3. Modified Cochrane Risk of Bias Tool

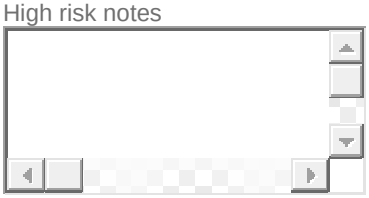
1. Was the allocation sequence (randomization method) adequately generated

There is a LOW RISK OF BIAS if the investigators describe a random component in the sequence generation process such as: referring to a random number table, using a computer random number generator, coin tossing, shuffling cards or envelopes, throwing dice, drawing of lots. There is a HIGH RISK OF BIAS if the investigators describe a non-random component in the sequence generation process, such as: sequence generated by odd or even date of birth, date (or day) of admission, hospital or clinic record number; or allocation by judgement of the clinician, preference of the participant, results of a laboratory test or a series of tests, or availability of the intervention. IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- ● Low risk (yes)
- ● High risk (no)
- ● Unclear

Clear Response

High risk notes



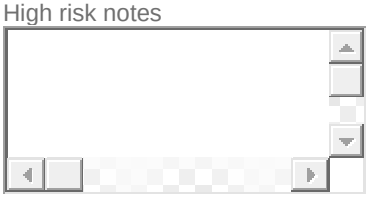
2. Was ALLOCATION adequately concealed (prior to assignment)?

There is a LOW RISK OF BIAS if the participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance; or sequentially numbered, opaque, sealed envelopes. There is a HIGH RISK OF BIAS if participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; or other explicitly unconcealed procedures. IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- ● Low risk
- ● High risk
- ● Unclear

Clear Response

High risk notes



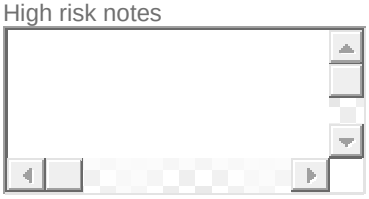
3. Were PARTICIPANTS adequately BLINDED?

There is a LOW RISK OF BIAS if blinding of participants was ensured and it was unlikely that the blinding could have been broken; or if there was no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding.

- Low risk
- High risk
- Unclear

Clear Response

High risk notes



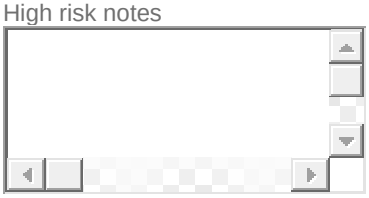
4. Were OUTCOME ASSESSORS adequately BLINDED?

There is LOW RISK OF BIAS if the blinding of the outcome assessment was ensured and it was unlikely that the blinding could have been broken; or if there was no or incomplete blinding, but the outcome is unlikely to be influenced by lack of blinding (ie, lab tests--lipids--inherently low risk of bias, but not blood pressure).

- Low risk
- High risk
- Unclear

Clear Response

High risk notes

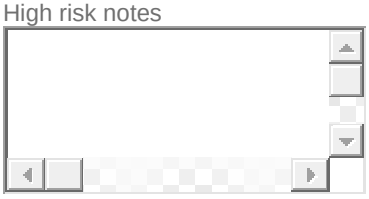


5. If outcome assessor blinding risk of bias is different for different outcomes (eg, lipids vs. MI), choose HIGH risk of bias and describe in Notes

- Low risk
- High risk
- Unclear
- Not applicable

Clear Response

High risk notes



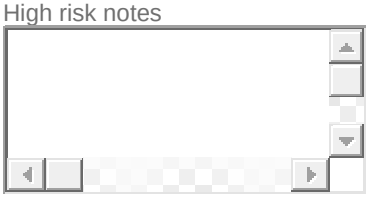
6. Incomplete outcome data (ATTRITION BIAS) due to amount, nature or handling of incomplete outcome data

There is a LOW RISK OF BIAS if there were no missing outcome data; reasons for missing outcome data were unlikely to be related to the true outcome; missing outcome data were balanced in numbers, with similar reasons for missing data across groups (****The percentage of withdrawals and drop-outs should not exceed 20% for short-term follow-up [<=1 year] and 30% for long-term follow-up [>1 year]****). IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- Low risk
- High risk
- Unclear

Clear Response

High risk notes

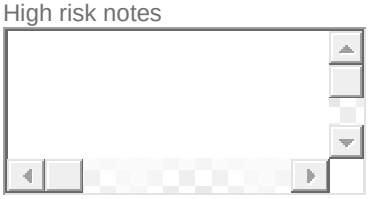


7. If attrition risk of bias is different for different outcomes (eg, lipids vs. MI) or different time points (eg, 1 year vs. 5 years), choose HIGH risk of bias and describe in Notes

- Low risk
- High risk
- Unclear
- Not applicable

Clear Response

High risk notes



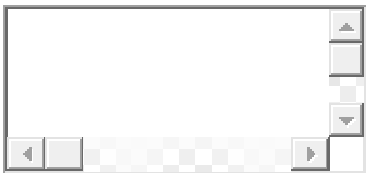
8. Is there evidence of SELECTIVE OUTCOME REPORTING bias (Yes/No)?

For LIPIDS, are only selected lipids/lipoproteins reported, were lipids measured at baseline and was a blood sample taken at follow-up but follow-up lipids were not reported, were subgroup lipid outcomes omitted? For BLOOD PRESSURE, was BP measured at baseline and was there a follow-up clinical encounter (where follow-up BP would have been measured), but BP is not reported, were subgroup BP outcomes omitted? For CLINICAL OUTCOMES, are all outcomes in the Methods section (all pre-specified outcomes) reported, were all components of composite outcomes reported? DESCRIBE ISSUES IN NOTES.

- Yes
- No
- Unclear

Clear Response

Notes



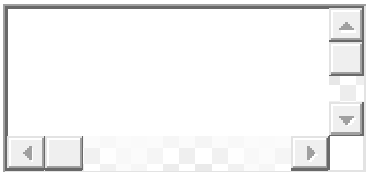
9. INTENTION-TO-TREAT analysis? (Yes/No)

YES if they state ITT and methods used were actually ITT, or **all** participants were analyzed in the group to which they were allocated by randomization (no cross-over). IF NO ITT, EXPLAIN IN NOTES.

- Yes
- No
- Unclear

Clear Response

Notes



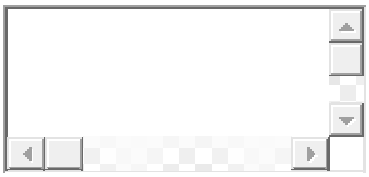
10. Group SIMILARITY AT BASELINE (GENERAL**)**

There is LOW RISK OF BIAS if groups are similar at baseline for demographic and other factors ("Table 1"). Also LOW risk of bias if any baseline differences were adjusted for in all relevant analyses. IF HIGH RISK OF BIAS, EXPLAIN IN NOTES.

- Low risk
- High risk
- Unclear

Clear Response

Notes



11. Group SIMILARITY AT BASELINE (OMEGA-3**)**

There is LOW RISK OF BIAS if groups were similar (or statistical adjustments were made to account for differences) in omega-3 intake or status (biomarkers) at baseline. There is HIGH RISK OF BIAS if groups had different omega-3 intake/status at baseline that was not accounted for. There is UNCLEAR RISK OF BIAS if baseline omega-3 status was not reported.

- Low risk
- High risk
- Unclear

Clear Response

Notes

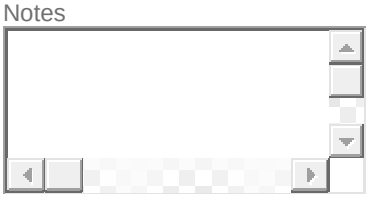
12. Was there incomplete COMPLIANCE with interventions across groups?

There is LOW RISK OF BIAS if compliance with the interventions was acceptable (>=80% across intervention duration), based on the reported actual compliance compared to protocol or increased biomarker levels were reported during or at the end of the intervention. There is HIGH RISK OF BIAS if compliance was low (<80%) or no change in biomarker levels were found during or at the end of the intervention. There is UNCLEAR RISK OF BIAS if these data were not reported.

- Low risk
- High risk
- Unclear

Clear Response

Notes



13. Additional Bias: Bias due to problems not covered elsewhere in the table.

- Yes
- No

Clear Response