GUIDELINES FOR SYSTEMATIC LITERATURE SEARCH

Prepared by the Technology Assessment Unit of the McGill University Health Centre (MUHC)

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1. **BACKGROUND**

The following document serves as a guideline for carrying out a systematic literature search to support health technology assessment (HTA) reports prepared by the Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC). It has been prepared in consultation with a number of authoritative references cited at the end, and is supplemented by links to resources and explanatory pages found on the MUHC TAU blog (http://muhctau.wordpress.com).

2. **TYPES OF REPORT**

Reports prepared by the TAU can be classified as follows:

1. Full HTA: Includes a systematic literature review and cost analysis, and if appropriate a meta-analysis.

2. Brief HTA: Typically based on a non-systematic summary of previously published systematic reviews and key studies.

3. Mini HTA: Consists of a structured questionnaire completed by the individual requesting the technology followed by a brief commentary by TAU.

3. **SCOPING SEARCH**

There is no standard definition or protocol for a scoping search\(^1,2\). It is a preliminary search carried out to support a decision as to whether to undertake a report, to decide on the type of report, to prepare for a meeting with a subject matter expert, or to gather keywords and most useful sources for the complete search. It is not intended to be systematic, but it is intended to produce an impression of the available information.

If the scoping search is being undertaken to support a decision to undertake the review, then it should include at least a search of registered and ongoing HTAs and systematic reviews.

- **PROSPERO** (registration of systematic reviews), at the CRD [http://www.crd.york.ac.uk/NIHR_PROSPERO/](http://www.crd.york.ac.uk/NIHR_PROSPERO/)
- **CADTH** in-progress reports [http://www.cadth.ca/products/projects-in-progress](http://www.cadth.ca/products/projects-in-progress)
- **National Institute for Health Research HTA programme**, research in progress [http://www.nets.nihr.ac.uk/projects](http://www.nets.nihr.ac.uk/projects)
- Technology Assessment in Québec from INESSS, including current projects http://www.inesss.qc.ca/index.php?id=105&L=1

A scoping search may involve searches for HTAs, as described below (Sections 4.3.1 and 4.3.2), a limited bibliographic database search (PubMed, OVID Medline/EMBASE), and/or a Google/Google Scholar search to identify a set of highly cited and readily available references. Other strategies might involve manual scanning of recent references, and use of citation searches, manual searches, and “related articles” links to find closely related articles.

The scoping search will generally not be documented in the report.

4. LITERATURE SEARCH

The literature search usually progresses in increasing detail from a scoping review through the core search, to a search of topic-specific databases, if appropriate.

4.1. Developing the search protocol

Before commencing the full search, a search protocol should be established, with the following steps as a guideline.

- Present topic (technology to be reviewed plus indications)
- Construct specific research question(s)
- Identify target population
- Define inclusion and exclusion criteria (specific measure of outcome of interest, covariates, adverse events, comorbidities... etc)
- Plan the search
  - Determine the databases to be used according to the topic (disease condition and the technology) under review
  - Determine search keywords to be used; consult clinical experts to provide search keywords (including variations and synonyms)

The search may be structured according to the PICO framework

- P, target population
- I, intervention (disease of technology)
- C, comparator or comparators
- O, outcome or outcomes

Depending on the size of the evidence-base, or whether there are accepted standard treatments and outcomes, it may be appropriate to search without specifying comparators or outcomes.
The protocol is liable to be modified, particularly during the initial stages of a search. Once study selection has begun, the reasons for such changes should be documented.

4.2. Developing searches

4.2.1. Disease- and intervention-specific search terms

Search terms for the disease and intervention may be gathered from:

- Subject experts
- Textbook chapters and review articles
- Articles retrieved during the initial scoping search
- Other systematic searches on the same subject, if available (Cochrane reviews, other detailed systematic reviews)
- Disease dictionary entries in indexed databases, eg.,
  - Medical Subject Headings (MeSH®) from PubMed
    https://www.nlm.nih.gov/mesh/meshhome.html and
    http://hlwiki.slais.ubc.ca/index.php/Medical_Science_Headings_%28MeSH%29
  - The Elsevier Life Sciences Thesaurus (Emtree)
    http://www.elsevier.com/online-tools/embase/emtree
  - The individual entry for each term describes the other terms included under it, the date of first introduction of the term, and the date of back-indexing.
- MeSH or Emtree subject headings for articles found by other means, eg, by hand-searching, or via a PubMed related articles link
- GoPubMed, an interface for PubMed which provides ordered lists of the indexing terms of references retrieved in a search http://gopubmed.com/
- Google Scholar and general Google searches for websites dedicated to the topic

Note:

- Preferred terminology may change over time
- There are regional variations in terminology and spelling
- Eponyms may be required (particularly if the search is expected to include non-indexed resources which will require text word searches).
- For indexed terms (eg, MeSH), check the dates major search terms were introduced, which keywords have been included, and how far any back indexing has been carried.

4.2.2. Search terms describing study-type and methodology

Numerous filters and hedges⁴ have been developed to refine search results according to study-design, methodology, patient characteristics and type of publication, eg,
• Filters collected by the InterTASC Information Specialists' Sub-Group Search Filter Resource https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home
• Search filters from the Scottish Intercollegiate Guidelines Network http://www.sign.ac.uk/methodology/filters.html
• Highly sensitive search filters for RCTs from the Cochrane Handbook (online version) http://handbook.cochrane.org/chapter_6/6_4_11_search_filters.htm

Which filter is most appropriate (or whether any is suitable) depends on the type of report and the type of studies being sought. Filters may emphasize sensitivity (for specialized systematic reviewers accustomed to screening large reference-sets, probably more appropriate for a full HTA) or specificity (intended for working clinicians who require a few quality references, probably more appropriate for a limited review) or aim for best precision. Filters for RCTs and systematic reviews are the most numerous and refined (eg, McKibbon et al⁵ compared the performance of 38 published filters for retrieving RCTs from MEDLINE). Conversely, filters for searches of diagnostic studies have received mixed reviews, with some assessors supporting their use⁵, and others considering them insufficiently mature⁷-⁹.

CADTH¹⁰ and the UK InterTASC Information Specialists’ Sub-Group (ISSG)¹¹ have both developed search filter appraisal tools.

4.2.3. Creating efficient searches

• Structure the search by grouping terms for the components of the PICO (or other structured question) together, then combining the retrieved sets (AND/OR/NOT) and, finally, applying filters or limits
• Use a combination of indexed terms and plain text terms
• Avoid redundancy, one of the faults identified on a critical review of published searches¹². Check which terms are included within other terms, eg, MeSH keyword search automatically includes the same term as a text word. Look up the hierarchy of MeSH and Emtree terms
• Use search truncation symbols and wildcards to reduce the number of individual terms. See the UBC HLWiki http://hlwiki.slais.ubc.ca/index.php/Search_truncation_%26_wildcards
• Use NOT to increase the precision (especially the sensitivity) of a search, by excluding irrelevant subsets¹³.

4.2.4. Peer review of search

Particularly for a complex search, consider a peer review. CADTH has prepared evidence-based practice guideline for the peer review of electronic search strategies (Sampson et al, 2009) and peer review checklist, http://www.cadth.ca/en/resources/finding-evidence-is/peer-review-search-strat
4.2.5. Involvement of a health librarian

The TAU has access to experienced librarians at both the MUHC library (RVH site) and the McGill library (Life Sciences library, generally) who can assist with searches.

- MUHC libraries http://www.muhclibraries.ca/contact-us/

Both libraries offer regular workshops on general strategies for search and specific resources in particular (MEDLINE/EMBASE, CINAHL, others), as well as on the use of bibliographic software and other tools to assist search, retrieval and review. See the library websites for details.

4.3. Complete search

For a full HTA, the complete search of the literature and selection of relevant articles should ideally be performed independently by two individuals to increase the chances of capturing all relevant articles and to minimize risk of bias.

4.3.1. Core search

In general, every search (systematic or non-systematic) should include the following resources, although it need not be restricted to them.

- Search for HTAs:
  - Centre for Reviews and Dissemination (CRD, http://www.york.ac.uk/inst/crd/)
  - CADTH federated search http://www.cadth.ca/search/federated
- Search for systematic reviews
  - Cochrane library (through MUHC libraries) http://www.muhclibraries.ca/
  - CRD
  - EMBASE (through MUHC libraries)
- Search for single studies (RCTs and other study types)
  - Cochrane CENTRAL (through MUHC libraries)
  - PubMed or MEDLINE
  - EMBASE (through MUHC libraries)

Although not part of a systematic search, a general Google search on selected keywords may be useful as a check for important omissions in the strategy.

4.3.2. Additional sources for health technology assessment

- Institut national d’excellence en santé et en services sociaux (INESSS) http://www.inesss.qc.ca
4.3.3. Sources for guidelines

- National Institute for Health and Care Excellence (NICE, UK) [http://www.nice.org.uk/]

4.3.4. Additional bibliographic databases

Although the question of “How much searching is enough?” still requires an authoritative answer, the research done to date suggests that an extensive search across multiple databases may not significantly improve retrieval.

Nevertheless, we list additional potential resources here which may be applicable to specific questions. Unless otherwise indicated, these are available through MUHC Libraries at [http://www.muhclibraries.ca]

- Biological and biomedical sciences database (BIOSIS Previews; McGill library)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Current Contents. Collections of articles from the world’s major core journals, subsets including: agriculture, biology, environmental sciences, social and behavioural sciences, clinical medicine, life sciences (McGill library)
- Global health. Collection of articles of human health and disease, including: communicable diseases, tropical disease, parasitic disease and parasitology, human nutrition, community and public health, medicinal and poisonous plants (McGill library)
- Health and Psychosocial Instruments. Database of articles focused on measurement instruments (i.e. questionnaires, index measures, rating scales, assessment guidelines… etc.)
- PsychINFO. Psychology, behavioural and social sciences database
- ISI Web of Science. Covers the scientific and medical literature, includes conference abstracts. (McGill library)

### 4.3.5. Citation searching

The main options for automated search for articles that have cited an article of interest are,

- ISI Web of Science (McGill library)
- Google Scholar [http://scholar.google.com](http://scholar.google.com)

Comparisons of the performance of the three (eg, Bakkalbasi et al, 2005\textsuperscript{17}) have not produced a clear favourite across all domains, although all three continue to evolve.

### 4.3.6. Grey literature/unpublished data

“Grey literature”\textsuperscript{18} is a generic term for all material that has not undergone academic peer review. Grey literature is a principal source of “unpublished” data, and might be used to address publication-lag in a fast-moving field\textsuperscript{19}, to detect selective publication of favourable results (and changes between abstract and full publication)\textsuperscript{20,21}, and to expand a sparse evidence-base\textsuperscript{22}. In addition, grey literature searches may be required for a fuller accounting of adverse events\textsuperscript{23,24}.

Grey literature varies widely in quality, and arguments against its use centre on the lack of quality control over reporting, and the potential for bias or inaccuracies in the absence of formal peer review\textsuperscript{19}. Conversely, regulatory documents provide fuller documentation than articles on randomization and blinding methods\textsuperscript{25}.

For information on searching grey literature and lists of grey literature resources, see


### Conference abstracts

- Biological and biomedical sciences database (BIOSIS, via MUHC libraries)
- ISI Web of Science (via MUHC libraries)
- Hand (paper or on-line) searching of supplements for conferences
• Conferences of interest may be identified by mentions within reviews and commentaries, subject searches, expert recommendations, and Google searches
• Google, Google Scholar

Searches of abstracts would usually be limited to the past three to five years, although in the case of a sparse dataset, the search may need to be extended. Be alert to the possibility of duplicate publication, since abstracts are frequently not cited in the corresponding articles, and there is no control of duplicate publication in reports and other materials.

Other data sources

• Manufacturers’ websites and industry clinical trials registries.
• Regulatory websites, for example,
  • The Food and Drug Agency (FDA) http://www.fda.gov/
  • Health Canada http://www.hc-sc.gc.ca/dhp-mps/index-eng.php
  • Individual country sites, as available.
• Registries of procedures (potentially an increasingly important resource in the future, given open data initiatives).

4.3.7. Identification of ongoing and unpublished studies

Databases of ongoing and unpublished studies should be searched to identify potential publication bias and get a sense of when technology might need to be reassessed (eg, to be aware of reporting dates – particularly upcoming ones – for trials expected to address identified evidence deficits).

There is overlap between databases, so it is not necessary to search all resources. ClinicalTrials.gov is likely to be sufficient for a core search of a pharmaceutical or device, with possible addition of Current Controlled Trials, since the latter allows searching across multiple registries.

• ClinicalTrials.gov; US National Institutes of Health registry of controlled trials http://clinicaltrials.gov/
• Current controlled trials; A registry of controlled trials, both ongoing and completed, can also search by “International Standard Randomised Controlled Trial Number (ISRCTN)” http://controlled-trials.com/
• HSRProj; Health services research registry database http://www.nlm.nih.gov/hsrproj/
• CORDIS; European-funded research project database http://cordis.europa.eu/projects/home_en.html
• International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) http://clinicaltrials.ifpma.org/clinicaltrials/no_cache/en/myportal/index.htm
• Cancer research or new drug therapies research databases:
  o http://www.cancer.gov/clinicaltrials
  o http://www.centerwatch.com/
• WHO International Clinical Trials Registry Program
  http://www.who.int/ictrp/en/

4.3.8. Additional general references on searching for systematic reviews and HTAs

• Cochrane Handbook of Systematic Reviews of Interventions, particularly chapters 5-7. On line version available at http://handbook.cochrane.org/
• Finding studies for systematic reviews: a checklist for researchers. Centre for Reviews and Dissemination, University of York. http://www.york.ac.uk/inst/crd/finding_studies_systematic_reviews.htm
• Finding the evidence: Literature Searching Tools in Support of Systematic Reviews from Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/en/resources/finding-evidence-is

4.4. Abbreviated searches for brief reports or mini-HTAs

A brief report may be written when the evidence base is limited, or, conversely, when others have already extensively covered the question (or closely related questions). In the former case, the search may be as extensive as that for a full report to ensure the maximum retrieval of relevant information. In the latter case, the search may be more limited and more like that described in the literature for a rapid or expedited review.26,27 The search should include the core resources as described above (although need not be limited to them), but may be restricted by date, eg, to the last five years, or by study type, eg, HTAs, SRs, or RCTs. In each instance, the restrictions should be documented.

4.5. Particular topics

4.5.1. Diagnostic studies

Methods for systematic searches and health technology assessments for diagnostic studies are less mature than those for interventional studies\textsuperscript{28}. There are at present no curated databases equivalent to Cochrane CENTRAL for RCTs the indexing of diagnostic studies is acknowledged to be incomplete. Full evaluation of diagnostic technologies involves progression through several different study designs, ranging from pre-clinical to health care systems and economic; searches must necessarily be broad enough to retrieve them all\textsuperscript{28}.

- The Diagnostic test accuracy working group of the Cochrane Collaboration [http://srdta.cochrane.org/](http://srdta.cochrane.org/), and the draft on-line Handbook of Diagnostic Test Accuracy, [http://srdta.cochrane.org/handbook-dta-reviews](http://srdta.cochrane.org/handbook-dta-reviews)
- See the filters section (Section 4.2.2) for a discussion and references to filters for identifying diagnostic studies

4.5.2. Therapeutic devices and surgical procedures

Hartling et al\textsuperscript{29} discussed a variety of challenges in systematic reviews of therapeutic devices and procedures that have implications for search. The evidence for therapeutic devices and surgical procedures frequently comes in the form of non-randomized or open-label trials. These are potentially less likely to be published, and if published, are less likely to be retrieved on indexed search. Standard search strategies may perform less well when retrieving uncontrolled studies.

4.5.3. Complementary and alternative medicines

Complementary and alternative medicine research is unevenly distributed between the allopathic and complementary medical journals and across languages, and the majority of journals are non- or poorly indexed in the standard bibliographic databases\textsuperscript{30}. Searches of CAM-specific databases and non-English language reports may be required. In addition, CAM treatments are frequently individualized to the patient and non-standardized.

Resources to search,

- Allied and Complementary Medicine (AMED, via McGill library)
4.5.4. Health economics

Health economics studies are generally retrieved as part of an HTA, either by hand screening a general search (if the number of references is not overly large), or by a dedicated search. Several filters for health economics materials have been developed (listed in the resources in Section 4.2.2). See also the dedicated Economics Evaluation Database (EED) and information resources at the CRD.

- Information resources on health economics, from the CRD
  http://www.york.ac.uk/inst/crd/econ.htm

5. DOCUMENTING THE SEARCH

When documenting the search, whether on paper, in a spreadsheet, or in a text or Word file, the following key items should be captured.

- The full name of the resources searched, the resource provider, version, and date of last update
- The date of the search, and the dates covered by the search
- Search terms (indexed and keyword) and combinations of terms. For ease of reuse, variants for each resource may be stored in a plain text – not Word – document, from which they can be cut/pasted into the appropriate search box
- Filters used (eg, for study type, or population). If these were provided by the search engine (eg, PubMed Clinical Queries), citation, version and date
- Any limits applied, eg, language limits
- If there is a possibility of publication, the number of terms retrieved in the search (to complete the PRISMA flowchart)

A descriptive summary of the search (see the MUHC TAU template and PRISMA guidelines) will appear in the report, with more detail, as required, in the appendices.

6. UPDATING THE SEARCH

One or more update searches should be conducted during the report writing to capture recently-added citations (eg, newly indexed citations, or electronic preprints – particularly of studies reported in abstract).

There are also numerous options for ongoing monitoring and updating using ‘push’ technology or RSS feeds.

- PubMed automated search, with emailed results
• OVID (Medline and EMBASE) autoalerts
  om=9&subsection=13
• Journal RSS feeds

7. WORKFLOW

Some suggestions.

• PubMed, OVID (MEDLINE and EMBASE), Cochrane Collaboration, DARE, and others, allow search results to be downloaded to the desktop in formats compatible (.ris) or specific to individual desktop bibliographic databases, which can then be loaded into EndNote, Reference Manager, RefWorks, RevMan, etc.
• For grey literature, Zotero (http://www.zotero.org/, which comes as a plug-in for Firefox, or in a standalone version) offers a wide variety of filters and scrapers that can be used to capture metadata for grey literature (including Google Scholar searches). This can then be exported in a generic format suitable for importation into other databases. RefWorks (http://www.refworks.com/, a cloud-based reference manager available through McGill) also has an option to create a citation entry from any web-page.
• Combining the results from searching multiple sources inevitably leads to duplicates. EndNote offers an option to remove duplicates, but variations in capitalization (eg, titles in sentence case from PubMed versus title case from OVID), formatting of author names, and journal abbreviations means that there is no single, optimal search for duplicates. A workable strategy is to do repeat searches, gradually decreasing stringency of matching.
• EndNote allows one-click retrieval of PDFs (conditional on having retrieved a working URL and having a subscription to the library). Pubget (http://www.pubget.com) is another option for retrieving multiple citations at once.

REFERENCES


