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Appendix S4. A Framework for Assessing the Risk of Bias in Individual Studies

Adapted from the framework presented by Altman (Egger M, Smith GD, Altman D, eds. *Systematic Reviews in Health Care: Meta-analysis in Context*. Wiley-Blackwell; 2001).

Study feature	Qualities sought				
1. Sample of patients	Eligibility criteria defined	Good	Poor	N/R	N/A
	Sample selection explained (setting, locations and periods of recruitment)	Good	Poor	N/R	N/A
	Clinical and demographic characteristics fully described	Good	Poor	N/R	N/A
	Representative (unbiased selection of controls)	Good	Poor	N/R	N/A
	Assembled at a common stage in the course of their disease	Good	Poor	N/R	N/A
	Completeness	Good	Poor	N/R	N/A
2. Follow	Sufficiently long	Good	Poor	N/R	N/A

up of patients					
3. Outcome	Fully defined	Good	Poor	N/R	N/A
	Known for all or a high proportion of patients	>80%	60-79%	<60%	N/R
	Outcome assessor blinded to exposure status	Good	Poor	N/R	N/A
4. Prognostic variable	Fully defined, including details of method of measurement (maternal HBsAg study: when maternal serology was investigated?)	Good	Poor	N/R	N/A
	Available for all or a high proportion of patients	>80%	60-79%	<60%	N/R
	Exposure assessor blinded to outcome status	Good	Poor	N/R	N/A
5. Analysis	Continuous predictor variable analysed appropriately	Good	Poor	N/R	N/A
	Appropriate control for	Good	Poor	N/R	N/A

	confounding factors				
	Appropriate statistical method	Good	Poor	N/R	N/A
6.	Fully described	Good	Poor	N/R	N/A
Treatment subsequent to inclusion in cohort	Treatment standardized or randomised	Good	Poor	N/R	N/A

Abbreviations: N/A, not applicable; N/R, not reported.