Author’s response to reviews

Title: Fatty fish intake and attention performance in 14-15 year old adolescents: FINS-TEENS - a randomized controlled trial

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Author’s response to reviews:

Dear reviewers and editor.

Thank you for reviewing this manuscript and we appreciate your constructive and helpful comments. We have revised the manuscript according to the reviewers’ comments with revisions in the manuscript highlighted in yellow. This letter explains point-by-point the details of the revisions in the manuscript and our responses to the reviewers’ comments.
Reviewer reports:

Reviewer #1: The enclosed manuscript investigates the effect of fatty fish intake on attention ability and processing speed among adolescents. While considerable data is available for the effect of fatty fish intake/ N3 fatty acids on cognitive performance of elderly or middle aged adults, the relationship has not been sufficiently established among adolescents. The authors are commended for their efforts in elucidating this interesting relationship in this age group. This is especially important because adolescence is a time when academic expectations begin to demand greater cognitive discipline.

Overall, it is a well written manuscript. The authors present their arguments in a logical sequence and this helps with the readability of the article. Minor rephrasing in some places will help with further improving the manuscript.

The term “developing adolescents” is repeated in the manuscript. I find the word “developing” redundant. Also when the authors say "typical developing adolescents" there is an element of ambiguity. The authors are encouraged to rethink these descriptions.

Response: The term “developing adolescents” is changed or removed from the manuscript. In the methods section, we have replaced it with the term “adolescents from a mainstream school population” (lines 67-68). In the title, “developing adolescents” is replaced with “14-15 year old adolescents”.

Abstract: - Results- the authors talk of greater improvement in processing speed/ total performance in the fish vs. meat or supplement group, but present the results as negative numerals. The authors should reconsider this presentation.

Response: We have changed this in the abstract to: “The improvement in processing speed was significantly lower in the meat (-11.8; 95% CI: -23.3, -0.4) and supplement (-13.4; 95% CI: -24.9, -1.8) group compared to the fish group (reference). The supplement group also showed inferior improvement in total performance (-10.4; 95% CI: -20.0, -0.7) compared to the fish group (reference).” lines: 15-18, and similar changes have been done in the results section (lines 236-238).

The abbreviation IRR appears first in the abstract without expansion of the abbreviation.

Response: This is now corrected in the abstract (line 19).
Abstract: - Conclusions- The first sentence needs improvement in terms of clarity.

Response: We have changed this sentence to: “There were a small beneficial effect of fatty fish, compared to meat meals and supplements on attention performance related to processing speed” in the abstract (lines 22-23) and similarly in the conclusion (lines 371-372).

Main Text:

Methods

Subjects and Randomization: First sentence needs to be rewritten using proper syntax to improve readability.

Response: The sentence is rephrased and now reads: “Inclusion criteria were that the adolescents were attending 9th grade at the schools participating in the study, and that they knew the Norwegian language orally and written.” Lines 76-77.

Dietary Intervention procedure- 'The supplement group continued to eat their habitual lunch'. So was this a standard lunch provided by the school? Did this lunch contain fatty fish? If so how much of n3-PUFA did it contain?

Response: In Norway, the schools do not provide lunch to the pupils, thus, the school lunch usually consist of a packed lunch from home. According to one study conducted in Norwegian adolescents, the packed school-lunch often contains medium dark or dark bread or crispbread with meat, cheese or liver pate as spread, and sometimes a fruit or vegetable. Fish is hardly ever used as bread spread in these packed lunch meals. This information is now included (with reference) in the text, in lines 91-93.

While the authors mention that the fish meal was matched to the supplements for n3-LCPUFA, the mean weight of the fish meal contained more n3-LCPUFA than one capsule. How many capsules were the supplement group students advised to consume?

Response: The supplement group received seven capsules per serving. This is now specified in the text, in line 103.
Can the test outcomes and the tools used be listed in a table for ease of reference when reading the results section?

Response: Yes, thank you for this good suggestion. The test outcomes with their respective description is now listed in a table instead of in the text, (table 1, page 28).

Statistical analysis: line 238- additional analyses with further adjustments. What were these adjustments?

Response: The additional analyses included further adjustments for parental education level, at home omega-3 supplement use and fatty fish intake as dinner or as bread spread at baseline. This is described in the statistical analyses section (lines 197-200), and in the results section (lines 247-248).

Main Text- Results

Dietary Compliance and background diet- dietary compliance showed that the total intake was significantly lower in the fish group? What intake does this refer to? Dietary compliance for fish meal was very low. This limitation needs to be discussed in greater detail.

Response: The recording of dietary compliance was conducted by trained research assistants, who served the study meals and supplements to the participants and collected leftovers. The intake records refer to assessments of the specific amount of fish and meat consumed by each participant in the fish and meat group, respectively, and the number of capsules consumed by each participant in the supplement group.

We absolutely agree with you that the dietary compliance in the fish group is important to discuss. Therefore, this is described in the results section (lines 256-259) and discussed in three different places in the discussion: 1) it is emphasized that the results are difficult to interpret, and that we cannot conclude on the relationship between fish intake and attention due to the compliance issue in lines 313-315. 2) The difference between intervening with supplements or food in relation to compliance in intervention trials is discussed in lines 340-342, and a possible reason for the lower compliance in the fish group is given in lines 344-347. 3) Dietary compliance is highlighted as the main limitation of the study in lines 348-349. Thus, we think that this topic is thoroughly discussed and highlighted continuously and in sufficient detail. More information about the dietary compliance is published in the manuscript by Skotheim et al., which is reference number 18 in the manuscript.
Main Text- Discussion

First paragraph- 2nd sentence: "This corresponds to approximately 2% of the characters...". It would be helpful to add details on the length of the test provided and the duration of the test.

Response: In lines 129-133 in the methods section it now reads: “The test comprises 47 interspersed target- and distraction characters×14 rows. It is conducted under time pressure, as participants are only allowed 20 seconds on each row before they must move down to the next, independent of how far they had reached on the current row. The test, including instructions, was administered within eight minutes.” In the discussion section, we have also included that there were a total of 658 characters in the test, in line 277.

The second paragraph in discussion section talks of association reported in earlier studies. It would be helpful if the direction of the associations are mentioned. The authors could also consider shortening this paragraph. This can be done by grouping all the studies that showed positive association and further identifying the outcomes that were positively associated with fatty fish intake and the age groups in which the associations were observed.

Response: We have now specified the direction of the associations, and grouped the description of the studies by Kaljmin et al. and Nurk et al., (lines 289-293), and rewritten the sentence in lines 303-305.

Paragraph 4 in discussion suggests heterogeneity in dosage as a possible reason for contradictory results in studies investigating the association of interest. Could the discrepancy in the results between the fish and supplement group in this study be due to additional bioactives (other than n3-LCPUFA) in the fatty fish?

Response: Yes we agree, and have included a discussion of this in lines 335-337 in the discussion section.

Strengths and Limitations

The last sentence in this section mentions that the study did not exclude those with cognitive disorders etc…. However, were subjects with anomalies in this aspect equally distributed among the three groups? Could some learning disorders have had implications on the type of tasks required of subjects in this study?

Response: Of the 372 parents/caregivers who responded to the questionnaire sent to them by e-mail, five reported that their child was diagnosed with a cognitive disorder, and ADHD was the
only disorder reported. Two of these were in the meat group, two were in the fish group and one was in the supplement group. Thus, they were equally distributed among the intervention groups, and excluding them from the analysis did not significantly affect the results.

In a separate publication (see Skotheim et al. supplemental file for peer review only), results from the mental health screening tool Strengths and Difficulties Questionnaire (SDQ) are reported. As seen in page 13 line 267-269 in that manuscript, we did not find any systematic differences between intervention groups in the baseline level of symptoms related to emotional difficulties, behavioral problems or hyperactivity/inattention as measured by the SDQ.

The fact that improvement of outcomes in this study is not correlated with compliance is problematic to comprehend. Since the authors only talk of standardising the lunch at school, and obtained reported intake of fish at other meals the validity of these self-reported dietary intake requires needs discussion, especially among adolescents.

Response: We agree that it is difficult to comprehend why there is no correlation between the dietary compliance measure and improvement in the attention outcomes. We do however, not think that incorrect reporting of the background diet in the FFQ can explain this because, we have in a previous publication (see Handeland et. al., reference number 29) tested the agreement (reliability) of the responses to the FFQ between pre- and post-intervention, which shows high level of agreement, i.e. good reliability. The questions regarding fish and omega-3 consumption in the FFQ have also been validated previously (see references in the manuscript). And, if it was the case that incorrect reporting occurred in some participants, this should have been equally distributed between the intervention groups due to the randomization and thus, not affected the differences between groups.

Reviewer #2: This paper describes a RCT aiming to investigate whether consumption of fatty fish 3 times/WE during 12 WE could improve attention performance in Norwegian adolescents ages 14-15 compared to similar meals with meat or omega-3 supplements. So far, no other RCTs have approached the relation between fatty fish intake and cognition in the adolescent population, which is a major strength of this research. The research question is well crafted and contains all the major elements to properly assess the quality of both the intervention and its findings (population, intervention, comparisons, and outcomes). Background diet was consider in the analysis, which should be consider another major strength of this study since many RCT's assessing nutritional supplementations do not include this important confounder. The statistical analysis is well described, step-by-step, and the approached used by the authors is correct. The paper is well written, no language editing is needed, and it was easy to read it, so the findings
should be easily communicated to a non-academic audience, let’s say, parents, teacher/educators, and health policymakers. I have a few minor suggestions which are mostly intended to add to the paper.

1. Overall in the text, please, replace gender with sex, since gender is not a biological category.

Response: The word gender is replaced with sex throughout the manuscript, highlighted in yellow.

2. Introduction: It really surprised me that Norwegian adolescents have a low intake of fish, and so I’d like to see more details on this. Perhaps stats from a population health or food consumption survey and/or comparison with other European countries.

Response: Yes it is perhaps surprising as we are a country with a vast coastline and a history in fisheries. However, data suggests that the Norwegian population do not meet the recommended 2-3 dinner portions of fish per week. Among the data on adolescents, The Norwegian National dietary survey among 8th graders (“Ungkost”) was conducted in 2015. This included food-diary data from n=687 adolescents aged 13 years old, from different parts of Norway. In this sample, the mean (SD) intake of fish and shellfish was 24 (37) g/day, corresponding to 168 g/week, which is below the recommended amount of 200-300g fish/week.

EFSAs Food Consumption Database contains data on seafood consumption from dietary surveys carried out in 17 EU Member States. It shows that for children and adolescents, the daily intake of ‘fish-meat’ was 10-15 g/day in Denmark and Finland, which are countries comparable to Norway. In Italy and Spain on the other hand, the intake was 50-60 g/day. Norway is not part of this database.

The reference to The Norwegian National dietary survey (“Ungkost”) is given in the manuscript, reference number 17.

3. Methods: Authors may want to merge the subjects and randomization subsection with the sample size subsection.

Response: We have considered your suggestion, but we prefer to keep it separately.

4. Methods: because the sample is made of male and females participants, BMI for age and sex (BMI z-score) should be reported instead of raw BMI. And just for description purposes, I’d like to see the prevalence of participants having and unhealthy weight (overweight/obesity).
Response: We agree that raw BMI score is not descriptive enough, and have included Cole’s age and sex-specific BMI cut off points for underweight, and overweight and obesity for adolescents 14.5 years old. These changes can be seen in table 2, and in line 224 in the text.

5. Discussion: I'd like the authors could dig deeper into the topic of bioavailability of fish omega-3 LCPUFAs vs. supplement omega-3 LCPUFAs. Because the fish group have a relatively low compliance compared to meat and supplement groups, and in spite of that, they had better cognitive performance it may be that bioavailability is the missing piece of this equation.

Response: Yes we agree, and have included bioavailability in the discussion in lines 331-335.

6. Discussion: Be more specific about the implications of your results for research, practice and policymaking. In fact, you may want to include a subsection.

We have included a section about the implications for research and practice in lines 338-342. Because this is one of the first intervention studies assessing the impact of school-meals on cognitive outcomes in healthy adolescents, we think that more research and evidence is needed on this field before it can give implications on policy making.

7. Because the amount of fish/meat eaten was estimated by eye rather than using an objective measure such as weighing out food portions, state this as a limitation.

Response: We have included this as a limitation in the discussion section, lines 359-361.