td>Diabetes department outpatient clinic</td>
<td>12 (0%)</td>
<td>14 (0%)</td>
<td>1,080/720</td>
<td>60</td>
</tr>
<tr>
<td>Kunesova et al. (28)</td>
<td>Czech Republic</td>
<td>Unclear</td>
<td>11 (0%)</td>
<td>9 (0%)</td>
<td>Total 2,800</td>
<td>21</td>
</tr>
<tr>
<td>Marques-Vidal et al. (72)</td>
<td>Spain</td>
<td>Follow up from SEAFOODPlus YOUNG Study</td>
<td>14 (100%)</td>
<td>7 (100%)</td>
<td>Total 1,070</td>
<td>56</td>
</tr>
<tr>
<td>Munro and Garg (13)</td>
<td>Australia</td>
<td>General population</td>
<td>18 (17%)</td>
<td>14 (21%)</td>
<td>420/1,620</td>
<td>98</td>
</tr>
<tr>
<td>Munro and Garg (12)</td>
<td>Australia</td>
<td>General population</td>
<td>20 (25%)</td>
<td>19 (21%)</td>
<td>420/1,620</td>
<td>56</td>
</tr>
<tr>
<td>Paniagua et al. (8)</td>
<td>8 European countries</td>
<td>LIPEGENE study</td>
<td>83 (48%)</td>
<td>77 (44%)</td>
<td>Total 1,240</td>
<td>84</td>
</tr>
<tr>
<td>Thorsdottir et al. (18)</td>
<td>Iceland, Spain, Ireland</td>
<td>SEAFOODPlus YOUNG Study</td>
<td>244 (43%)</td>
<td>80 (40%)</td>
<td>Total: cod: 300, salmon: 3,000, capsules: 1,500</td>
<td>56</td>
</tr>
<tr>
<td>Troseid et al. (32)*</td>
<td>Norway</td>
<td>Follow-up from Oslo Diet and Antismoking Study</td>
<td>282 (100%)</td>
<td>281 (100%)</td>
<td>840/480</td>
<td>1,095</td>
</tr>
<tr>
<td>Yamaoka et al. (19)</td>
<td>Japan</td>
<td>Female college students</td>
<td>57 (0%)</td>
<td>46 (0%)</td>
<td>0/700</td>
<td>35</td>
</tr>
</tbody>
</table>

*Not included in the meta-analyses.
the meta-analysis showed a greater decrease in the intervention groups than in the control groups (−0.49%, 95% CI: −0.97 to −0.01, \( P = 0.047 \)). Outcome waist circumference (seven studies) was also reduced more in the intervention groups than in the control groups (−0.81 cm, 95% CI: −1.34 to −0.28, \( P = 0.003 \)).

For the outcome fat mass (three studies), the meta-analysis showed no statistically significant difference between intervention and control groups (−0.36 kg, 95% CI: −0.96 to 0.24, \( P = 0.24 \)). Similarly, for the outcome lean body mass (three studies), the meta-analysis showed no statistically significant difference between intervention and control groups (−0.19 kg, 95% CI: −0.72 to 0.33, \( P = 0.47 \)).

### Sensitivity analyses and meta-regressions

Results were not modified by exposure characteristics (type of exposure [fish or fish oil], EPA/DHA ratio, dose per day, study time or additional interventions such as calorie-restricted diet or exercise), or participant characteristics (ethnicity, setting, age, nutritional stage, health condition, gender). We found that length of study (less than 60 d vs. more than 60 d) had a significant effect on the meta-regression for the outcome BMI (\( P = 0.028 \)): the effect was stronger in shorter studies (see also Fig. 3). Stratified analyses by gender showed stronger effects of n3-PUFA on reduction of obesity-related measures in men than in women, but this difference generally did not reach statistical significance (\( P > 0.17 \)). An exception was waist circumference (\( P = 0.050 \)): the meta-regression showed a stronger effect in men than in women (based upon three studies).

### Discussion

We found evidence that intake of fish or fish oil capsules can decrease weight in adults. When considered on their own, most studies did not show a statistically significant

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**Table 2  Methodological quality of studies**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sequence generation</th>
<th>Concealment of allocation</th>
<th>Blinding participants</th>
<th>Blinding investigator</th>
<th>Blinding outcome assessor</th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abete et al. (17)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>NA</td>
<td>NA</td>
<td>Unclear</td>
<td>Unclear</td>
</tr>
<tr>
<td>Bays et al. (29)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
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<tr>
<td>Crochemore et al. (14)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>DeFina et al. (68)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
</tr>
<tr>
<td>Ebrahimi et al. (6)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
<td>No</td>
<td>Unclear</td>
<td>No</td>
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<tr>
<td>Emsley et al. (69)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
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<td>Hill et al. (70)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Unclear</td>
<td>Unclear</td>
<td>No</td>
</tr>
<tr>
<td>Itariu et al (71)</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>Unclear</td>
<td>Yes</td>
</tr>
<tr>
<td>Kabir et al. (11)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Kunesova et al. (28)</td>
<td>Unclear</td>
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<td>Yes</td>
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<tr>
<td>Marques-Vidal et al. (72)</td>
<td>Yes</td>
<td>Unclear</td>
<td>NA</td>
<td>NA</td>
<td>Unclear</td>
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<tr>
<td>Munro and Garg (13)</td>
<td>Yes</td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Munro and Garg (12)</td>
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<td>Unclear</td>
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<td>Yes</td>
<td>Yes</td>
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<td>Paniagua et al. (8)</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
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<td>Thorsdottir et al. (18)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Troseid et al. (32)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Unclear</td>
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<tr>
<td>Yamaoka et al. (19)</td>
<td>Unclear</td>
<td>Unclear</td>
<td>NA</td>
<td>NA</td>
<td>Unclear</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

ITT, intention-to-treat analysis performed; NA, non-applicable.

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**Figure 2** Results of meta-analyses performed for different outcomes on the association between fish or fish oil intake and body composition. WC, waist circumference; BMI, body mass index.
difference: our meta-analyses documented effects that previous reviews had not detected (15,16). We included only RCTs that explicitly examined body composition-related measures as primary or secondary outcomes and used n3-PUFA of fish provenience. Our analysis was therefore not compromised by the possibility that n3-PUFA derived from vegetal sources had different effects than n3-PUFA derived from fish (33). Our study was, however, limited by poor reporting in the studies we examined. This made it difficult to assess the impact of study quality on the results.

The effect found in our meta-analyses was modest: 590 g mean difference in body weight between intervention and control groups. This finding was consistent for other body composition-related outcomes such as BMI, body fat percentage and waist circumference. For outcomes body fat mass and lean body mass, the direction of results was the same. However, results were not statistically significant, probably because of a lack of statistical power, as only few studies reported on these outcomes.

A modest weight loss of 5–10% body weight has been shown to be effective in improving risk factors such as hyperinsulinaemia, hypertension and dyslipidaemia (34–36). Indeed, Klein concluded that modest weight loss can affect the whole cluster of cardiovascular risk factors simultaneously (37). Troseid et al. found that despite small to moderate decreases in BMI, triglycerides and inflammatory markers such as IL-18 decreased after an n3-PUFA intervention, and an overall positive effect was obtained, probably by a combination of mechanisms (32). As obesity is associated with a low-grade inflammation state with mild elevation of several inflammatory markers expressed in adipose tissue, such as tumour necrosis factor-α or interleukin-6 (38–40), the anti-inflammatory effect of n3-PUFA might have a beneficial effect. In fact, n3-PUFA was shown to reduce insulin resistance in rats and humans (41,42) and proposed as a potential anti-inflammatory strategy to decrease obesity-related disease (43).

At a population level, the effect of a small change in a risk factor on an outcome can be substantial. This phenomenon is known as the ‘prevention paradox’ (44) and relates to the fact that a large number of people exposed to a low risk produce more cases of disease than a small number of people exposed to a high risk. In fact, the population attributable risk depends upon the individual attributable risk and the prevalence of the risk factor in the population. It is therefore more effective to shift the distribution of the risk factor (in this case overweight) in the whole population than to treat only those at high risk (obese people), even if the shift in the population is modest. We found that taking n3-PUFA for less than 2 months may be more effective than longer interventions. This finding questions the long-term effect of n3-PUFA on body composition, but as only few studies reported on these outcomes.
studies lasted longer than 2 months and only one study lasted more than a year (32), more long-term studies are needed to clarify this point.

In the present study, we found some indications that the effect might be greater in men than in women for the outcome waist circumference, which is a measure for visceral adiposity. This is relevant, as visceral fat is strongly associated with metabolic disease risks (45–47). Several studies reported that n3-PUFA had a stronger effect on weight loss in men than in women (e.g. Thorsdottir et al. (18)), whereas other studies found stronger effects in women (12). Difference between the sexes in the physiological response to n3-PUFA is plausible because men and women have a different fat tissue anatomy and physiology. For example, women may convert more α-linoleic acid into DHA than men do (48,49). A population-based study in New Zealand showed higher DHA levels and lower EPA levels in serum lipids in women compared to men (50). Future studies on the effect of n3-PUFA on body composition should examine gender differences in order to clarify possible differences in health benefits.

A further question is the relative importance of EPA and DHA. We did not find a dose–response relationship or an effect modification depending upon the EPA/DHA ratio, despite both animal studies (51,52) and human studies (28) suggesting this possibility. Several mechanisms have been proposed to explain the weight loss effect of n3-PUFA, for example, increased lipolysis and reduced lipogenesis. In rodents (53) and in humans (54), n3-PUFA stimulate β-oxidation, and inhibit fatty acid synthesis and very-low-density lipoprotein secretion, partially by regulating gene expression. In rats, there is indication that n3-PUFA might reduce lipogenesis in adipose cells by reducing lipoprotein lipase activity (55). In addition to n3-PUFA, fish protein might have an effect on body weight. For example, the amino acid taurine, which is abundant in fish protein, showed a weight-lowering effect in mice (56,57) and humans (58). In our meta-regressions, we did not find a difference between the effects of whole fish or of fish oil on body composition. However, only three studies included in our analysis used whole fish as exposure (17,18,59), so that more studies are needed using whole fish or fish protein to clarify the possible specific roles of fish oil and fish protein, and the different components of fish protein.

Our meta-analysis and other studies showed that n3-PUFA might influence body composition and health in a favourable way. Evolutionary considerations are also relevant in this context. Based upon estimates from studies on Palaeolithic nutrition and modern-day hunter-gatherer populations, it seems likely that humans have evolved with a diet that contained small and approximately equal amounts of n6- and n3-PUFA and lower amounts of trans-fatty acids and linoleic acid (60). A nutrition rich in n3-PUFA and other nutrients typical for the Palaeolithic diet, such as polyphenols, fibre and plant sterols, was therefore proposed to improve health outcomes (61). Of several early Homo species (such as Homo habilis, Homo erectus and early Homo sapiens), it is assumed that they consumed fish and seafood (62–64). However, the exploitation of aquatic food resources is still a neglected field in paleoanthropology (65,66) and more research on the reconstruction of our ancient natural nutrition, including aquatic food, is needed (67). This knowledge should contribute to a better understanding of modern human nutrition and health.

Conclusions

Our meta-analysis showed that consumption of n3-PUFA can decrease weight in adults. Further research is needed to reveal which components of fish and fish oil are most beneficial. In particular, the documented positive effects of n3-PUFA on cardiovascular diseases, dyslipidaemia and obesity suggest that we should continue to explore the effects of fish-derived n3-PUFA on human health.

Conflict of interest statement

No conflict of interest was declared.

Acknowledgement

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Supporting information

Additional Supporting Information may be found in the online version of this article, http://dx.doi.org/10.1111/obr.12189

Appendix S1. Search strategy for the database Medline. The search strategies for Embase and CENTRAL were similar.

Appendix S2. Funnel plots of studies for the outcomes BMI and body weight.

Appendix S3. Forest plots of meta-analyses.

References


