Searching for studies for Cochrane Systematic Reviews of Diagnostic Test Accuracy

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Key Challenges

○ Incomplete and inconsistent reporting by authors of DTA studies (Mallett 2006)

○ Incomplete and inconsistent indexing of DTA studies in databases (van der Weijden 1997, Fielding 2002, Vincent 2003)

○ Efficiency of methodology search filters designed to identify DTA studies is hampered by incomplete and inconsistent reporting and indexing (Doust 2005, Mitchell 2005, Leeflang 2006, Ritchie 2007, Whiting 2008b)

Authors of diagnostic test accuracy reviews are likely to retrieve thousands of records to scan for potentially relevant studies for their review

Meeting the challenges

- Sources to search

- Search methods to use
  - Structure of search
  - Problematic terminology
  - Methodology search filters for DTA studies

- Screening records to decide relevance

- Managing references

- Documenting and reporting search methods and results

Sources to search

○ Cochrane Register of Diagnostic Test Accuracy Studies

- centralized, study-based and managed by Ruth Mitchell, Trials Search Co-ordinator for the Cochrane Renal Group, Sydney, Australia
- improve access to DTA studies (**2535 studies** published between 1951 and 2008 as of August 2008)
- assist with lobbying for improved indexing – e.g. Publication Type for DTA studies
- resource for methodological research into DTA studies
- not yet publicly available www.cochrane.org/docs/DiagnosticTestRegisterPlan.doc

Cochrane Register of Diagnostic Test Accuracy Studies

- Studies from existing non-Cochrane DTA systematic reviews (MEDLINE, DARE, HTA, MEDION) – **1667**

- Studies from pilot Cochrane DTA reviews – **62**

- Studies from Cochrane Renal Group's renal-related DTA database (including studies from journals that have been handsearched) – **727**

- Studies identified in MEDLINE using "Sensitivity and Specificity/" –
    - results downloaded (14,611) (from 2005 backwards in time)
    - 5000 screened
    - 10 to 15% are eligible for inclusion in Register
    - 352 entered with coding
    - Total **2535** published 1951-2008
  - auto alert search for new records since 2005, as they are added to MEDLINE
  - analysing DTA search terms (text words and database subject headings) for future testing in development of DTA filter
  - developing screening protocols

Sources to search

- A range of biomedical databases to avoid missing relevant studies (Whiting 2008a)

  - examined 8 systematic reviews and their database searches
  - MEDLINE, EMBASE, BIOSIS, Science Citation Index, LILACS all uniquely contributed relevant studies
  - none of the searches in a specific database identified all studies included in a review
  - over 20% of the included studies were not found by searching MEDLINE
  - 6% of the included studies were not found by the electronic searches

Sources to search

- Other approaches
  - Reference checking (relevant primary studies, other related DTA reviews) (Whiting 2008a, Davenport 2008)
    - the majority of relevant diagnostic accuracy studies that had not been found by database searching or that were included in databases but not retrieved by the database searches were identified by scanning reference lists

  - Citation searches
  - Handsearching

  - Grey literature sources (e.g. conference abstracts (Brazzelli 2008), dissertations)
  - Unpublished, ongoing studies

Search methods to use

○ Contact the Trials Search Co-ordinator of your Review Group to discuss the sources to search and the development of database search strategies for your review

○ Consult Chapter 7 'Searching for studies' in the *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy* (http://srdta.cochrane.org)

○ Look out for further training opportunities offered by your regional Support Unit (http://srdta.cochrane.org)

Structure of Search

○ Design a search strategy to reflect the key components of the review question

- **Index Test(s)**

- **Target Condition**

- Reference Standard

- Patient Description

○ <u>Search structure examples</u>:

- Index Test(s) AND Target Condition

- Index Test(s) AND Target Condition AND Patient Description

- (Index Test(s) OR Reference Standard) AND Target Condition

- (Index Test(s) OR Reference Standard) AND Target Condition AND Patient Description

○ Routine use of methodological search filters for diagnostic test accuracy is not currently recommended (Doust 2005, Mitchell 2005, Leeflang 2006, Ritchie 2007, Whiting 2008b)

Structure of Search

"Clinical assessment for diagnosing congenital heart disease in newborn infants with Down Syndrome"

- **Index test(s):** physical examination, auscultation, palpation, pulse, observation, electrocardiography, chest radiograph

- **Target condition**: congenital heart disease

- Reference standard: echocardiography

- **Patient description**: newborn infants with Down Syndrome

Structure of search:
Index test(s) AND Target condition AND Patient description

(Index test(s) OR Reference standard) AND Target condition AND Patient description

Search methods to use

○ Check **related DTA systematic reviews**, evidence-based guidelines etc for reported search strategies for useful terms (subject headings and text words)

○ Search for **known relevant studies** in the database - check to see how these are indexed and look for any useful text words in the titles and abstracts (where available) to cover each concept

○ Check the **search tools** provided with the **database** (e.g. MeSH database option in PubMed; Permuted Index under Search Tools in Ovid)

Search methods to use

○ Aim for the search to be highly sensitive (likely to result in low precision)

- Use a range of terms (text words and subject headings e.g. MeSH, EMTREE)

- Advanced search techniques (e.g. 'explode' subject headings to retrieve more specific terms as well, use of floating subheadings)

- Synonyms, related terms, variant spellings, acronyms, abbreviations

- Truncation, wildcards

Search methods to use

○ If search results are too many to deal with pragmatically seek advice from your Trials Search Co-ordinator on methods to test out to improve precision

- Restricting to studies involving humans

- Excluding irrelevant publication types such as case reports

- Careful use of proximity operators, where available
  e.g. ((spleen or splenic) adj3 diamet$)

- Use of subheadings with specific subject headings rather than use floating subheadings
  e.g. Chest/radiography rather than radiography.fs.

Problematic terminology

Target condition

- named disease (e.g. myasthenia gravis)
- disease stage (e.g. early stage breast cancer)
- any of a number of related conditions (e.g. urinary tract infections)

Target condition: myasthenia gravis

Text words: MeSH terms:

myasthen$ OR MG OR ocular-myasthen$ Myasthenia gravis/

OR generali?ed-myasthen$

Problematic terminology

Target condition: urinary tract infections

Text words:
(infection$ adj3 (urinary OR
urine OR urethra OR bladder
OR ureter$ OR kidney OR kidneys
OR renal)

etc...

MeSH terms:
exp Urinary Tract Infection/

(Bacterial infection/ OR
Gram negative infection/ OR
Enterobacter infection/ OR
Staphylococcus infection/ OR exp
Leukocyte/ OR vesicoureteral
reflux/ OR exp pyelonephritis/ OR
Bacteriuria/ OR exp Cystitis/)
AND
exp Urinary tract/

Problematic terminology

Index test(s)

- physiological - signs and symptoms (e.g. clinical examination)
- serological - assays to detect substances in serum (e.g. antibodies)
- pharmacological - substances administered for diagnostic rather than therapeutic use (e.g. edrophonium)
- electrophysiological – e.g. nerve conduction tests
- imaging techniques – e.g. ultrasonography, MR, CT, PET (Mijnhout 2000, 2004 – approximately 70 ways of describing a single test)

Many diagnostic technologies are used across a wide range of fields in medicine and may also be routinely mentioned in abstracts of RCTs for example, in descriptions of entry criteria, thus retrieving large numbers of irrelevant studies.

Search methods to use

Index test(s): clinical assessment

Text words
physical examination
auscultat*
palpat*
electrocardiogra*
ECG
chest radiograph*
chest roentgenogram
chest X-ray
Low oxygen saturation
Pulse oximet*

MeSH terms
Physical examination/ (explode)
Electrocardiography/
Chest/radiography
Oximetry/

Problematic terminology

'diagnostic' subheadings:
- diagnosis (di)
  - pathology (pa)
  - radiography (ra)
  - radionuclide imaging (ri)
  - ultrasonography (us)

Other potentially useful 'diagnostic' subheadings:
- diagnostic use (du)
- analysis (an)
  - blood (bl)
  - cerebrospinal fluid (cf)
  - isolation and purification (ip)
  - urine (ur)
- physiopathology (pp)
- cytology (cy)
- innervation (ir)

Problematic terminology

Example: Diagnostic imaging (Astin 2008)

Radionuclide Imaging/ — for general use only, non-specified

Disease or anatomical term/ri — preferred use

Tomography, Emission-Computed
 Positron-Emission Tomography
 Tomography, Emission-Computed, Single-Photon

some indexers may use name of imaging technique rather than "disease/ri" format

exp Magnetic Resonance Imaging/ — no 'diagnostic' subheading that covers this type of imaging

Problematic terminology

Examples:

Text words (ti,ab):

MeSH terms

Tensilon

Edrophonium/diagnostic use
Edrophonium/

Nerve conduction tests

Electromyography/
Electrodiagnosis/ AND Neural Conduction/
Hand/innervation OR Wrist/innervation

(urinalysis or urine analysis or
urine sample$ or urine specimen$ or
(urine adj3 collect$) or urine bags or
distick$ or dipstick$ or dip stick$ or
urine microscopy or reagent strip$)...

Urine/analysis
Urinalysis/

Search methods to use

○ Check **related DTA systematic reviews**, evidence-based guidelines etc for reported search strategies for useful terms (subject headings and text words)

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Methodology search filter for DTA studies

○ Routine use of methodological search filters for diagnostic test accuracy is not currently recommended (Doust 2005, Mitchell 2005, Leeflang 2006, Ritchie 2007, Whiting 2008b)

- Can lead to the omission of a considerable number of relevant studies

- Even the most sensitive filters have been found to miss relevant studies and perform inconsistently across subject areas and study designs

- Precision tends to be low – relevant records may be lost for no substantial reduction in the number needed to read (NNR)

Methodology search filter for DTA studies

Whiting et al. *Methods for Evaluating Medical Tests. Symposium*; 2008 Jul 24-25; University of Birmingham, Birmingham, UK: 20.

- 22 search filters versus index test(s) AND target condition searches tested in MEDLINE
- To find 523 studies in 7 reviews
- Index test(s) and target condition searches missed average 9% (0 to 13%)
- Filter searches missed 14 to 58% (range 3 to 88% across reviews)
- With filter searches NNR reduced from 55 to between 7 and 51 (median 27)
- For moderate sensitivity (>80%) the NNR not substantially reduced (range 29 to 51)

Currently available diagnostic filters are not recommended for use in identifying studies for inclusion in Cochrane DTA reviews because they are unable to offer both acceptable sensitivity and a substantially reduced NNR.

Methodology search filter for DTA studies

- Planned and ongoing research should produce further evidence on which to base search practice decisions (Alldred 2006, Franceschini 2006, Fraser 2006, Leeflang 2007, Astin 2008)

- Potential to develop new search filters
  - using objective, textual analysis methods - as for the Cochrane Highly Sensitive Search Strategy (revised) developed for identifying RCTs for intervention reviews (Glanville 2006)

- Search Filter Resource (UK InterTASC Information Specialists Subgroup)
  - www.york.ac.uk/inst/crd/intertasc/diag.htm - search filters for diagnostic studies
  - www.york.ac.uk/inst/crd/intertasc/surveys.htm
    - studies on performance of search filters
  - critical appraisals now available for some filters

Methodology search filter for DTA studies

○ Further research required:

- Further performance evaluations of recently published filters are required

- Are the studies missed by the search method materially different from those found and likely to affect the findings of the review?

Screening results to decide relevance

- More than one author should screen results of searches (Doust 2006)
  - Two authors screened results of searches for two systematic reviews
  - Good agreement between them
  - For one review either review author working alone would have missed one relevant study

- Some studies may be missed due to inadequate reporting of diagnostic accuracy terms in titles and abstracts (Fraser 2006)

- Where very large numbers of records need to be screened, likely agreement between review authors may be reduced and the probability of missing relevant articles may be higher

Managing references

- Suggest you use reference management software
  - Keep track of search results downloaded from databases
  - Seek advice from Trials Search Co-ordinator on which fields to download
  - Can store useful information on:
    - the name of the database or other source details from which a study was identified
    - when and from where an article was ordered and the date of article receipt
    - whether the study retrieved is to be included in or excluded from the review and the reasons for exclusion
- Please send included and excluded studies (if these are deemed to be DTA studies) to Ruth Mitchell for inclusion in the Cochrane Register of Diagnostic Test Accuracy Studies

Documenting and reporting search methods and results

○ **What was searched** (which databases - including date range of coverage, e.g. MEDLINE (1950 to October 2008); conference proceedings; journals etc)

○ **When they were searched** (date when you searched each database)

○ **How they were searched** (search strategy used for each database to be put in an appendix to the review)

○ **Results of the search** (proposal to use flow diagram – adapted from QUOROM (PRISMA) guidelines; or descriptive paragraph to include:

  • how many references were retrieved by the electronic searches, and other techniques

  • how many were excluded (with reasons)

  • how many were included in the analysis of the review

○ Refer to **Chapter 4** and **Chapter 7, Section 7.6** of the *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy* **http://srdta.cochrane.org/**

Meeting the challenge

- Standards for Reporting of Diagnostic Accuracy (STARD) initiative (Bossuyt 2003)
  - Further uptake of this guidance is needed to continue to improve the accuracy and completeness of reporting research methods in DTA studies by authors and journal editors

- Greater consistency in assigning available DTA subject terms in databases is also needed

- Standardization terms for Index test(s) would aid search efficiency (Cochrane Register of Diagnostic Test Accuracy Studies)

- Introduction of a specific study design term for DTA studies (such as a DTA Publication Type in MEDLINE, for example) would greatly help in the development of efficient and effective DTA search filters