PRISMA 2020 Checklist. Completed PRISMA 2020 checklist for this systematic review, indicating the page numbers or sections of the manuscript where each item is addressed.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page, p. 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract, p. 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	§ 1 Introduction, pp. 2–3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	§ 1 Introduction (final paragraph), p. 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	§ 2.2 Eligibility Criteria, pp. 3
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.	§ 2.3 Information Sources and Study Selection, p. 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Table S1
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.	§ 2.3 Information Sources and Study Selection, p. 4; Figure 1 (PRISMA flow diagram)
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.	§ 2.4 Data Extraction and Risk of Bias, p. 4
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.	§ 2.1 Protocol; § 2.2 Eligibility Criteria, pp. 3-4
	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.	§ 2.4 Data Extraction, p. 4
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	§ 2.4 Data Extraction and Risk of Bias, p. 4;

		worked independently, and if applicable, details of automation tools used in the process.	Supplementary Figures S2A–S2B
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.	§ 2.5 Synthesis and Certainty of Evidence, p. 4
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).	§ 2.5 Synthesis and Certainty of Evidence, p. 4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	§ 2.5 Synthesis and Certainty of Evidence, p. 4
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	§ 2.5 Synthesis and Certainty of Evidence, p. 5
	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.	§ 2.5 Synthesis and Certainty of Evidence, p. 4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	§ 2.5 Synthesis and Certainty of Evidence, p. 4
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	§ 2.5 Synthesis and Certainty of Evidence, p. 4
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	§ 2.5 Synthesis and Certainty of Evidence, p. 4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	§ 2.5 Synthesis and Certainty of Evidence, p. 4; Table 2 (GRADE Summary)
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.	§ 3.1 Study Selection, p. 5; Figure 1 (PRISMA flow diagram)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	§ 3.1 Study Selection, p. 5
Study characteristics	17	Cite each included study and present its characteristics.	§ 3.2 Randomized Controlled Trials – 3.3 Open-label trials – 3.4 Summary of findings; Table 1, pp. 8-10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	§ 2.4 Data Extraction and Risk of Bias, p.4;

			Table 2
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.	§ 3.2 Randomized Controlled Trials – 3.3 Open-label trials – 3.4 Summary of findings ; Table 1, pp. 8-10
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	§ 3.4 Summary of Findings, pp. 10–11
	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.	§ 3.4 Summary of Findings, p. 10, Table 2.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	§ 3.4 Summary of Findings; § 4.3 Strengths and Limitations, pp. 10 and 11-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	§ 3.4 Summary of Findings, p. 10, Table 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	§ 2.5 Synthesis and Certainty of Evidence and § 3.4 Summary of Findings, pp. 4 and 10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	§ 3.4 Summary of Findings, p 10, Table 2 (GRADE Summary)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	§ 4.1 Efficacy – 4.2 Safety and Tolerability – 4.3 Strengths and limitations of the evidence base – 4.4 Clinical Implications – § 5 Conclusions and Future Perspectives, pp. 11 – 12
	23b	Discuss any limitations of the evidence included in the review.	§ 4.3 Strengths and limitations of the evidence base, pp. 11-12
	23c	Discuss any limitations of the review processes used.	§ 4.3 Strengths and limitations of

			the evidence base, pp. 11-12
	23d	Discuss implications of the results for practice, policy, and future research.	§ 4.4 Clinical Implications; § 5 Conclusions, p. 12
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.	§ 2.1 Protocol, p. 3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	§ 2.1 Protocol (OSF link), p. 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	§ 2.1 1 Protocol (none reported), p. 3
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding, p. 13
Competing interests	26	Declare any competing interests of review authors.	Conflicts of Interest, p. 13
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.	Supplementary Materials, p. 12

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