Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

METHOD – RAPID REVIEWS

KCE PROCESS NOTES
METHODS

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METHOD – RAPID REVIEWS

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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AHRQ	US Agency for Healthcare Research and Quality
CADTH	Canadian Agency for Drugs and Technologies in Health
HTA	Health Technology Assessment
RR	Rapid review
RRMG	Cochrane Rapid Reviews Methods Group
SR	Systematic review

SCIENTIFIC REPORT

1 WHAT IS A RAPID REVIEW?

A rapid review (RR) is a type of knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a short period of time[1]. There is today no clear-cut definition of a RR. Instead, this denomination covers a range of products characterized by varying depth and breadth of steps involved[1-3]. This document focuses on RRs understood as rapid systematic reviews of the literature. They can be either used as stand-alone documents or included in Rapid Health Technology Assessments or Rapid Guidelines. Other methodological aspects of such reports are out of scope of this process note.

The US Agency for Healthcare Research and Quality (AHRQ) provides a neat overview of dimensions of standard systematic reviews that may be altered in RRs[4] (see Table 1). Similarly, an international survey of 40 RR producers reported the most frequently used approaches in the production of RRs: updating the literature search of previous reviews (92%); limiting the search strategy by date of publication (88%); and having only one reviewer to screen (85%), excluding abstract data (84%), and excluding the assessment of the quality of the included studies (86%)[2].

Other ways of categorizing RRs also exist. For example, Polisena and colleagues divided RRs into six groups: accelerated, condensed, focused, form of evidence synthesis, modified and tailored RRs[5] (see appendix). The Canadian Agency for Drugs and Technologies in Health (CADTH) (https://www.cadth.ca/about-cadth/what-we-do/products-services/rapid-response-service) also proposes a range of products tailored to meet the specific requirements and time-frame of decision-makers, from a simple reference list to a rapid HTA (see appendix).

In spite of this variety of products, two characteristics are constant.

- First, a RR should be executed more rapidly than a full systematic review. According to Schunemann et al., rapid systematic reviews should be conducted in less than 8 weeks[6]. However, other authors described rapid HTAs as taking between 1 and 6 months[7].
- Second, RRs should be of high quality, i.e. rapidity should not be a risk factor for poor, overly simplistic, or misconducted systematic reviews[6]. RRs must adhere to core principles of systematic reviews that avoid bias in the inclusion, assessment, and synthesis of studies. Transparency in the description of the methods is very important[6, 8, 9].

There is today no formally established methodology guidance on how to conduct RRs. In October 2015, the Cochrane RRs Methods Group (RRMG) was formed[10]. Its primary objective is to provide guidance on RR conduct, i.e. complement the Cochrane handbook in that domain. However, although a number of workshops have already been organised by this group, clear guidelines are still lacking (http://methods.cochrane.org/rapidreviews/about-us).

2 WHY ARE RAPID REVIEWS NEEDED?

Increasingly, healthcare decision makers demand high-quality evidence in a short timeframe to support urgent and emergent decisions related to procurement, clinical practice, and policy[3]. One consistently identified barrier to implementing results from evidence syntheses is an incongruence between the time required to produce a full systematic review and the time within which policy and other decision makers must render decisions[3, 6]. The concern regarding a timely decision on health care and policies is thus the driving force for RRs.

This is why HTA agencies have embraced RRs. While the HTA community and producers such as the CADTH have been conducting RRs for a long time (https://www.cadth.ca/rapidresponse-service), the Cochrane Collaboration (http://innovations.cochrane.org/response) and McMaster Health Forum (http://mcmasterhealthforum.org/policymakers/rapidresponse-program) have also recently initiated programmes to conduct RRs[7]. The use of RRs is not limited to HTA, but can also be a component of GCP or HSR projects.

In the current Belgian context of increasing stakeholder demands and limited human resources, the appropriateness for KCE to produce a RR should be carefully considered at the beginning of a project. In those cases in which a RR is considered appropriate, the choices made to speed up the process should always be clearly described and justified in the report (see point 4.4).

3 DO WE HAVE EVIDENCE THAT RAPID REVIEWS ARE VALID?

In a scoping review of RR methods, Tricco et al. retrieved four studies comparing the results of RRs to full systematic reviews (SRs)[1]. Three of these found that the results for both knowledge synthesis products were in agreement. However, the results of these studies should be interpreted with caution because they included a very small sample of reviews (ranging from 1 to 8) and it was unclear whether the authors of the full systematic reviews used the RR as a starting point to identify articles for inclusion or vice versa[1].

Another explorative study applying individual shortcuts to 3 systematic reviews reported that in most instances, the shortcuts resulted in at least one relevant study being omitted from the review. When meta-analysis was possible, the omission of studies generally resulted in less precise pooled estimates that did not differ in direction from the original estimate[11].

Further research on RRs is warranted as the conclusions from RRs may be less generalizable or provide less certainty than standard SRs[7]. In particular, the consequences of various methodological shortcuts should be investigated[1, 7, 12], notably in terms of impact on the clinical or policy decision-making.

4 HOW TO PRODUCE RAPID REVIEWS AT KCE?

When looking at elements of RRs in the frame proposed by the AHRQ[4](Table 1), it becomes apparent that KCE already applies some of them in virtually all its reports (i.e. lack of dual study selection and data extraction) to speed up the delivery of evidence-informed recommendations.

The process of RRs may combine one or several of these shortcuts depending upon the information needs of the knowledge users, timeliness, but also availability of pre-existing high-quality SRs or HTAs. Therefore, a range of products may come under the umbrella of RRs. For example, the *KCE has read for you* product is exclusively based on offering a very short summary of a recent high-quality SR. However, the authors of this report consider that some of the shortcuts listed in Table 1 could hinder the quality of our work at KCE and thus recommend to avoid them (see Table 1).

Table 1 – Dimensions of standard SR that may be altered in a rapid review[4]

Dimension	Shortcuts	Option at KCE?
Scope	Limit the type of questions (e.g. efficacy only, new technology only, single technology only)	Yes
	Limit number of questions	Yes
	Limit the number of studies that can be included	Yes
Comprehensiveness	Limit search strategy (e.g. number of databases, grey literature, date, setting, language)	Yes
	Limit study types included (e.g. existing systematic reviews only, RCTs only)	Yes
	Limit textual analysis (e.g. no full-text review, limit number of extracted items)	Limit number of items
Rigor/Quality control	Eliminate dual study selection	Yes*
	Eliminate dual data extraction	Yes*
	Limit or eliminate internal or external review of final product (e.g. peer review)	Limit to internal
Synthesis	Limit or eliminate risk of bias/quality assessment of individual studies	No
	Limit or eliminate either quantitative or qualitative analysis	No
	Limit of eliminate strength/quality of evidence assessments (e.g. using GRADE)	No
Conclusions	Simplify or eliminate any conclusive statements about the direction of the evidence	No

** done systematically at KCE*

We detail hereafter some of the shortcuts that could be considered on a project by project basis at KCE.

4.1 Scope

Limiting the scope of RRs is the most efficient shortcut as it has a direct impact on the number of articles to retrieve, screen, assess and synthesize. However it is important to work closely with the knowledge users i.e. to apply an integrated knowledge translation[13]. The scope of the question should be clearly defined with them, as well as the purpose for which the evidence summary will be used, and the availability and commitment of the knowledge user for collaboration during the project period. This process serves the dual objective of refining the scope such that it is suitable for a RR method, and ensuring that the final product is useful for its intended audience and their objectives[7, 13].

A research question with a limited scope is appropriate in a number of cases, notably for review of effective (clinical) interventions, e.g. what is the performance of protein S-100B for excluding brain injury after head trauma. Limiting the breadth of the research question might be more difficult for complex interventions, economic implications, ethics, safety, and social policy[7].

Limiting the number of studies included in a review is often done at KCE when the primary search yields an 'unreasonable' amount of hits. Under such circumstances, a more focused search strategy is developed with an adapted sensitivity-specificity balance to limit the number of hits to a manageable amount. However, this should never be done at the expense of a too low sensitivity.

4.2 Comprehensiveness

4.2.1 Limit the search strategy

In order to save some time, one may decide to limit the number of references retrieved by using various shortcuts. It is important to realize that each of these shortcuts has drawbacks and may lead to missed relevant evidence.

4.2.1.1 By date

In the case of a new topic, (e.g. review of an innovative therapy recently launched in the market, or review in a therapeutic area where standard practice has recently changed), a search date can be set before the first publication on that topic to limit the noise (false positives) with no loss of evidence. However, on a rapidly changing topic, setting up an appropriate cut-off date should always be done in discussion with experts in the topic to avoid this strategy resulting in a direct loss of relevant evidence.

4.2.1.2 By number of databases consulted

The current approach followed at KCE recommends to search on Medline, Embase and CENTRAL databases. For RRs, the number of databases consulted could be reduced[12, a]. If this approach is to be followed a check should be performed in other databases by looking at the abstracts to ensure no relevant evidence is being missed e.g. no contradicting results (see section 0 for a structure approach of signal detection).

Skipping the grey literature search can also be considered, provided this does not contradict the information needs (see point 1.1). This decision must account for the benefits and risks at stake. For example, for assessing harms of new drugs, the grey literature (e.g. conference abstracts) should be checked, whereas this might be less crucial for a SR on behavioural changes following a health promotion program.

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[a] Some authors proposed that the number of databases could be reduced (i.e. limited to Medline), particularly for reviews of randomized trials of health interventions[12]. But there is currently no agreement on that point[14, 15].

4.2.1.3 By language

KCE authors often use language as an exclusion criteria during the screening process (English, French, Dutch and other languages mastered by the team). Limiting the search strategy to a reduced set of languages has a limited impact on the total number of references retrieved. A limit to English only misses 4.5% of the references published in Pubmed (Nicolas Fairon, data for year 2015) and 5.5% in Embase (for articles published in 2015, but 8.6% for 2010).

4.2.1.4 By developing a more specific strategy

Building a search strategy aims for the best sensitivity and precision or in other words, to retrieve a maximum number of relevant references with minimal noise. A more specific strategy in a RR process will lead to less sensitivity. A search strategy can be more specific by using narrower MeSH terms, using major topic MeSH headings (see https://www.nlm.nih.gov/bsd/disted/meshtutorial/principlesofmedlinesubjectindexing/majortopics/) or by dropping less common keywords. The difficulty is to be able to drop those keywords with the potentially worst signal/noise ratio. When a search strategy is more specific, it should be complemented with a good snowballing. Further research comparing specific vs sensitive strategies including snowballing may be necessary to draw conclusions. Building the search strategy may consider the use of published search filters, if their sensitivity and specificity are considered to be acceptable.

4.2.1.5 By type of publication

A decision can be made to limit the search by the type of publication. For RRs the exclusion of conference abstracts, letters and editorials can be considered, since in most cases such publications do not provide enough data to ultimately include these studies in a review.

4.2.2 Using a published systematic review as the core document

When recent, good quality SRs exist on the topic of interest, a possible strategy already frequently used at KCE is to use those documents as the starting point of KCE's review[b].

Two important aspects must be considered to ensure the validity of this strategy: the quality of the core SR and the need for update.

4.2.2.1 High-quality SR

The core SR should be of high-quality based on AMSTAR results. The results of the AMSTAR assessment should be reported with a mention of all potential weaknesses of the core SR. The researcher will evaluate if these weaknesses could have a significant impact on its results SR and, even more importantly, on the strength of its conclusions.

4.2.2.2 Update of the SR

The need for an update of the core SR should be assessed. The search date of the core SR may be months or even years old. That does not necessarily mean that the SR is out-of-date as several lines of evidence demonstrate that reviews become obsolete at different rates[16]. The need to update can be assessed formally following two methods (Ottawa and RAND methods): a formal comparison of these two methods showed they produce similar results[17]. However, the authors of this document recommend the Ottawa method because it is more transparent, consistent and suitable for experts not specialists in the report's topic.

[b] The same strategy can be pursued starting from a high quality HTA.

Ottawa method

The Ottawa method[17] ascertains if there are updating signals in the published literature (Table 2), but also recommends to consult clinical content experts and to examine safety alerts (from MedWatch, the FDA's Safety Information and Adverse Event reporting system etc).

To identify signals/triggers for updating, qualitative and/or quantitative criteria to the abstracted evidence are applied for each conclusion in the original SR[16]. For each conclusion, Ahmadzai et al. recommend to first document the absence of new evidence (that is, no new evidence or new evidence showing the same or similar conclusion as the original SR) or the presence of new evidence meeting the pre-defined criteria of signal(s) indicating a need for updating (Table 2).

Table 2 – Criteria for determining that a conclusion from a SR is out-of-date[16]

Ottawa's label	Ottawa method
	Qualitative criteria for potentially invalidating signals
A1	Opposing findings: a pivotal trial or systematic review (or guidelines) including at least one new trial that characterized the treatment in terms opposite to those used earlier
A2	Substantial harm: a pivotal trial or systematic review (or guidelines) whose results called into question the use of the treatment based on evidence of harm or that did not proscribe use entirely but did potentially affect clinical decision-making
A3	A superior new treatment: a pivotal trial or systematic review (or guidelines) whose results identified another treatment as significantly superior to the one evaluated in the original review, based on efficacy or harm
	Qualitative criteria for signals of major changes
A4	Important changes in effectiveness short of 'opposing findings'
A5	Clinically important expansion of treatment
A6	Clinically important caveat
A7	Opposing findings from discordant meta-analysis or non-pivotal trial
	Quantitative criteria signals of changes in evidence
B1	A change in statistical significance (from non-significant to significant)
B2	A change in relative effect size of at least 50 percent

- What is a qualitative signal ?

Examples of a qualitative signal might include finding a newly published "pivotal trial" with results opposite to that of the original SR with respect to an efficacy outcome (for example, effective versus ineffective or vice versa) or a harm (for example, a newly identified risk of harm that outweighs the previously observed benefits). In this context the original definition of a pivotal trial was one published in one of the top five general medical journals (Annals of Internal Medicine, BMJ, JAMA, The Lancet, and New England Journal of Medicine) or a trial whose sample size was at least triple that of the largest trial in the original SR. Other examples of qualitative signals include a superior new treatment (for example, a new treatment significantly more effective than one assessed in the SR); or a new population subgroup (that is, the treatment assessed in the SR has subsequently been tested on a new population).

- What is a quantitative signal?

New evidence generates a quantitative signal if its incorporation into a SR's original meta-analysis changes a statistically non-significant pooled estimate into a statistically significant one or vice versa.

If none of these signals is detected, the results of the core SR can be used without update.

RAND method

The RAND method[17] combines external domain expert opinion with an abbreviated search of the literature published since the original SR. The RAND method uses a four category scheme ("definitively out of date", probably out of date", possibly out of date" or "still valid"). Experts (at least 4) receive a summary of past report conclusions. They are asked if these are still valid and if no, to provide new evidence to support their statement. At the end of the process, report's conclusions are compared to the summary of findings in the experts' input and to the summary of findings in new studies.

4.2.3 Limit textual analysis

This is very dependent of the scope of the research question. For example, if the question relates to specific outcomes, the number of items extracted can be limited to address that specific question. However, the text should always be reviewed in full to assess the quality of the methods and detect limitations.

4.3 Quality control

4.3.1 Only one reviewer for title/abstract screening and data extraction

This is already common practice for KCE reports to save researchers' time. However, the authors of this document recommend that given the importance of the quality of any literature review, a partial check would provide a valuable tool to ensure the final quality of KCE's RRs. Such check can be done by a second reviewer, for example on the list of the rejected studies if their number is limited. A second possibility is to perform the check at the start of the process on a limited subsample (e.g. 10% of citations). Any discrepancy in exclusion or inclusion between the 2 reviewers should be duly examined (are exclusion/inclusion criteria unclear?). The same check could be done at the stage of data abstraction. This check must be clearly explained in the review protocol.

4.3.2 Limit or eliminate internal or external review of final product (e.g. peer review)

For RRs, skipping or modifying the external review may be considered to save time, particularly since our experience shows that there are usually few remarks on the methods of a literature review. An interesting alternative is an internal review (validity check) conducted at each step of the review by a (senior) KCE colleague (see an example in 4.3.1).

4.4 Transparent reporting

Transparency in the description of the methods used is essential[6, 8, 9]. Potential limitations or any potential bias that may have been introduced by methodological concessions should be described and discussed.

However, the compliance with PRISMA and AMSTAR checklists is poor in most published RRs[8]. It is difficult to ascertain whether the reporting omissions are attributable to the RR approach followed or simply to the poor reporting. Highlighting where the PRISMA criteria were omitted or modified will increase transparency[6]. PRISMA-RR 2017, an extension to PRISMA for RRs, is currently under development (http://www.equatornetwork.org/library/reporting-guidelines-under-development/#51).

5 CONCLUSIONS

KCE as many other agencies[2,18], strives to balance efficiency with methodological rigour and already applies various shortcuts in full SRs. This document is a road map to orient this process in a standardised way. Table 1 summarises the dimensions of standard SRs that may be considered in future KCE RRs[4].

Given the current lack of internationally validated guidance for RRs, using further shortcuts cannot be recommended at this stage. This document that explores different possible methods to conduct RRs should be further updated in December 2018: at this date the ongoing work by the Cochrane group and the extension to PRISMA for RRs will be more advanced.

However, when a request for evidence-based recommendations is urgent, organizational aspects could/should also be considered to speed-up the process. These include for example: allocating human resources, potentially at the expense of other projects; selecting experienced researchers; limiting quality checks to an internal peer-review; changing the extended synthesis into an abstract; or translating in the national languages only the recommendations, not the full synthesis.

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APPENDICES

APPENDIX 1. TYPOLOGY OF RAPID REVIEW PRODUCTS

Description
Accelerated: • accelerated evidence synthesis/ abbreviated systematic review methods • expedited evidence review/ report or jurisdiction Condensed: • broad brush review of review-level literature • condensed/ restricted time frame • not an in-depth analysis of the data • not a comprehensive systematic review • short reports based on limited search of electronic databases • succinct review • systematic review methodology within a restricted timeframe Focused: • detailed and objective assessment and synthesis of the current research evidence • focused on specific technology • limited in scope/ methodology • pre-reimbursement single technology assessment for hospital • single technology assessment Form of evidence synthesis: • review conducted by one reviewer with no meta-analysis, modeling or GRADE • review of full HTA reports from other organizations

- review of medical method (non-drug) the use of which hospitals are planning to introduce or spread
- summary of available data/ summary of published literature/ summary of evidence
- listing of potentially relevant information
- overview of existing evidence/ current state of the evidence
- provides a detailed and objective assessment and synthesis
- provides 'best evidence'
- provides evidence-based answers
- rapid response provides access to up-to-date research evidence
- support evidence-informed programs, service delivery and advocacy
- synthesis of data
- systematically review and summarize existing evidence

Modified:

- does not formally appraise the methodological quality of the included studies
- knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a timely manner
- modified systematic review
- no formal appraisal of methodological quality
- systematic review methodology simplified or omitted
- trade-off between robust methodology and the need for rapidity

Tailored:

- tailored to decision makers/ provide recommendations to decision makers

Source: Polisena et al. [5]

Report Type	Description Products tailored to meet the needs and timelines of the requester.
Reference list	List of the best available evidence with abstracts and links to full-text documents, if available.
Summary of abstracts	Summary based on the abstracts of the best available evidence. Includes the abstracts and links to full-text documents, if available.
Summary with critical appraisal	Written summary of the evidence from full-text articles, with a critical appraisal and policy implications.
Peer-reviewed summary with critical appraisal	Summary of systematically selected evidence with a critical appraisal and policy implications. An external peer review is conducted.
Systematic review and meta-analysis	A systematic review of the evidence and a meta-analysis is performed, where appropriate. Authorship includes a content expert, and an external peer review is conducted.
Rapid health technology assessment	A systematic review of clinical studies and an economic component that includes a systematic review of economic studies, an economic evaluation or a budget impact analysis. It excludes a review of the health services impact. Authorship includes a content expert, and an external peer review is conducted.

Source: CADTH Rapid Response Service https://www.cadth.ca/about-cadth/what-we-do/products-services/rapid-response-service