Section/topic	No.	Checklist item	Reported in:
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both	Title page
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	Executive summary
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	*Chapter 1*, *Conditions and aetiologies*
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS)	*Chapter 2*, *Objectives*
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g. website address) and, if available, provide registration information including registration number	Protocol available at: http://guidance.nice.org.uk/DT/3/FinalProtocol/pdf/English
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	*Chapter 3*, *Inclusion and exclusion criteria*
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	*Chapter 3*, *Search strategy*
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	*Appendix 1*
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)	*Chapter 3*, *Inclusion screening and data extraction*
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	*Chapter 3*, *Inclusion screening and data extraction*
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made	*Chapter 3*, *Inclusion screening and data extraction*
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was carried out at the study or outcome level), and how this information is to be used in any data synthesis	*Chapter 3*, *Inclusion screening and data extraction*
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means)	*Chapter 3*, *Inclusion screening and data extraction* and *Quality assessment*
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if undertaken, including measures of consistency (e.g. I^2) for each meta-analysis	*Chapter 3*, *Methods of analysis/synthesis*

Section/topic	No.	Checklist item	Reported in:
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)	NA
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if carried out, indicating which were prespecified	NA
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	*Figure 1*
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations	*Appendix 4* and *Table 1*
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item no. 12)	*Appendix 3*, *Tables 2, 4*, *6*, *8* ,*10*, *12* and *14*
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 CIs, ideally with a forest plot	*Tables 3*, *5*, *7*, *9*, *11*, 13 and *15*
Synthesis of results	21	Present results of each meta-analysis undertaken, including CIs and measures of consistency	*Table 16*
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item no. 15)	*Figure 10*
Additional analysis	23	Give results of additional analyses, if done [e.g. sensitivity or subgroup analyses, meta-regression (see item no. 16)]	NA
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. health-care providers, users and policy-makers)	*Chapter 4*, *Summary*
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)	*Chapter 5*, *Statement of principal findings* and *Strengths and limitations of assessment*
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	*Chapter 5*, *Uncertainties*
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	*Executive summary*

NA, not applicable.