

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.	



Section/topic	#	Checklist item	Reported on page #	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).		
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.		
RESULTS				
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10-11 Fig 1.	
Study characteristics	18			
Risk of bias within studies	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).			
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.		
Synthesis of results	thesis of results 21 Present results of each meta-analysis done, including confidence intervals and measures of consistency.		16-21 Table 3, Fig 2, fig 3, fig 4 and Fig 5.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).		
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Table 5	
DISCUSSION				
Summary of evidence	mary of evidence 24 Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).		23-28	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	27-28	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	28	
FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Submission system	



PRISMA-P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic #	#		Information reported		Page and Line
			Yes	No	number(s)
ADMINISTRATIVE IN	FORMA	TION			'
Title					
Identification	1a	Identify the report as a protocol of a systematic review	Х		Page (1) Line numbers (4-5)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such		X	-
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	Х		Page (5) Line numbers (91)
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	X		Page (1) Line numbers (6-20)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Х		Page (1) Line numbers (21)
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments		X	-
Support					
Sources 5a	Fo	Indicate courses of financial or other cumpert for the review	X		No funding
	Ja	Indicate sources of financial or other support for the review			Submission system

Section/topic	#	Checklist item	Information reported		Page and Line	
			Yes	No	number(s)	
Sponsor	5b	Provide name for the review funder and/or sponsor	х		No funding Submission system	
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	X		No funding Submission system	
INTRODUCTION						
Rationale	6	Describe the rationale for the review in the context of what is already known	X		Page (4-5) Line numbers: (52-85)	
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	x		Page (5) Line numbers: (85-87)	
METHODS						
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	х		Page (5, 6-7) Line numbers: (93-99, 122- 135)	
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	x		Page (5) Line numbers: (101-104)	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	x		Page (6) Line numbers: (105-120)	
STUDY RECORDS	STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	X		Page (7) Line numbers: (140-141, 144-147)	



Section/topic	#		Information reported		Page and Line
			Yes	No	number(s)
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	х		Page (7) Line numbers: (137-147)
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Х		Page (10) Line numbers: (226-230) #(see Fig 1)
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	x		Page (5) Line numbers: (95-99)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	х		Page (5) Line numbers: (99)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Х		Page (9) Line numbers: (189-196)
DATA					
	15a	Describe criteria under which study data will be quantitatively synthesized	Х		Page (9-10) Line numbers: (198-218)
Synthesis	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., f , Kendall's tau)	Х		Page (10) Line numbers: (220-224)
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)		Х	-
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	X		Page (19) Line numbers: (326-329) - fig 3 Page (20) Line numbers: (346-351) - fig 4

Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	Х	Page (22) Table 4 and 5.
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	Х	Page (21-22) Line numbers: (374-389)