CADTH RAPID RESPONSE

Rapid Response Systematic Review and Meta-Analysis Process

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This document will be periodically revised as part of ongoing process improvement activities. The following version control table, as well the version number and date on the cover page, are to be updated when any updates or revisions are made.

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<thead>
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<tbody>
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</tr>
</tbody>
</table>
# Table of Contents

Revision History .......................................................................................................................... 2

1. Introduction............................................................................................................................. 4
   1.1 About Rapid Response Systematic Review and Meta-Analysis ........................................... 4
   1.2 Scope .................................................................................................................................. 4
   1.3 Target Audience and Application for Decision-Making ..................................................... 5
   1.4 Transparency and Stakeholder Engagement ....................................................................... 5
   1.5 Timelines............................................................................................................................. 6

2. Process ................................................................................................................................... 7
   2.1 Process Overview ............................................................................................................... 7
   2.2 Topic Identification ............................................................................................................ 8
      2.2.1 Identify and Filter Topic ............................................................................................. 8
      2.2.2 Refine Topic ............................................................................................................... 8
   2.3 Research ............................................................................................................................ 9
      2.3.1 Engage Canadian Manufacturers and/or Suppliers and Content Experts ................. 9
      2.3.2 Draft Scoping Search and Protocol ........................................................................... 9
      2.3.3 Finalize Protocol ........................................................................................................ 9
      2.3.4 Conduct Literature Search ....................................................................................... 9
      2.3.5 Screen and Appraise Literature .............................................................................. 10
      2.3.6 Externally Review Included Studies ........................................................................ 10
      2.3.7 Conduct Meta-Analysis (Optional) ......................................................................... 10
      2.3.8 Draft Report ............................................................................................................. 10
   2.4 Review ............................................................................................................................... 10
      2.4.1 Internal Review ......................................................................................................... 10
      2.4.2 External Peer Review ............................................................................................... 10
      2.4.3 Post Draft Report for Feedback .............................................................................. 11
      2.4.4 Director Approval .................................................................................................... 11
   2.5 Delivery .............................................................................................................................. 11
      2.5.1 Copy-Editing and Formatting .................................................................................. 11
      2.5.2 Post Report and Knowledge Mobilization Tools (As Required) ............................... 11

Appendix 1: Definitions ............................................................................................................ 12
1. Introduction

The purpose of this document is to outline a standardized process for producing Rapid Response Systematic Review and Meta-Analysis projects that meets the needs of publicly funded Canadian health care decision-makers. If possible, CADTH may adapt or supplement an existing Systematic Review or Meta-Analysis to shorten timelines.

1.1 About Rapid Response Systematic Review and Meta-Analysis

CADTH’s Rapid Response Service offers Canadian health care decision-makers quick and efficient access to the best publicly available health technology evidence.

A Rapid Response Systematic Review and Meta-Analysis report responds to specific stakeholder research questions using a comprehensive review of published evidence that meets predetermined inclusion criteria. If sufficient homogeneous studies that meet the inclusion criteria are identified, a meta-analysis is performed. The meta-analysis combines the data from the selected studies and provides a statistical summary of outcomes, such as safety and/or efficacy.

As well as identifying and summarizing existing and/or published evidence on a topic, these reports include possible implications for decision-making in order to better support CADTH customer information needs.

These projects also include a brief, plain-language summary and, depending on customer needs, additional knowledge mobilization tools may be developed to support implementation and outreach.

Systematic Review and Meta-Analysis reports attempt to be as comprehensive as possible and follow standard methodological guidelines for the production of systematic review and, when possible, Meta-Analysis reports.

1.2 Scope

In order to meet short timelines, the scope of research questions used in Systematic Review and Meta-Analysis reports tends to be narrower than the scope of questions used in CADTH Health Technology Assessment and Optimal Use projects (specifically, they typically address a focused clinical question and do not include an economic analysis or specific patient input process).

Topics suitable for Rapid Response reports include evaluations of medical, surgical, and dental technologies such as:

- drugs
- devices
- diagnostic tests
- medical, surgical, and dental procedures.

Please talk to the Liaison Officer in your jurisdiction to clarify if a topic is suitable for Rapid Response or is better suited to another product line offered by CADTH.
1.3 Target Audience and Application for Decision-Making

Rapid Response Systematic Review and Meta-Analysis reports are produced for federal, provincial (with the exception of Quebec, which does not participate in CADTH’s Rapid Response Service), and territorial health ministries, as well as health policy-makers working at regional health authorities and hospitals in Canada who make decisions on medical, surgical, and dental technologies. Rapid Response requests are made in confidence, and no identifying information is included when the reports are made public on the CADTH website.

The purpose of these reports is to provide detailed evidence-based support to policy and health care decision-makers by identifying and summarizing the existing, published evidence on a topic, and describing possible implications for decision-making.

Rapid Response Systematic Review and Meta-Analysis reports summarize available existing evidence in the most comprehensive manner possible given resources and timelines; however, they should not be construed as a recommendation for or against the use of a particular health technology, nor are they intended to replace professional medical advice. Readers are also cautioned that a lack of quality evidence does not necessarily mean a lack of effectiveness, particularly in the case of new and emerging health technologies for which little information can be found, but which may in future prove to be effective.

1.4 Transparency and Stakeholder Engagement

CADTH makes every reasonable attempt to be as transparent as possible within Rapid Response time constraints. The three principles of transparency, as defined by CADTH, are to:

1. solicit feedback from those affected by CADTH reports whenever possible given time constraints
2. facilitate the ability to reproduce or update CADTH reports by reporting the
   a. methods used to create reports
   b. sources searched and/or provided
3. publish CADTH reports in the public domain.

Reviews are conducted in an open and transparent fashion and, within timelines, every attempt is made for external feedback and review from interested stakeholders. In the Rapid Response Systematic Review and Meta-Analysis process, stakeholder feedback is solicited at the following stages:

- A content expert reviews the included studies.
- The report is externally peer-reviewed by content experts and, if applicable, manufacturers (see section 2.4.3).
- A draft report is posted for stakeholder comment.

At the start of each project, a protocol that documents the methodology that will be used is drafted, posted, and registered with the PROSPERO systematic review database. In each Rapid Response Systematic Review and Meta-Analysis report, the research questions, selection criteria, selection of included studies, evaluation tools used, methods, and search strategy are reported.
CADTH notifies interested parties of stakeholder feedback opportunities by posting a notice to its Calls for Feedback webpage and by issuing an email to subscribers of the CADTH E-Alert service. Instructions on providing feedback are included with every notification.

Rapid Response Systematic Review and Meta-Analysis reports are posted on the CADTH website for anyone to access and review (though, in exceptional circumstances, embargo periods may be considered). All drafts, search strategies, and working documents used to produce Rapid Response reports are archived for 15 years and may be requested, if required, with the exception of copyright-protected documents and of information provided in confidence by customers, manufacturers, or other agencies.

1.5 Timelines

Timelines will be negotiated between a CADTH representative and the requestor at the time of topic refinement. Exact timelines depend on the project scope, the number of research questions, and whether implementation tools are requested.
2. **Process**

2.1 **Process Overview**

### 2.2 Topic Identification
- 2.2.1 Identify and Filter Topic
- 2.2.2 Refine Topic

### 2.3 Research
- 2.3.1 Engage Canadian Manufacturers and Content Experts
- 2.3.2 Draft Scoping Search and Protocol
- 2.3.3 Finalize Protocol
- 2.3.4 Conduct Literature Search
- 2.3.5 Screen and Appraise Literature
- 2.3.6 ExTERNally Review Included Studies
- 2.3.7 Conduct Meta-Analysis (Optional)
- 2.3.8 Draft Report

### 2.4 Review
- 2.4.1 Internal Review
- 2.4.2 External Peer Review
- 2.4.3 Post Draft Report for Feedback
- 2.4.4 Director Approval

### 2.5 Delivery
- 2.5.1 Copy-Editing and Formatting
- 2.5.2 Post Report and KM Tools (As Required)

*KM = knowledge mobilization.*
2.2  Topic Identification

2.2.1 Identify and Filter Topic

Canadian publicly funded health care decision-makers (see section 1.3) can submit topics for Rapid Response reports by contacting a CADTH Liaison Officer or by independently submitting a request on the CADTH website. Topics for systematic review and meta-analysis can also be suggested by CADTH staff in conjunction with stakeholder feedback. Once a topic has been identified as a possible candidate for a Systematic Review and Meta-Analysis report, it is examined and filtered to ensure the topic meets CADTH’s mandate (health technology, patient outcomes, CADTH customer). Topics that do not meet CADTH’s mandate do not proceed, and those that do proceed continue to be refined and scoped.

2.2.2 Refine Topic

Information is gathered to determine if the topic is appropriate for a Systematic Review and Meta-Analysis report. The following criteria are reviewed to help judge the appropriateness of the topic for this higher-level Rapid Response product:

- existing evidence
- not a duplication of reviews completed by other agencies
- relevant to the Canadian health care context
- disease burden
- potential impact
- jurisdictional interest.

Topics determined to be highly relevant (per the above criteria) are prioritized for approval depending on operational capacity. CADTH will set up a meeting with customers and stakeholders (including the appropriate Liaison Officers) to refine the topic, define clear research questions, and create a timeline (taking into account when the information is required to most effectively support health care and policy decisions).

If the topic is not appropriate for a Systematic Review and Meta-Analysis report, or a previously published report answering the customer’s research needs is identified, the request does not proceed, though it may be considered for another CADTH product line.
2.3 Research

2.3.1 Engage Canadian Manufacturers and/or Suppliers and Content Experts

If the technology being reviewed is a drug or a device, Canadian manufacturers and/or suppliers are identified. The Project Manager prepares and sends emails or letters requesting industry input for the review. Any input received (i.e., studies or reports) is sent to the authors to screen and evaluate. A minimum of one content expert co-author is selected and identified to provide subject matter expertise throughout the project. The Project Manager coordinates the engagement of this expert and ensures that a conflict of interest form is filled out.

2.3.2 Draft Scoping Search and Protocol

A scoping search of the literature is conducted and the results are sent to the authors for review. The lead and secondary authors draft the project protocol using both the briefing note created during topic refinement and the supplemental scoping search. Occasionally, as part of the prioritization phase, a Reference List report is also created, and is a used to inform the protocol.

2.3.3 Finalize Protocol

A kick-off meeting is scheduled with all team members and the content expert co-author(s) to review the protocol. Once the final version of the protocol has been approved and posted, the lead author is responsible for registering it in the PROSPERO international database.1

2.3.4 Conduct Literature Search

An internally peer-reviewed literature search is conducted using key database resources, as well as topic-specific databases, when appropriate. Bi-weekly search alerts are set up until the final report is published. A focused grey-literature search is also conducted by searching relevant sections of the Grey Matters checklist. Literature searches are limited to published English-language articles in the human population. Rapid Response searches may also be limited by evidence-based study type, including some or all of the following (as negotiated with the customer):

- systematic reviews, meta-analysis, or health technology assessments
- randomized controlled trials
- non-randomized studies
- economic evaluations
- evidence-based guidelines.

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1 PROSPERO is an international database of prospectively registered systematic reviews in health and social care.
2.3.5 Screen and Appraise Literature

Once the results of the literature search are received, the two authors independently screen retrieved titles and abstracts and then come to a consensus on which pieces of literature to order. Both authors independently review the full-text articles selected, as well as any unique information made available by industry (if applicable, see section 2.3.1), and come to a consensus on which studies meet the inclusion criteria for the project (as documented in the protocol).

2.3.6 Externally Review Included Studies

The agreed-upon included studies list is sent to the team’s content expert co-author(s) to review and to offer suggestions, if necessary.

2.3.7 Conduct Meta-Analysis (Optional)

If sufficient studies are found meeting inclusion criteria with similar populations and outcomes, the primary author extracts data from the included studies to conduct a meta-analysis. The meta-analysis is a statistical summary of the selected studies that tests the pooled data for statistical significance.

2.3.8 Draft Report

Authors draft the report using a standardized template, the CADTH Style Guide, and specific author guidelines for Systematic Review and Meta-Analysis reports. Any limitations and potential biases identified are reviewed in the Discussion section of the report. Report examples can be found on the CADTH website.

2.4 Review

2.4.1 Internal Review

An internal quality check of the draft report content is conducted. Comments and revisions are sent back to the authors for incorporation into the report. References cited in reports will be verified, as will compliance to copyright guidelines. If personal communications (oral or unpublished information) have been included in the report, all of the required permission to publish forms must have been received. These steps are repeated until the report is deemed ready for external review.

2.4.2 External Peer Review

Comments and feedback from all external reviewers and stakeholders (which may include manufacturers) are forwarded to CADTH for review, followed by discussions with the authors on proposed revisions. The disposition form is filled out by the author, documenting feedback and CADTH’s response. The Scientific Advisor reviews the disposition form and scans the newly revised draft to ensure the external feedback has been accurately addressed. Once the final draft is deemed satisfactory, it is sent to the whole team for co-author review and approval.

All CADTH project team members (including the authors) review and approve the final draft. A final reference check is completed on the report, ensuring that the references follow CADTH standards and that copyright guidelines have been adhered to.
2.4.3 Post Draft Report for Feedback

A general electronic alert that announces to identified stakeholders that the draft report is available for comment is released. CADTH typically allows 10 working days (two weeks) to submit comments. At the same time, content expert(s) (selected from a list of potential external peer reviewers) are selected to peer review the draft report.

2.4.4 Director Approval

The final draft is sent to the Director of Health Technology Assessment and Rapid Response to review and approve.

2.5 Delivery

2.5.1 Copy-Editing and Formatting

After approval has been received, the report goes to the Publishing team to copy-edit and format (using the Rapid Response Systematic Review and Meta-Analysis template with the appropriate disclaimers). The title, key findings, research questions, and meta-data are translated into French.

2.5.2 Post Report and Knowledge Mobilization Tools (As Required)

The finalized report is posted on the CADTH website with a brief, plain-language summary. Depending on customer needs, additional knowledge mobilization tools may be developed to support implementation and outreach.

The CADTH Liaison Officer for the jurisdiction contacts the customers to get their feedback on the report and to gather data on how the report was used. The Liaison Officer also helps to disseminate the report findings to the appropriate stakeholders within their jurisdiction.
Appendix 1: Definitions

**CADTH:** CADTH is an independent, not-for-profit agency funded by Canada's federal, provincial, and territorial governments. CADTH's role is to deliver reliable, timely, and credible evidence-based information and impartial advice to Canada's health care leaders and decision-makers through a variety of customized products and services.

**Customer:** A CADTH customer is an entity or organization that requests CADTH’s products or engages CADTH’s services. (The customer is most often the first point of contact and requests knowledge from CADTH. The customers' needs may vary with specific topics, and they may request and/or choose between different products, services, and suppliers.)

**External Peer Reviewer:** An identified subject matter expert independent of or external to CADTH who is selected to provide comments and feedback on CADTH products, as required.

**Health Technology:** A device, medical procedure, or surgical procedure, and the administrative and supportive system in which health care is delivered.

**Jurisdictions:** The federal, provincial, and territorial health ministries from across Canada.

**Manufacturer:** A company that researches, develops, and markets drugs and/or medical devices to consumers and the health care system.

**Meta-Analysis:** A quantitative statistical analysis that is applied to separate but similar experiments of different and usually independent researchers, and that involves pooling the data and using the pooled data to test the effectiveness of the results.

**Product:** A deliverable that is provided to a client. An artifact that is produced, is quantifiable, and can be either an end item in itself or a component item.

**Request:** In the context of this document, a request is a question, suggestion, or submission received from a stakeholder external or internal to CADTH (reactive or proactive) in any format. A request could be a simple inquiry or could result in a large project.

**Stakeholders:** Stakeholders for the Rapid Response processes may include organizations, institutions, or individuals who have a strong and vested interest in specific Rapid Response products. Stakeholders may include:

- federal, provincial, and territorial ministries of health
- hospitals and health institutions
- health regions
- patients, consumers, and caregivers
- health professionals
- industry.
**Systematic Review:** A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review. Statistical methods (see meta-analysis) may or may not be used to analyze and summarize the results of the included studies.

**Topic:** A health technology or clinical or disease area that is being, has been, or will be investigated by CADTH to determine the suitable product or service to be provided. Essentially, it is a project idea that is being developed. The topic investigation could result in multiple products, projects, or requests.