

### Supplement 3. Original AMSTAR 2 questionnaire and description of the modifications

This section provides the original version of the AMSTAR 2 questionnaire. Detailed guidance and information can be found in: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA: AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008.

<b>1. Did the research questions and inclusion criteria for the review include the components of PICO?</b>		
For Yes:	Optional (recommended)	
<input type="checkbox"/> Population	<input type="checkbox"/> Timeframe for follow-up	<input type="checkbox"/> Yes
<input type="checkbox"/> Intervention		<input type="checkbox"/> No
<input type="checkbox"/> Comparator group		
<input type="checkbox"/> Outcome		
<b>2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?</b>		
For Partial Yes: The authors state that they had a written protocol or guide that included ALL the following:	For Yes: As for partial yes, plus the protocol should be registered and should also have specified:	
<input type="checkbox"/> review question(s)	<input type="checkbox"/> a meta-analysis/synthesis plan, if appropriate, <i>and</i>	<input type="checkbox"/> Yes
<input type="checkbox"/> a search strategy	<input type="checkbox"/> a plan for investigating causes of heterogeneity	<input type="checkbox"/> Partial Yes
<input type="checkbox"/> inclusion/exclusion criteria	<input type="checkbox"/> justification for any deviations from the protocol	<input type="checkbox"/> No
<input type="checkbox"/> a risk of bias assessment		
<b>3. Did the review authors explain their selection of the study designs for inclusion in the review?</b>		
For Yes, the review should satisfy ONE of the following:		
<input type="checkbox"/> <i>Explanation for including only RCTs</i>		<input type="checkbox"/> Yes
<input type="checkbox"/> OR <i>Explanation for including only NRSI</i>		<input type="checkbox"/> No
<input type="checkbox"/> OR <i>Explanation for including both RCTs and NRSI</i>		
<b>4. Did the review authors use a comprehensive literature search strategy?</b>		
For Partial Yes (all the following):	For Yes, should also have (all the following):	
<input type="checkbox"/> searched at least 2 databases (relevant to research question)	<input type="checkbox"/> searched the reference lists/bibliographies of included studies	<input type="checkbox"/> Yes
<input type="checkbox"/> provided key world and/or search strategy	<input type="checkbox"/> searched trial/study registries	<input type="checkbox"/> Partial Yes
		<input type="checkbox"/> No

- |   |  |
|---|--|
| <input type="checkbox"/> justified publication restrictions (e.g. language) | <input type="checkbox"/> included/consulted content experts in the field               |
|   | <input type="checkbox"/> where relevant, searched for grey literature                  |
|   | <input type="checkbox"/> conducted search within 24 months of completion of the review |

**5. Did the review authors perform study selection in duplicate?**

For Yes, either ONE of the following:

- |  |                              |
|--|------------------------------|
| <input type="checkbox"/> at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include                               | <input type="checkbox"/> Yes |
| <input type="checkbox"/> OR two reviewers selected a sample of eligible studies <u>and</u> achieved good agreement (at least 80 percent), with the remainder selected by one reviewer. | <input type="checkbox"/> No  |

**6. Did the review authors perform data extraction in duplicate?**

For Yes, either ONE of the following:

- |  |                              |
|--|------------------------------|
| <input type="checkbox"/> at least two reviewers achieved consensus on which data to extract from included studies  | <input type="checkbox"/> Yes |
| <input type="checkbox"/> OR two reviewers extracted data from a sample of eligible studies <u>and</u> achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer. | <input type="checkbox"/> No  |

**7. Did the review authors provide a list of excluded studies and justify the exclusions?**

For Partial Yes:

- provided a list of all potentially relevant studies that were read in full-text form but excluded from the review

For Yes, must also have:

- |   |                                      |
|---|--------------------------------------|
| <input type="checkbox"/> justified the exclusion from the review of each potentially relevant study | <input type="checkbox"/> Yes         |
|   | <input type="checkbox"/> Partial Yes |
|   | <input type="checkbox"/> No          |

**8. Did the review authors describe the included studies in adequate detail?**

For Partial Yes (ALL the following):

- described populations
- described interventions
- described comparators
- described outcomes
- described research designs

For Yes, should also have ALL the following:

- |  |                                      |
|--|--------------------------------------|
| <input type="checkbox"/> described population in detail                                    | <input type="checkbox"/> Yes         |
| <input type="checkbox"/> described intervention in detail (including doses where relevant) | <input type="checkbox"/> Partial Yes |
| <input type="checkbox"/> described comparator in detail (including doses where relevant)   | <input type="checkbox"/> No          |
| <input type="checkbox"/> described study's setting   |                                      |
| <input type="checkbox"/> timeframe for follow-up   |                                      |

**9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?**

**RCTs**

For Partial Yes, must have assessed RoB from:

For Yes, must also have assessed RoB from:

- |  |   |   |
|--|---|---|
| <input type="checkbox"/> unconcealed allocation, <i>and</i>  | <input type="checkbox"/> allocation sequence that was not truly random, <i>and</i>  | <input type="checkbox"/> Yes                |
| <input type="checkbox"/> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality) | <input type="checkbox"/> selection of the reported result from among multiple measurements or analyses of a specified outcome | <input type="checkbox"/> Partial Yes        |
|  |   | <input type="checkbox"/> No                 |
|  |   | <input type="checkbox"/> Includes only NRSI |

**NRSI**

For Partial Yes, must have assessed RoB:

For Yes, must also have assessed RoB:

- |   |   |   |
|---|---|---|
| <input type="checkbox"/> from confounding, <i>and</i> | <input type="checkbox"/> methods used to ascertain exposures and outcomes, <i>and</i>   | <input type="checkbox"/> Yes                |
| <input type="checkbox"/> from selection bias          | <input type="checkbox"/> selection of the reported result from among multiple measurements or analyses of a specified outcome | <input type="checkbox"/> Partial Yes        |
|   |   | <input type="checkbox"/> No                 |
|   |   | <input type="checkbox"/> Includes only RCTs |

**10. Did the review authors report on the sources of funding for the studies included in the review?**

For Yes:

- |  |                              |
|--|------------------------------|
| <input type="checkbox"/> Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies. | <input type="checkbox"/> Yes |
|  | <input type="checkbox"/> No  |

**11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?**

**RCTs**

For Yes:

- |  |   |
|--|---|
| <input type="checkbox"/> The authors justified combining the data in a meta-analysis   | <input type="checkbox"/> Yes                        |
| <input type="checkbox"/> AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present. | <input type="checkbox"/> No                         |
| <input type="checkbox"/> AND investigated the causes of any heterogeneity  | <input type="checkbox"/> No meta-analysis conducted |

**For NRSI**

For Yes:

- |   |   |
|---|---|
| <input type="checkbox"/> The authors justified combining the data in a meta-analysis  | <input type="checkbox"/> Yes                        |
| <input type="checkbox"/> AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present   | <input type="checkbox"/> No                         |
| <input type="checkbox"/> AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available | <input type="checkbox"/> No meta-analysis conducted |
| <input type="checkbox"/> AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review  |   |

**12. If meta-analysis was performed, did the review authors assess the potential impact RoB in individual studies on the results of the meta-analysis or other evidence synthesis?**

For Yes:

- |   |   |
|---|---|
| <input type="checkbox"/> included only low risk of bias RCTs  | <input type="checkbox"/> Yes                        |
| <input type="checkbox"/> OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect. | <input type="checkbox"/> No                         |
|   | <input type="checkbox"/> No meta-analysis conducted |

**13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?**

For Yes:

- |   |                              |
|---|------------------------------|
| <input type="checkbox"/> included only low risk of bias RCTs  | <input type="checkbox"/> Yes |
| <input type="checkbox"/> OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results | <input type="checkbox"/> No  |

**14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?**

For Yes:

- |  |                              |
|--|------------------------------|
| <input type="checkbox"/> There was no significant heterogeneity in the results   | <input type="checkbox"/> Yes |
| <input type="checkbox"/> OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review | <input type="checkbox"/> No  |

**15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?**

For Yes:

- |   |   |
|---|---|
| <input type="checkbox"/> performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias | <input type="checkbox"/> Yes                        |
|   | <input type="checkbox"/> No                         |
|   | <input type="checkbox"/> No meta-analysis conducted |

**16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?**

For Yes:

- |   |                              |
|---|------------------------------|
| <input type="checkbox"/> The authors reported no competing interests OR   | <input type="checkbox"/> Yes |
| <input type="checkbox"/> The authors described their funding sources and how they managed potential conflicts of interest | <input type="checkbox"/> No  |

**Description of and rationale for the modifications of AMSTAR 2**

This section details the modifications of AMSTAR 2 and provides the rationale for such modifications. AMSTAR 2 is based on the current state-of-the-art. For example, prospective registration of systematic reviews has only received considerable interest over the past few years. Our work includes also some older literature. If AMSTAR 2 is used correctly, it is so strict that most SRs included in our work would be rated as low quality, therefore modifications were considered necessary.

**Item 1:** The following modification was made:

- **The optional criterion on the "timeframe for follow-up" is excluded.**

**Item 2:** The following modifications were made:

- **The question is classified as a non-critical domain.**
- **While the a priori approach should be described in the publication, the methodology does not need to be pre-published.**

**Explanation:** Registration of study protocols of reviews is expected only recently, yet the protein guideline considers literature from the last 10 years.

**Item 3:** The following modification was made:

- **The question is not included in the AMSTAR 2 overall score.**

**Explanation:** For the protein guideline, it is sufficient to specify the types of studies included. This is already queried.

**Item 4:** The following modification was made

- **The subitem "justified publication restrictions" is deleted.**

**Explanation:** The reasons are usually obvious and often not stated.

- **The answers for "partial yes" are sufficient for "yes"**

**Items 5 and 6:** No modifications were made.

**Item 7:** The following modification was made

- **The answers for "partial yes" and "yes" are reworded as follows: „Provided a flow chart showing the number of excluded studies and reasons for exclusion. A study-specific list is not required“**

**Explanation:** The required information is often not available.

**Item 8:** The following modification was made:

- **The answers for "partial yes" are sufficient for "yes"**

**Item 9:** The following modification was made

- **The answers for "partial yes" and "yes" are reworded as follows: „A tool was used to evaluate the risk of bias of included studies“.**

**Explanation:** A large proportion of meta-analyses of RCTs use Cochrane's Risk of Bias tool, but there are other tools that do not assess "allocation concealment," for example. In addition, blinding is often challenging or not possible in nutrition studies.

**Item 10:** The following modification was made:

- **The question is not included in the AMSTAR 2 overall score.**

**Item 11:** The following modification was made

- **The answers for "yes" are reworded as follows: „Statistical heterogeneity between trial results was assessed and the results are provided“.**

**Item 12:** The following modification was made:

- **The question is not included in the AMSTAR 2 overall score.**

**Item 13:** The following modifications were made:

- **The question is classified as a non-critical domain.**
- **The answers for "yes" are reworded as follows: „Study quality is considered in the discussion and interpretation“.**

**Item 14:** The following modification was made:

- **The answer "no meta-analysis conducted" was added.**

**Item 15:** The following modifications were made:

- **The question was split into two questions**

**Explanation:** We based this question on the question on heterogeneity. The critical domain refers to whether publication bias has been investigated. The non-critical domain refers to whether any publication bias identified was discussed.

**1. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias)?**

- **This question is classified as a critical domain.**
- **The following part of the answer option for "yes" is deleted: "or an adequate reason is provided for not performing a test".**
- **The following is added to the answer option for "yes": „or an adequate reason is provided for not performing a test“.**

**Explanation:** Methods for assessing publication bias in SRs with fewer than 10 individual studies are not recommended.

**2. Did the review authors discuss the likely impact of publication bias on the results of the review?**

- **This question is classified as a non-critical domain.**
- **The answers for "yes" are defined as follows: "There was no significant publication bias" "OR if publication bias was present the authors discussed the likelihood and magnitude of impact of publication bias on the results of the review".**

**Item 16:** No modifications were made.