

AMSTAR 2

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:

- ☒ Population
- ☒ Intervention
- ☒ Comparator group
- ☒ Outcome

Optional (recommended)

- ☐ Timeframe for follow-up

- ☒ Yes
- ☐ No

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?

For Partial Yes:

The authors state that they had a written protocol or guide that included ALL the following:

- ☒ review question(s)
- ☒ a search strategy
- ☒ inclusion/exclusion criteria
- ☒ a risk of bias assessment

For Yes:

As for partial yes, plus the protocol should be registered and should also have specified:

- ☒ a meta-analysis/synthesis plan, if appropriate, *and*
- ☒ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

- ☒ Yes
- ☐ Partial Yes
- ☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:

- ☒ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

- ☒ Yes
- ☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):

- ☐ searched at least 2 databases (relevant to research question)
- ☐ provided key word and/or search strategy
- ☐ justified publication restrictions (eg, language)

For Yes, should also have (all the following):

- ☒ searched the reference lists/bibliographies of included studies
- ☒ searched trial/study registries
- ☒ included/consulted content experts in the field
- ☒ where relevant, searched for grey literature
- ☒ conducted search within 24 months of completion of the review

- ☒ Yes
- ☐ Partial Yes
- ☐ No

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

For Yes, either ONE of the following:

- ☒ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 per cent), with the remainder selected by one reviewer

- ☒ Yes
- ☐ No

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

For Yes, either ONE of the following:

- ☒ at least two reviewers achieved consensus on which data to extract

- ☒ Yes

from included studies <input type="checkbox"/> OR two reviewers extracted data from a sample of eligible studies <u>and</u> achieved good agreement (at least 80 per cent), 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: <input type="checkbox"/> 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: <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;"> <input type="checkbox"/> Justified the exclusion from the review of each potentially relevant study </div> <div style="width: 35%; text-align: right;"> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Partial Yes <input type="checkbox"/> No </div> </div>
8. Did the review authors describe the included studies in adequate detail?	
For Partial Yes (ALL the following): <input type="checkbox"/> described populations <input type="checkbox"/> described interventions <input type="checkbox"/> described comparators <input type="checkbox"/> described outcomes <input type="checkbox"/> described research designs	For Yes, should also have ALL the following: <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;"> <input checked="" type="checkbox"/> described population in detail <input checked="" type="checkbox"/> described intervention and comparator in detail (including doses where relevant) <input checked="" type="checkbox"/> described study's setting <input checked="" type="checkbox"/> timeframe for follow-up </div> <div style="width: 35%; text-align: right;"> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Partial Yes <input type="checkbox"/> No </div> </div>
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 <input checked="" type="checkbox"/> unconcealed allocation, <i>and</i> <input checked="" type="checkbox"/> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)	For Yes, must also have assessed RoB from: <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;"> <input checked="" type="checkbox"/> allocation sequence that was not truly random, <i>and</i> <input checked="" type="checkbox"/> selection of the reported result from among multiple measurements or analyses of a specified outcome </div> <div style="width: 35%; text-align: right;"> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Partial Yes <input type="checkbox"/> No <input type="checkbox"/> Includes only NRSI </div> </div>
NRSI	
For Partial Yes, must have assessed RoB: <input type="checkbox"/> from confounding, <i>and</i> <input type="checkbox"/> from selection bias	For Yes, must also have assessed RoB: <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;"> <input type="checkbox"/> methods used to ascertain exposures and outcomes, <i>and</i> <input type="checkbox"/> selection of the reported result from among multiple measurements or analyses of a specified outcome </div> <div style="width: 35%; text-align: right;"> <input type="checkbox"/> Yes <input type="checkbox"/> Partial Yes <input type="checkbox"/> No <input type="checkbox"/> Includes only RCTs </div> </div>
10. Did the review authors report on the sources of funding for the studies included in the review?	
For Yes <input checked="" 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	
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	
RCTs For Yes: <div style="display: flex; justify-content: space-between;"> <div style="width: 60%;"> <input checked="" type="checkbox"/> The authors justified combining the data in a meta-analysis <input type="checkbox"/> AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present </div> <div style="width: 35%; text-align: right;"> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> No meta-analysis </div> </div>	

<input type="checkbox"/> AND investigated the causes of any heterogeneity	conducted
For NRSI For Yes:	
<input type="checkbox"/> The authors justified combining the data in a meta-analysis <input type="checkbox"/> AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present <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"/> AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> No meta-analysis conducted
12. If meta-analysis was performed, did the review authors assess the potential impact of 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"/> 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 checked="" type="checkbox"/> Yes <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 checked="" 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 checked="" type="checkbox"/> Yes <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 checked="" 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"/> Yes <input checked="" 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 checked="" type="checkbox"/> performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	<input checked="" 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 checked="" type="checkbox"/> The authors reported no competing interests OR <input type="checkbox"/> The authors described their funding sources and how they managed potential conflicts of interest	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No