

SUPPLEMENTARY

Table S1. – PRISMA CHECKLIST

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			Lines
Title	1	Identify the report as a systematic review.	1-3
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	5-24
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	28 – 58
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	59 – 63
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	85-96
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	77 - 79
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	69 – 71
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	83-85
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	83 -85
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	98-116
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	98 -116
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	162-163
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	119-124
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	129-130

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	130-133
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	154 -157
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	134-149, 160-161
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	150-157
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	158-159
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	164-174
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	178-219
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Appendix 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	229-239, 241-270, 273-295, 298-309, 347-358
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	312-334, 360-371
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	335-345, 372-382
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	384-411
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	414-439, 444-454, 470-476
	23b	Discuss any limitations of the evidence included in the review.	440-443, 455-469, 476-482
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future	483-488

Section and Topic	Item #	Checklist item	Location where item is reported
		research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not registered
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	None
Competing interests	26	Declare any competing interests of review authors.	None
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Require from the corresponding author

Figure S1.- AMSTAR CHECKLIST

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

<p>1. Did the research questions and inclusion criteria for the review include the components of PICO?</p>		
<p>For Yes:</p> <p><input checked="" type="checkbox"/> Population</p> <p><input checked="" type="checkbox"/> Intervention</p> <p><input type="checkbox"/> Comparator group</p> <p><input checked="" type="checkbox"/> Outcome</p>	<p>Optional (recommended)</p> <p><input type="checkbox"/> Timeframe for follow-up</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>
<p>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?</p>		
<p>For Partial Yes:</p> <p>The authors state that they had a written protocol or guide that included ALL the following:</p> <p><input type="checkbox"/> review question(s)</p> <p><input type="checkbox"/> a search strategy</p> <p><input type="checkbox"/> inclusion/exclusion criteria</p> <p><input type="checkbox"/> a risk of bias assessment</p>	<p>For Yes:</p> <p>As for partial yes, plus the protocol should be registered and should also have specified:</p> <p><input checked="" type="checkbox"/> a meta-analysis/synthesis plan, if appropriate, <i>and</i></p> <p><input checked="" type="checkbox"/> a plan for investigating causes of heterogeneity</p> <p><input checked="" type="checkbox"/> justification for any deviations from the protocol</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> Partial Yes</p> <p><input type="checkbox"/> No</p>
<p>3. Did the review authors explain their selection of the study designs for inclusion in the review?</p>		
<p>For Yes, the review should satisfy ONE of the following:</p> <p><input type="checkbox"/> Explanation for including only RCTs</p> <p><input type="checkbox"/> OR Explanation for including only NRSI</p> <p><input checked="" type="checkbox"/> OR Explanation for including both RCTs and NRSI</p>		<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>
<p>4. Did the review authors use a comprehensive literature search strategy?</p>		
<p>For Partial Yes (all the following):</p> <p><input checked="" type="checkbox"/> searched at least 2 databases (relevant to research question)</p> <p><input checked="" type="checkbox"/> provided key word and/or search strategy</p> <p><input checked="" type="checkbox"/> justified publication restrictions (e.g. language)</p>	<p>For Yes, should also have (all the following):</p> <p><input type="checkbox"/> searched the reference lists / bibliographies of included studies</p> <p><input type="checkbox"/> searched trial/study registries</p> <p><input type="checkbox"/> included/consulted content experts in the field</p> <p><input type="checkbox"/> where relevant, searched for grey literature</p> <p><input type="checkbox"/> conducted search within 24 months of completion of the review</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> Partial Yes</p> <p><input type="checkbox"/> No</p>
<p>5. Did the review authors perform study selection in duplicate?</p>		
<p>For Yes, either ONE of the following:</p> <p><input checked="" type="checkbox"/> at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include</p> <p><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.</p>		<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>

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6. Did the review authors perform data extraction in duplicate?		
For Yes, either ONE of the following:		
<input checked="" type="checkbox"/> at least two reviewers achieved consensus on which data to extract from included studies	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
<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.		
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:	<input checked="" type="checkbox"/> Justified the exclusion from the review of each potentially relevant study
<input checked="" 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):		
<input checked="" type="checkbox"/> described populations <input checked="" type="checkbox"/> described interventions <input type="checkbox"/> described comparators <input checked="" type="checkbox"/> described outcomes <input checked="" type="checkbox"/> described research designs	For Yes, should also have ALL the following:	<input type="checkbox"/> described population in detail <input type="checkbox"/> described intervention in detail (including doses where relevant) <input type="checkbox"/> described comparator in detail (including doses where relevant) <input type="checkbox"/> described study's setting <input type="checkbox"/> timeframe for follow-up
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> Partial Yes <input type="checkbox"/> No		
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:	<input type="checkbox"/> allocation sequence that was not truly random, <i>and</i> <input type="checkbox"/> selection of the reported result from among multiple measurements or analyses of a specified outcome
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> Partial Yes <input type="checkbox"/> No <input type="checkbox"/> Includes only NRSI		
NRSI		
For Partial Yes, must have assessed RoB:		
<input checked="" type="checkbox"/> from confounding, <i>and</i> <input checked="" type="checkbox"/> from selection bias	For Yes, must also have assessed RoB:	<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
<input type="checkbox"/> Yes <input checked="" 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 checked="" type="checkbox"/> No

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<p>11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?</p>	
<p>RCTs For Yes:</p> <p><input checked="" type="checkbox"/> The authors justified combining the data in a meta-analysis</p> <p><input checked="" type="checkbox"/> AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.</p> <p><input checked="" type="checkbox"/> AND investigated the causes of any heterogeneity</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> No meta-analysis conducted</p>
<p>For NRSI For Yes:</p> <p><input checked="" type="checkbox"/> The authors justified combining the data in a meta-analysis</p> <p><input checked="" type="checkbox"/> AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present</p> <p><input checked="" 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</p> <p><input type="checkbox"/> AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> No meta-analysis conducted</p>
<p>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?</p>	
<p>For Yes:</p> <p><input type="checkbox"/> included only low risk of bias RCTs</p> <p><input checked="" 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.</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> No meta-analysis conducted</p>
<p>13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?</p>	
<p>For Yes:</p> <p><input type="checkbox"/> included only low risk of bias RCTs</p> <p><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</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>
<p>14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?</p>	
<p>For Yes:</p> <p><input type="checkbox"/> There was no significant heterogeneity in the results</p> <p><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</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>
<p>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?</p>	
<p>For Yes:</p> <p><input checked="" type="checkbox"/> performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias</p>	<p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> No meta-analysis conducted</p>

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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 checked="" type="checkbox"/> Yes
<input type="checkbox"/> The authors described their funding sources and how they managed potential conflicts of interest	<input type="checkbox"/> No