

Effectiveness of educational interventions on vaccine hesitancy: a systematic review and meta-analysis

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Annex 1: risk of bias assessment of randomized controlled trials using the Cochrane Risk of Bias 2 (RoB 2) tool						
Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Huang <i>et al.</i>	Low	Low	Some concerns	Low	Low	Some concerns
Roussos-Ross <i>et al.</i>	Low	Low	Low	Low	Low	Low
Frew <i>et al.</i>	Low	Low	Low	Low	Low	Low
Kriss <i>et al.</i>	Low	Low	Low	Low	Low	Low
Kester <i>et al.</i>	Low	Low	Some concerns	Low	Low	Some concerns
Meharry <i>et al.</i>	Low	Low	Low	Low	Low	Low
Herrett <i>et al.</i>	Low	Low	Low	Low	Low	Low
Sun <i>et al.</i>	Low	Low	Low	Low	Low	Low
Bennett <i>et al.</i>	Low	Low	Low	Low	Low	Low
O'Leary <i>et al.</i>	Low	Low	Low	Low	Low	Low
Nyhan <i>et al.</i>	Low	Low	Low	Low	Low	Low
Dudley <i>et al.</i>	Low	Low	Low	Low	Low	Low
Stockwell <i>et al.</i>	Low	Low	Low	Low	Low	Low

Annex 2: methodological quality assessment of observational studies using the Newcastle-Ottawa Scale (NOS)					
Study	Selection (4 ★)	Comparability (2 ★)	Outcome/exposure (3 ★)	Total score	Quality rating
Hebballi <i>et al.</i>	★★★★	★★	★★	8	Good/high quality
Costantino <i>et al.</i>	★★★	★★	★	6	Fair/moderate quality
Preston <i>et al.</i>	★★★★	★★	★★★	9	Good/high quality
Abebe <i>et al.</i>	★★★★	★★	★★	8	Good/high quality
Mascaro <i>et al.</i>	★★★	★★	★★	8	Good/high quality
Drokow <i>et al.</i>	★★	★★★★*	★★	7	Fair/moderate quality
Marinda <i>et al.</i>	★★★★	★★	★★★	9	Good/high quality
Ahmed <i>et al.</i>	★★★★	★★	★★★	9	Good/high quality
Abdullah <i>et al.</i>	★★★★	★★	★★★	9	Good/high quality



Annex 3: grading of recommendations assessment, development and evaluation (GRADE) evidence profile for the primary outcomes									
Outcome	No. of Studies (design)	Participants (n)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence (GRADE)	Justification
Behaviour (vaccine uptake/behaviour)	11 RCTs suitable for meta-analysis*	858	Not serious	Serious ↓	Not serious	Not serious	Undetected	Moderate	Of the 13 eligible RCTs, 11 provided data suitable for quantitative synthesis. Most contributing studies were assessed as having low risk of bias, with some concerns in a small number of studies. Certainty was downgraded one level for substantial heterogeneity across intervention types, vaccine categories, populations, and settings. The populations, interventions, comparators, and outcomes were directly relevant to the review question. Effect estimates were generally sufficiently precise. No definitive evidence of publication bias was identified, although borderline funnel plot asymmetry was observed.
Knowledge	7 studies (RCTs and observational studies)	461	Not serious	Serious ↓	Not serious	Not serious	Undetected	Moderate	Overall methodological quality was acceptable, with few concerns regarding risk of bias. Certainty was downgraded one level because of substantial variation in intervention formats, outcome measurement, and study characteristics. The evidence directly addressed educational interventions designed to improve vaccine knowledge. Sample sizes and confidence intervals were generally adequate, and no convincing evidence of publication bias was identified.



Vaccination intention	5 RCTs	349	Not serious	Serious ↓	Not serious	Not serious	Undetected	Moderate	Most contributing trials were assessed as having low risk of bias. Certainty was downgraded one level because of differences in intervention delivery, follow-up periods, participant characteristics, and other sources of between-study heterogeneity. The interventions and outcomes were directly applicable to the review objectives. Effect estimates were generally sufficiently precise, with no clear evidence of publication bias.
GRADE domain judgements									
GRADE domain			Behaviour	Knowledge	Vaccination intention	Justification			
Risk of bias			Not serious	Not serious	Not serious	RoB 2 assessment showed that 11 of the 13 eligible RCTs were at low risk of bias and 2 had some concerns. Observational studies assessed using the NOS were predominantly of high methodological quality, although two were rated as fair quality.			
Inconsistency			Serious ↓	Serious ↓	Serious ↓	Substantial heterogeneity was observed across intervention modalities, vaccine types, populations, settings, follow-up periods, and outcome measurement. Therefore, the certainty of evidence was downgraded by one level for inconsistency.			
Indirectness			Not serious	Not serious	Not serious	The included populations, interventions, comparators, and outcomes directly addressed the review question.			
Imprecision			Not serious	Not serious	Not serious	The pooled estimates were generally based on adequate sample sizes and had reasonably precise confidence intervals.			
Publication bias			Undetected	Undetected	Undetected	Funnel plot inspection and Egger's test did not provide definitive evidence of publication bias, although borderline asymmetry was observed for some analyses.			
Overall certainty			Moderate	Moderate	Moderate	Evidence for all three primary outcomes was judged to be of moderate certainty, primarily because of concerns regarding inconsistency across studies.			