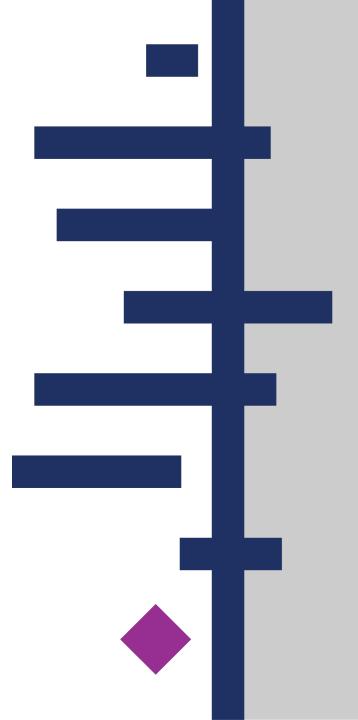


MECIR

Toby Lasserson April 2016

Trusted evidence. Informed decisions. Better health.





Session overview

MECIR: brief history

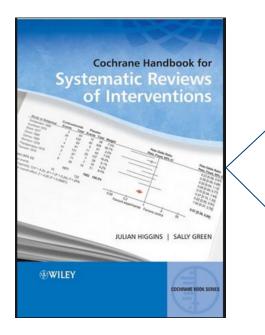
CEU review screening & use of MECIR

MECIR 2.0



MECIR standards

Developed from existing Handbook guidance



Chapter 5: Defining the review question and developing criteria for including studies Chapter 6: Searching for studies Chapter 7: Selecting studies and collecting data Chapter 8: Assessing risk of bias in included studies Chapter 9: Analysing data and undertaking meta-analyses Chapter 10: Addressing reporting biases Chapter 11: Presenting results and 'Summary of findings' tables Chapter 12: Interpreting results and drawing conclusions

Chapter 6: Searching for studies

Authors: Carol Lefebvre, Eric Manheimer and Julie Glanville on behalf of the Cochrane Information Retrieval Methods Group.

Key points

- Review authors should work closely from the start with the Trials Search Co-ordinator (TSC) of their Cochrane Review Group (CRG).
- Studies (not reports of studies) are included in Cochrane reviews but identifying reports of studies is currently the most
 convenient approach to identifying the majority of studies and obtaining information about them and their results.
- Trials registers and trials results registers are an increasingly important source of information.
- The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE (if access is available to either the review author or TSC) should be searched for all Cochrane reviews, either directly or via the CRG's Specialized Register.
- · Searches should seek high sensitivity, which may result in relatively low precision.
- Too many different search concepts should be avoided, but a wide variety of search terms should be combined with OR within each concept.
- · Both free-text and subject headings should be used (for example Medical Subject Headings (MeSH) and EMTREE)
- Existing highly sensitive search strategies (filters) to identify randomized trials should be used, such as the newly revised Cochrane Highly Sensitive Search Strategies for identifying randomized trials in MEDLINE (but do not apply these filters in CENITRAL).

	Searching f	or studies			
C24	Mandatory	Searching key databases	Search the Cochrane Review Group's Specialized Register (internally, e.g. via the Cochrane Register of Studies, or externally via CENTRAL, Ensure that CENTRAL and MEDLINE (e.g. via PubMed) have been searched (either for the review or for the Review Group's Specialized Register).	Searches for studies should be as adminive as possible in order to reduce the risk of publication bias and to identify an anul network web regime as possible. The minimum databases to be covered are the Codrame Review Group's Specialized Rectange of the studies of the studies of the studies of the studies of the Rectange of the studies of the studies of the studies of the registration of the studies of the registration of the studies of the registration of the registration of the registration of the registration of registration of r	6.2.1.1 6.3.3
C25	Highly desirable	Searching specialist bibliographic databases	Search appropriate national, regional and subject specific bibliographic databases.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Databases relevant to the review topic should be covered (e.g. CINAHL for nursing- related topics, PsychiNFC for psychological interventions), and regional databases (e.g. LLIACS) should be considered.	6.2.1.4 6.2.1.5 6.4.1
226	Mandatory	Searching for different types of evidence	If the review has specific eligibility criteria around study design to address adverse effects, economic issues or qualitative research questions, undertake searches to address them.	Sometimes different searches will be conducted for different types of evidence, such as for non-randomized studies for addressing adverse effects, or for economic evaluation studies.	13.3 14.5 15.3 20.3.2.1
C27	Mandatory	Searching trials registers	Search trials registers and repositories of results, where relevant to the topic through Clinical Trials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) portal and other sources as appropriate.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Although ChincalTrials gov is included as one of the registers within the VHAO ICTRP portal, it is recommended that both ChincalTrials.gov and the ICTRP portal are searched separately due to additional features in ChincalTrials.gov.	6.2.3.1 6.2.3.2 6.2.3.3

Search m	ethods for identification	of studies		
R34	Mandatory	Search sources	List all sources searched, including: databases, trials registers, web sites and grey literature. Database names should include platform/provider name and dates of coverage, web sites should include full name and URL. State whether reference lists were searched and whether individuals or organizations were contacted.	MECIR conduct standard 36 (Document the search process in enough detail to ensure that it can be reported correctly in the review.) Also MECIR conduct standards 24 – 31. [PRISMA item 7]
R35	Mandatory	Latest searches	Provide the date of the last search and the issue / version number (where relevant) for each database whose results were evaluated and incorporated into the reviewif a search was re-run prior to publication, the results of which were not incorporated, explain how the results were dealt with and provide the date.	The review should provide the search date from which studies have been retrieved and assessed for inclusion. This is the date up to which the conclusions of the review are valid. It should reflect the date of the most recent set of searches from which all records have been screened for relevance and any studies meeting the eligibility criteria have been fully incorporated into the review (studies may be awaiting classification if, for example, the review authors are awaiting translation or clarification from authors or sponsors). Since the review is likely to have drawn on searches conducted across multiple databases, it is possible that searches were performed on more than one date. The earliest date of the most recent set of searches should be provided in the review text and as the hard-coded date of the last search. The remaining dates for other databases should be reported in an appendix.



MECIR standards

Developed from existing Handbook guidance

Extensive consultation process

Development of methodological standards for the conduct of intervention reviews

Annex 2: Feedback and response to consultation

ltem number	Status	Item description	Expectation (now Standard)	conditional on	Rationale	Agree?	Disagree?	Change status to? [or omit?]	Change status to? [or omit?] MG	Comments	Response	New Item number
101	Mandat ory	Pre-defining objectives	Define in advance the objectives of the review, including participants, interventions, comparators and outcomes.		Objectives give the review focus and must be clear before appropriate eligibility criteria can be developed.	CRG: 31 C:7 F:4 M:6	CRG: 0 C: 0 F: 0 M: 0	CRG29: omit		CRG29: obvious CRG25: Query whether the outcomes must be listed in the Objectives CRG21: Surely this is built into the protocol/review format, and happens already? If not, it shouldn't be a Cochrane product CRG36: May need some flexibility in exact wording. CRG36: this hould be simply stated under Expectation Define in advance the primary objective(s) of the review?, because the intention here is to highlight the need of pre-defining the objective(s), not what the objective should include. The second bit of the sentence ('including participants, interventions, comparators and outcomes?) would not only go beyond this proposed standard, but could also cause confusion, since. It is handbook advice that a primary/main objective is 16 defined (including in its format: interventions, comparison, health problem, participants type, and setting if appropriate), and that the main objective MIGHT be followed by a series of specific objectives relating to different outcome measures. Thus, it looks like that a primary objective should be mandatory, but specific ones, which may vay according to participants, interventions, comparisons OR (rather than AUD) outcomes, should not, and the Expectation statement is not really reflecting his all present. MG8: Either this item or item 112 should ask reviewers to clarify whether the aim of the IK is to compare two or more interventions.	Status and standard unchanged. Details of the review question, and where they are stated, is a reporting issue. Rationale extended to comment on comparisons of multiple interventions.	2
102	Highly desirabl e	Formulating review questions	Ensure that the review question, and particularly the outcomes of interest, address issues that are important to stakeholders such as consumers		Cochrane reviews are intended to support clinical practice and policy, not just scientific curiosity. Qualitative research, i.e. studies that explore the experience of those involved in providing and	CRG: 20 C: 7 F: 4 M: 5	CRG: 5 C: 0 F: 0 M: 0	CRG35: Mandatory CRG32: mandatory CRG31: Mandatory CRG29: omit CRG5: Omit, stick to health science CRG34:		CRG32: It is essential that our reviews are addressing issues that are relevant to stakeholders and end-users. CRG32: The big efforts to produce a high-quality Cochrane review should primarily focus on patient-relevant outcomes (additional outcomes might be reported). No Cochrane review should be published investigating surrogate outcomes only. CRG30: Should there be a separate section to acknowledge consumer or stakeholder comments to the review question? CRG29: can not be checked or implemented	Status changed to Mandatory. Standard modified to expand on types of stakeholders. Rationale extended to incorporate extended to mention the interests of consumers.	1

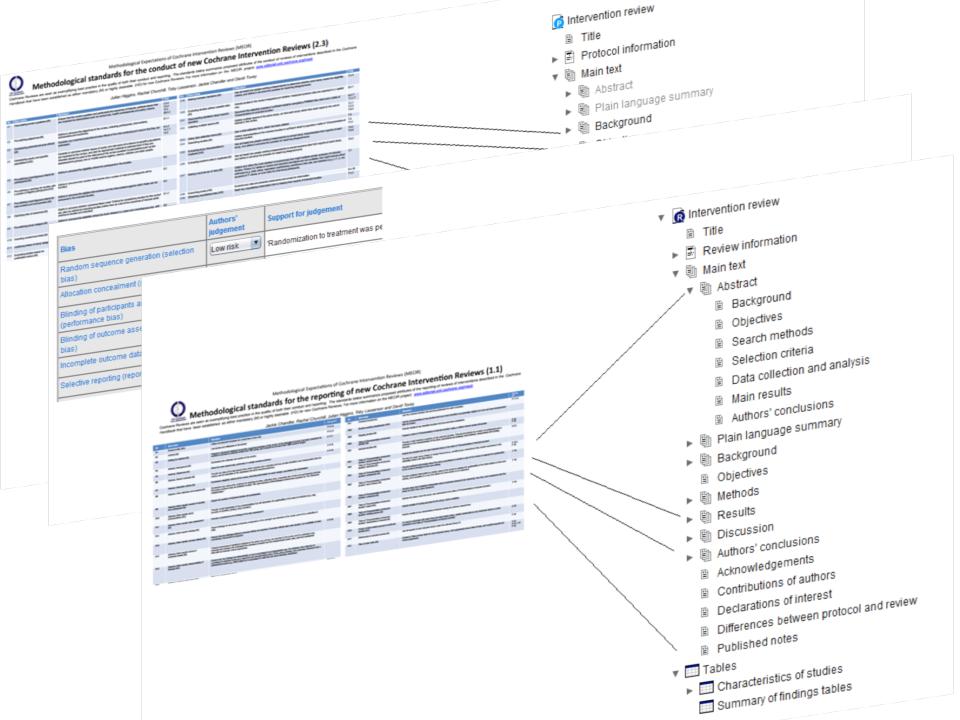


MECIR standards

Developed from existing Handbook guidance

Extensive consultation process

Never apply all at once





MECIR standards

Developed from existing Handbook guidance

Extensive consultation process

Never apply all at once

Supported: Software prompts for users

	Text of Review 🔀 1.2 Machine usage	X Guidance
		MECIR Reporting
1	04 September 2008 Updated V Literature search re-run.	Abstract, Main results: number of studies and participants
		R9, Mandatory
	Add Event	Report the number of included studies and participants.
	Add Link	
	History	Abstract, Main results: study characteristics
		R10, Highly desirable
	Abstract	Provide a brief description of key characteristics that will determine the applicability of the body of evidence (e.g. ag severity of condition, setting, study duration).
	Background	Details
	Continuous Positive Airways Pressure (CPAP) is considered to be the cornerstone of therapy for obstructive sleep apnoea (OSA). However, compliance with this treatment is frequently poor, which may lead to ongoing symptoms of sleep disruption, daytime sleepiness and poor waking	Abstract, Main results: bias assessment
	cognitive function. Mechanical interventions which involve changing the way that positive pressure is delivered, and the addition of humidification,	R11, Mandatory
	might improve compliance.	Provide a comment on the findings of the bias assessment.
	Objectives	Details

To determine the efficacy of pressure level modifications and additional humidification in increasing CPAP machine usage.

Search methods

We searched the Cochrane Airways Group Specialised Register (September 2008).

Selection criteria

Randomised controlled trials (RCTs) assessing interventions to improve compliance with CPAP usage. Control groups received fixed pressure CPAP

Data collection and analysis

Two authors assessed articles for inclusion in the review and extracted data. We made attempts to obtain additional unpublished data from the trialists.

Main results

Forty-five studies met the inclusion criteria (1874 participants). Auto-CPAP (30 studies, 1136 participants): a statistically significant difference in machine usage of 0.21 hours/night (0.08 to 0.35) was observed in favour of auto-CPAP from cross-over studies. This difference is of questionable clinical significance. Pooled effect estimates from parallel group trials detected a similar sized difference for average nightly machine usage, but this was not statistically significant. Evidence from parallel group studies did not identify a statistically significant difference between pressure modes in Epworth Sleepiness Scores, but there was an overall reduction of 0.64 units with cross-over studies (-0.12 to -1.16) in favour of auto-CPAP. Parallel group studies did not identify a significant difference. More participants preferred auto-CPAP to fixed CPAP where this was measured. Bi-level PAP (six studies, 285 participants): no significant differences were observed in machine usage. One small study found no difference in preference. C-Flex (six studies, 318 participants): no significant difference was observed in machine usage. Humidification (three studies, 135 participants): there were conflicting findings between the studies. Two parallel group trials found no significant difference in machine usage, whereas a cross-over study found a significant difference.

Authors' conclusions

Improvement in average machine use of auto-CPAP was superior in studies with a cross-over design; the point estimate in parallel group trials was similar, but did not reach statistical significance. It is uncertain how use of machines in study settings relates to 'real world' use. Where

Abstract. Main results: findings

R12, Mandatory

Report findings for all primary outcomes, irrespective of the strength and direction of the result, and of the availability of data.

Abstract, Main results: adverse effects

R13, Mandatory

Ensure that any findings related to adverse effects are reported. If adverse effects data were sought, but availability of data was limited, this should be reported.

Abstract, Main results: format of numerical results

R14, Mandatory

Present summaries of statistical analyses in the same way as they are reported in the review and in a standard way, ensuring that readers will understand the direction of benefit and the measurement scale used, and that confidence intervals are included where appropriate.

Abstract, Main results: interpretability of findings

R15. Highly desirable

Ensure that key findings are interpretable, or are re-expressed in an interpretable way. For instance, they might be re-expressed in absolute terms (e.g. assumed and corresponding risks, NNTs, group means), and outcomes combined with a standardized scale (e.g. SMD) might be re-expressed in units that are more naturally understood. Details



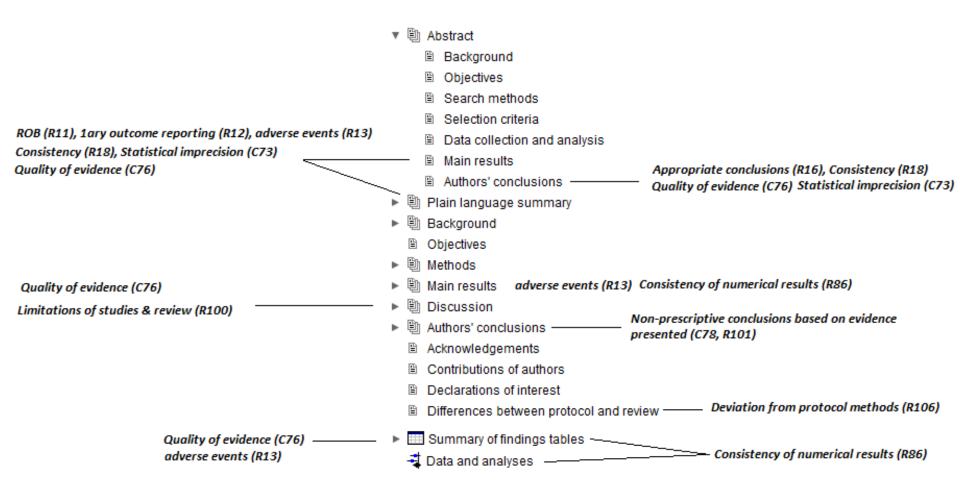
Screening



Spot the missing piece

ltem No.	ltem	n name		Standard	Met?			Comment	
	Implen	mentatio	n of protocol me	thods					
C27	Searchin registers		through ClinicalTrials	s and repositories of results, where relevant to the topic .gov, the WHO International Clinical Trials Registry tal and other sources as appropriate.					
C37	Rerunnin	ltem No.	Item name	Standard			Met?		Comment
		C76	Assessing the quality of the body of evidence	imprecision, indirectness and publication bias) to ass	the five GRADE considerations (study limitations, consistency of effect, recision, indirectness and publication bias) to assess the quality of the / of evidence for each outcome, and to draw conclusions about the quality ridence within the text of the review.				
	Excluding without u data		'Summary of findings' table	Present a Summary or Findings table according to re described in Chapter 11 of the Cochrane Handbook (Specifically: include results for one clearly defined population grou indicate the intervention and the comparison intervent include seven or fewer patient-important outcomes; describe the outcomes (e.g. scale, scores follow.un)	version 5 or later). ıp (with few exceptions); ion;				
068	Compari subgroup	C73	Interpreting results	Interpret a statistically non-significant P value (e.g. lar finding of uncertainty unless confidence intervals are out an important magnitude of effect.	ger than 0.05) as a				
		C78 Formulating implications for practice Base conclusions only on findings from the synthesis (quantitative or narrative) of studies included in the review.							
	R101 Implicat Item No. Item name							Met?	
				Completeness of reporting in the abstrac	ct & Internal consis	tency			

R11	Abstract, Main results: bias assessment	Provide a comment on the findings of the bias assessment.	
R12	Abstract, Main results: findings	Report findings for all primary outcomes, irrespective of the strength and direction of the result, and of the availability of data.	
R13	Abstract, Main results: adverse effects	Ensure that any findings related to adverse effects are reported. If adverse effects data were sought, but availability of data was limited, this should be reported.	
R18	Consistency of summary versions of the review	Ensure that reporting of objectives, important outcomes, results, caveats and conclusions is consistent across the text, the abstract, the plain language summary and the 'Summary of findings' table (if included).	
R86	Consistency of results	Ensure that all statistical results presented in the main review text are consistent between the text and the 'Data and analysis' tables.	



Key learning points

Implementation of protocol methods	Interpretation	Inconsistency
Excluding studies due to outcome reporting Unacknowledged departures from protocol Subgroups (misuse & interpretation) Analysis errors	SoF tables footnotes/ downgrading decisions Use of GRADE Prescriptive conclusions	Results in text/tables Mismatch between full- text & summary versions
Subgroups (misuse & interpretation)	Prescriptive conclusions	

Feedback loop for MECIR

CEU screening programme: Overview of common errors & good practice in Cochrane intervention reviews

Since September 2013, the CEU has been responsible for pre-publication screening of new intervention reviews. Based on these experiences this resource has been compiled to draw attention to the most prominent challenges faced by authors and editors in the production of Cochrane Reviews. Where possible it also identifies how they might be addressed.

Toby Lasserson, Senior Editor

Section of the review	Common error	Good practice
	Unclear or misleading title.	Clear link between the review title and review question.
Global	In empty reviews, too much prominence can be given to findings from ineligible studies, or extrapolation of positive results from other reviews.	Emphasis on the lack of evidence to address the review question and acknowledgement of any ongoing studies.
	Inconsistent messages across conclusions, PLS, Discussion & implications for practice & research.	Using GRADE ratings to inform the review abstract, Summary of Findings (SoF) tables, PLS, Effects of interventions, Discussion (especially quality of evidence) and conclusions.
Abstract main results	Primary outcomes and harms under-reported, often with emphasis on positive secondary endpoints.	Reporting main outcomes of interest irrespective of the strength of evidence. As a general approach, outcomes important enough to feature in the Summary of Findings table should be considered for the abstract and vice versa.

Feedback loop for MECIR

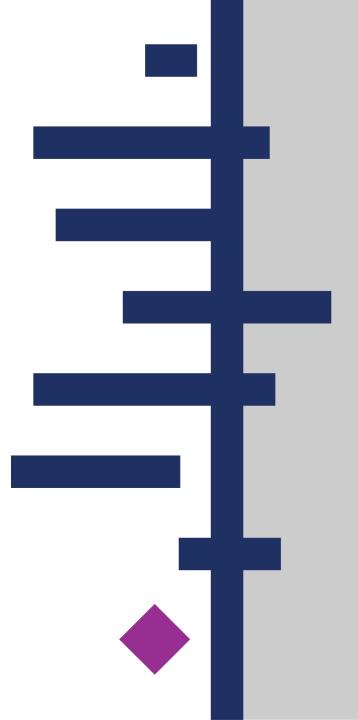
Incorporating GRADE in Cochrane Reviews: Feedback from the CEU screening programme

- Describing methods for assessing the quality of the evidence under the 'Data collection & analysis' section of protocols and full reviews.
- 2. Explaining decisions about the quality of the evidence in reporting of results.
- 3. Incorporating information about the quality of evidence in the Discussion.
- Drawing on quality of evidence ratings when summarising and interpreting the results e.g. abstracts, plain language summaries and implications for practice sections.



MECIR 2.0

Of sets & standards...





New developments

4 sets (conduct; reporting protocol; reporting review & updating)

Booklet format

Standards revised to reflect what screening has taught us

	Contents	
Metho Cochra	1. Introduction	3
MECIR	2. Standards for the conduct	
	of new Cochrane Intervention Reviews	5
	3. Standards for the reporting of protocols	
	for new Cochrane Intervention Reviews	34
Standard Cochrane and the <i>p</i>	4. Standards for the reporting	
	of new Cochrane Intervention Reviews	22
	5. Standards for the planning, conduct and reporting of updates of Cochrane Intervention Reviews	55



Changes to conduct standards

5 fewer conduct standards (75 versus 80)

Surviving standards draw on learning points from screening & related audit work

Mandatory

C756 Assessing the quality of the body of evidence

Use the five GRADE <u>considerations</u> (<u>risk of</u> <u>biasstudy limitations</u>, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome, and to draw conclusions about the quality of evidence within the text of the review. GRADE is the most widely used <u>approach system</u> for summarizsing confidence in effects of the interventions by outcome across studies. It is preferable to use the GRADE tool (as implemented in <u>GRADEprofiler or GDT</u> and described in the help system of the software). This should help to ensure that author teams are accessing the same information to inform their judgments. Ideally, two people working independently should assess the quality of the body of evidence <u>and</u> <u>reach a consensus view on any downgrading decisions</u>. The five GRADE considerations should be addressed irrespective of whether the review includes a 'Summary of <u>#F</u>Eindings' table. It is helpful to draw on this information in the <u>Discussion, in the conclusions and to convey the certainty in the evidence in the</u> <u>abstract and Plain Language Summary</u>. See Handbook 12.2

C7 <u>8</u> 9	Avoiding recommendations	-Mandatory
Avoid p practic	providing recommendations for e.	Cochrane <u>Intervention</u> <u>R</u> reviews should not attempt to tell people which interventions should or should not be used, since local considerations may be relevant. However, the implications of the findings should be discussed, and decision-making can be helped by laying out different scenarios. See Handbook 12.7.2
C <u>79</u> 80	Formulating implications for research	Highly desirable
addres includii	re the implications for research to s the nature of evidence required, ng population intervention rison, outcome, and type of study.	Anyone wishing to conduct a study in the topic area of the review should be provided with a clear sense of what the remaining uncertainties are. A useful framework for considering implications for research is EPICOT (evidence, population, intervention, comparison, outcome and time stamp). See Handbook 12.7.3



New set for reporting protocol

44 standards to mirror Conduct Standards

Investing effort in formulating question

Standard		Ration	ale and elaboration			
R3 Background	'			Mandatory		
	n addressed by the	reasoned rationale w existing knowledge. C useful to readers and	nould have a clearly defir hich has been developed Outlining the context of th helps to establish key un liness	in the context of he review question is		
he four standard he	PR14 Outcome doma	ins of interest			Mandatory	
	State which outcomes and which are seconda	are primary outcomes ary outcomes,	그는 그 지금 한 것을 수 있는 것을 가지 않는 것을 것을 수 있다. 않는 것을	should be pre-specified fo table (see PR40); it may be		
		PR39 Quality of the evid	dence			Mandatory
		State the methods to be quality of the body of ev GRADE considerations).		If the current GRADE gui followed in its entirety (reference to this is suffic make judgements.	see Handbook Chapt	er 12), then a
				MECIR conduct standard considerations (risk of b imprecision, indirectnes quality of the body of ev draw conclusions about text of the review.)	bias, consistency of el ss and publication bia vidence for each outc	ffect, as) to assess the ome, and to
		PR40 'Summary of findi	ngs' table			Mandatory
		State which outcomes a are intended to be inclue findings' table.	다른 말 다양 같이 다 같이 많이 많이 많이 다 같다. 것은 것이 없이 많이	Up to a maximum of s pre-specified for inclu If possible, sources of a 'Summary of finding	ision in a 'Summary o any assumed risks to	of findings' table. b be presented in
				MECIR conduct stando to be used for assession and summarizing the	ng the quality of the l	body of evidence,



Changes to reporting standards

Reporting standards revised to incorporate learning points from review screening

Clarification based on user feedback

R12 Abstract, Main results: findings

Mandatory

Report findings for all <u>important primary</u> outcomes, irrespective of the strength and direction of the result, and of the availability of data. Findings should typically include concise information about the <u>size of effect and</u> quality of the body of evidence for the outcome (such as <u>study limitationsrisk of</u> <u>bias</u>, consistency of effect, imprecision, indirectness and publication bias), for example using GRADE.

Outcomes <u>reported in the abstract</u> should not be selected solely on the basis of the findings. <u>In general, the same outcomes in the abstract should be presented</u> <u>in the Plain Language Summary and Summary of Findings tables.</u> If no studies measured the <u>primary</u> outcomes, then a comment should be made to that effect.

R99100 Limitations

Discuss limitations of the review at study and outcome level (e.g. regarding risk of bias), and at review-level (e.g. incomplete identification of studies, reporting bias). Review authors must explicitly state the limitations of their review. One aspect that is easily overlooked is that of adverse effects. In particular, if the review methods do not allow for detection of serious and/or rare adverse events, the review authors must explicitly state this as a limitation. <u>Additional considerations here include currency and completeness of the search, completeness of data collection processes, assumptions regarding classification of interventions, outcomes or subgroups, and methods to account for missing data.</u>

MECIR conduct standard 74 (Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.) [PRISMA item 25]

Mandatory



Updating

Challenge notion that updating = adding studies

Start with a re-evaluation of the original research question (new protocol if necessary)

Separation of standards between planning & considerations for reporting

DECIDING ON AND PERFORMING AN UPDATE

Planning the update

		Standard		Rat	ionale and	elab	oration		
	U1	Reconsidering review	questic	ons				Mandatory	
	Confirm or amend review question (PICO) and objectives.			Consider whether it is impo the review relevant to its us		odify o	or add new objectiv	es to make	
				otherwise changed substan and the <i>MECIR conduct stan</i> update standards. It will be	Consider whether the review will be split, merged with another review or otherwise changed substantially. If so, a new protocol might be warranted and the <i>MECIR conduct standards</i> should be followed rather than these <i>update standards</i> . It will be necessary to agree the approach to updating the review with the Cochrane Review Group.				
Reconsiderir	ng elig	ibility criteria						U11 Assessi	ing quality of the evide
firm or ame	nd eliş	gibility criteria.						consideration inconsistency	y of evidence using GR ns of risk of bias, y, imprecision,
								indirectness	and publication bias.
U2 Reco	nsider	ing outcomes				U5	Reconsidering dat		
Confirm o interest.	or ame	end outcomes of				colle	and analysis meth sider whether meth ection and analysis	ods for data (including a	
			U4	Planning the search		ame	DE assessment) nee nded in the light of nodological develop	recent	
			Decid	le appropriate search methods.					

UR2 Changes to scope

1

Explain any changes to questions, objectives or eligibility criteria.

		•
UR4 Flow	of studies	Mandatory
Flow of studies		 Provide information on the flow of studies into the updated review, ideally using a flow diagram. There are two broad options for providing information about how studies were identified that are included in the updated version of the review: The results of previous searches can be retained in the review and supplemented with information about studies identified in the update. Alternatively, only information about searches in the current update can be presented, with the previous version of the review serving as one particular source of studies.
	UR7 What's new?	Manda
	Explain what's new.	It is important that changes are explained to inform returning readers about what's new. This should be achieved in several ways.
		A comment should be inserted to explain that the review is an update o previously published review. This might be placed at the beginning or e of the Background or the start of the section 'Search methods for identification of studies'. It can be helpful to explain also whether the article describes the first, second, third and so on update of the review.
		Changes in review questions, eligibility criteria and methods should be reported in the section 'Differences between protocol and review', maki it clear that they are changes since the previous version.

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Where next?



Supporting implementation

Finalise & circulate the final sets as booklet

Handbook & software integration

Update learning resources

Produce targeted guidance on aspects of conduct & reporting that pose greatest challenge



Summary

MECIR should not be seen in isolation from Handbook guidance

Shared ownership

Some standards easier to attain than others

Recent changes encourage earlier adherence to standards & reinforce good practice