SYSTEMATIC REVIEWS

Asking the Question
Finding the Best Answer
IN THIS CLASS

• Provide a practical, usable sense of what a systematic review is and does.
• List of the steps.
• Why they are important.
• Some excellent examples.
• A detailed explanation of the steps that will guide you to undertaking and completing this important research study.
• Resources that will assist you along the way.
• Questions?
DEFINITION

From the Cochrane Handbook for Systematic Reviews of Interventions, 2011:

• A systematic review attempts to collate **all** empirical evidence that fits pre-specified eligibility criteria in order to **answer a specific research question**. It uses explicit, systematic methods that are selected with a view to **minimizing bias**, thus providing more **reliable findings** from which **conclusions** can be drawn and **decisions** made.
IN A NUTSHELL

• It is a research study, requiring a carefully thought out question, an investigative team, and a study protocol to guide you along the way until it is completed and published.

• An analysis, evaluation, and summary of all the research studies as they pertain to a specific scientific question, such as a condition, or treatment of a condition.

• A properly conducted systematic review faithfully summarizes the evidence from all relevant studies on the topic of interest, and it does so concisely and transparently. (Cook, 1997)

• The word, “all” is important, because bias may result if you don’t identify all relevant studies. Systematic Reviews consolidate all of the high quality evidence.
SUMMARY OF STEPS

- Formulate Topic and Refine Question.
- Assess Need/Does one exist?
- Assemble Team: SR methods, info retrieval, subject expertise, statistics.
- Create Protocol.
  - Describe reason for SR.
  - Eligibility Criteria: Define inclusion/exclusion criteria: Types of Studies, Types of Participants, Types of Interventions, Date range.
  - Describe the critical appraisal process for evaluating studies.
- Register Protocol.
- Begin a comprehensive search as outlined in your protocol. You will have a lot of results then you screen based on your criteria. Document search and include date and number of results.
  - At least three bibliographic databases, as well as grey literature, subject specific and regional databases.
  - Search clinical trial registries.
  - Contact researchers to clarify information about their studies.
- Screening and Selection based on your inclusion/exclusion criteria. Two or more members of the team working independently.
  - Level 1: Review Title/Abstract. Select based on your protocol’s criteria.
  - Level 2: Read full text of the keepers. Give reasons for those you exclude.
SUMMARY OF STEPS (cont’d)

- Critical Appraisal: Assessing the quality of each study.
  - Look for bias with the author.
  - Assess the quality of the study/methodology. Funnel Plot.
  - Relevance to the research question. Does it answer the question?

- Manage citations and data that have been selected.
  - Endnote or Refworks allows you to export to Excel and then to Google Sheets.
  - Google Drive offers web based collaboration.

- Data Extraction.

- Data Synthesis:
  - Meta-Analysis and/or narrative analysis.

- Summarize the Evidence.
  - Forest Plot
VERSUS REVIEW ARTICLES

• A **Review Article** is an overview or **BROAD examination** of the published literature on a broader topic usually from one author’s perspective. **There is no critical appraisal of the research.**

• **Scoping Review**: Purpose is to establish what is currently known about the topic and perhaps identify what needs further research. They can be conducted prior to any new scientific project to assess research need and/or **scope** of the project.
SOME GOOD EXAMPLES

• METHODS: Transparent and reproducible. So Specific that it can be reproducible. Shows HOW IT WAS DONE.
  • Clearly Stated Objective
  • Search Methods: The Where
    • Which electronic databases
  • Selection Criteria (inclusion/exclusion): The What. It sets the boundaries for the systematic review.
    • Types of participants, sample size, study design, date range
    • Interventions, exposures, outcomes.
• Data Collection and Analysis
  • Independence to reduce bias in selection
The PRISMA checklist offers guidelines on forming a strategy and writing the METHODS section as well as other sections of your paper.

Abstract

Background

Aripiprazole is a relatively new antipsychotic drug, said to be the prototype of a new third generation of antipsychotics; the so-called dopamine-serotonin system stabilisers. In this review we examine how the efficacy and tolerability of aripiprazole differs from that of typical antipsychotics.

Objectives

To evaluate the effects of aripiprazole compared with other typical antipsychotics for people with schizophrenia and schizophrenia-like psychoses.

Search methods

We searched the Cochrane Schizophrenia Group Trials Register (November 2007) which is based on regular searches of BIOSIS, CENTRAL, CINAHL, EMBASE, MEDLINE and PsycINFO. We inspected references of all identified studies for further trials. We contacted relevant pharmaceutical companies, drug approval agencies and authors of trials for additional information.

Selection criteria

We included all randomised trials comparing aripiprazole with typical antipsychotics in people with schizophrenia or schizophrenia-like psychoses.

Data collection and analysis

We extracted data independently. For dichotomous data we calculated relative risks (RR) and their 95% confidence intervals (CI) on an intention-to-treat basis, based on a random effects model. We calculated numbers needed to treat/harm (NNT/NNH) where appropriate. For continuous data, we calculated weighted mean differences (WMD) again based on a random effects model. We have contacted representatives of Bristol Myers Squibb pharmaceuticals (UK) for additional data.
Ultrasound guidance for peripheral nerve blockade.
Walker KJ, McGrattan K, Aas-Eng K, Smith AF.

Author information

Update in
Ultrasound guidance for upper and lower limb blocks. [Cochrane Database Syst Rev. 2015]

Abstract

BACKGROUND: Peripheral nerve blocks can be performed using ultrasound guidance. It is not yet clear whether this method of nerve location has benefits over other existing methods.

OBJECTIVES: To assess whether the use of ultrasound to guide peripheral nerve blockade has any advantages over other methods of peripheral nerve location.

SEARCH STRATEGY: We searched the following databases for relevant published trials: the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2008, Issue 3); MEDLINE (1966 to July 2008); EMBASE (1974 to July 2008); ISI Web of Science (1945 to 2008 ); CINAHL (1982 to July 2008); and LILACS (1980 to July 2008). We also handsearched meeting supplements.

SELECTION CRITERIA: We included all identified randomized controlled trials (RCTs) comparing ultrasound-guided peripheral nerve block with at least one other method of nerve location.

DATA COLLECTION AND ANALYSIS: Two authors independently assessed trial quality and extracted data. We attempted to contact study authors for additional information, where necessary.

MAIN RESULTS: We included 18 trials containing data from 1344 patients. Ten trials assessed upper limb blocks and eight assessed lower limb blocks. Most compared ultrasound with peripheral nerve stimulation. All trials were assessed as having a moderate risk of bias due to inability to blind the practitioner. Meta-analysis was not performed because of the variety of blocks, techniques, and outcomes, and the review was based on the authors' assessment of the trials. Ultrasound guidance produced similar success rates in providing surgical anaesthesia (72% to 98.8%) when compared with peripheral nerve stimulation (58% to 93.1)
WHY ARE THEY NEEDED?

• “The systematic review lies at the heart of evidence-based health care” (Beverley 2003).
• Important in making informed decisions that may improve quality of care and health outcomes.
• Consolidates evidence to solve problems:
  • For Health Administrators: “Does our hospital have enough nurses?”
  • For Clinicians: “What age do women benefit the most from having a mammogram?”
  • For Public Health: “Is calorie labeling necessary to reduce obesity?”
UNCOVERS THE BEST EVIDENCE TO SUPPORT THE BEST HEALTH CARE AND OUTCOMES

• “The most reliable way to identify benefits and harms associated with various treatment options is a systematic review of comparative effectiveness research.”


• If you want to treat a disease and there are 1 or 2 drugs to use, SR’s attempt to pool together all of the treatments and analyze them to help you make the best decision based on the best evidence.
HOW DO WE BEGIN?

Here are some excellent resources to follow from PRISMA (preferred reporting items for systematic reviews and meta-analyses).

• It consists of a 27-item checklist and a four-phase flow diagram that will help you document your exclusions.
• Here is a very detailed outline from the National Academy of Medicine: Finding What Works in Health Care, Standards for Systematic reviews.
  • Standard 2.2 and 3.2
    • As you look at this detailed outline notice the emphasis on reducing bias, both as it pertains to study selection and within the team itself. Transparency and impartiality is key.
FIRST STEP:
WHAT IS YOUR QUESTION?
WHAT IS THE PROBLEM YOU ARE ADDRESSING?

• Is there a need for an answer? Does it lend itself to a systematic review?
• Follow the PICO format, or other logical designs, or models, in order to refine your question.
• Here is an excellent article that can help you organize your topic:
  Formulating the Evidence Based Practice Question: A Review of the Frameworks
  https://journals.library.ualberta.ca/eblip/index.php/EBLIP/article/view/9741/8144
DOES ONE ALREADY EXIST?

• CHECK A FEW PLACES: REMEMBER REVIEWS CAN REGISTER ANYTIME PRIOR TO DATA EXTRACTION
  • Cochrane Database of Systematic Reviews:
    https://community.cochrane.org/editorial-and-publishing-policy-resource/overview-cochrane-library-and-related-content/databases-included-cochrane-library/cochrane-database-systematic-reviews-cdsr
  • PROSPERO: International prospective register of systematic reviews:
    https://www.crd.york.ac.uk/PROSPERO/
ASSEMBLE YOUR TEAM

• Expertise:
  • You want someone who is good at research and information retrieval, statistics and/or quantitative data retrieval (if you are including a Meta-Analysis) and someone who is very familiar or even an expert in the subject area.

• Transparency of professional and financial COI.
  • To uncover any intellectual bias that would reduce the credibility of the review.
CREATE A PROTOCOL:

In other words, how will you be accomplishing your project? Be specific. What is the question and need for the research and what is your plan of action in filling that need to answering the question?

• Define your strategy in finding the best evidence specific to the question:
  
  • Refine research question. Why are you doing this?
  • Describe the study screening criteria:
    • How will you choose what studies to include and what to exclude?
  • Describe search strategy:
    • What and where you will search? How will you search?
  • How will you be extracting the data?
  • How will you critically appraise each study?
  • How will you synthesize and summarize?

More on the specifics of the how and the what and the where in a bit ...
REGISTER YOUR PROTOCOL

• Access to information about ongoing reviews should help avoid the unintended duplication of reviews and wasting of resources/funding.

• By keeping a public record, methods are transparent, reproducible, reduces bias.

• Remember to add amendments to review or registration updates as you go forward and indicate why you are making the change.


  • “When the review is published, the final results can be compared with what was intended at registration.”

  • “As with clinical trial registration, there is a need to register reviews prospectively at a point in time when the review protocol has been completed, but ideally before screening for eligibility has begun. This timing will reduce the opportunity for conscious or subconscious manipulation of inclusion criteria to include certain studies to mold a review to reach a desired conclusion.”

  • Practically should be done when the main elements of the review have been agreed upon, such as inclusion/exclusion criteria.
HOW TO REGISTER

- Registration should take place once the systematic review protocol has been finalized, but ideally before screening studies for inclusion begins. However, reviews are currently accepted for registration as long as they have not progressed beyond the completion of data extraction.

- Completed reviews should **not** be registered. Only protocols.

- Guidelines on How to Register:
  - [https://www.crd.york.ac.uk/prospero/#aboutregpage](https://www.crd.york.ac.uk/prospero/#aboutregpage)
  - [http://collections.plos.org/reporting-guidelines](http://collections.plos.org/reporting-guidelines)
WHERE TO REGISTER:
http://www.crd.york.ac.uk/PROSPERO/

• PROSPERO is an international database of prospectively registered systematic reviews in health and social care, welfare, public health, education, crime, justice, and international development, where there is a health related outcome. Key features from the review protocol are recorded and maintained as a permanent record. PROSPERO aims to provide a comprehensive listing of systematic reviews registered at inception to help avoid duplication and reduce opportunity for reporting bias by enabling comparison of the completed review with what was planned in the protocol.
Some Excellent Examples

• Define Inclusion/Exclusion Criteria:
  • What types of studies will you include? RCT’s? Cohort?
  • Demographic of population or participants. What are the ages? What is the problem?
  • What type of intervention?
  • What publication types? Clinical trial, Government Publication, etc.

• Search Strategy:
  • This will also be written in the methods section so make sure you document how you searched. Try to make it reproducible.
Criteria for considering studies for this review

Types of studies

We included randomized controlled trials. Where a trial was described as ‘double-blind’, but it was only implied that the study was randomized, we included those trials in a sensitivity analysis. If there was no substantive difference within primary outcomes (see types of outcome measures) when those ‘implied randomisation’ studies were added, then we included these in the final analysis. If there was a substantive difference, we only used clearly randomised trials and described the results of the sensitivity analyses in the text. We excluded quasi-randomised studies, such as those allocating by using alternate days of the week.

Types of participants

We included people with schizophrenia and other types of schizophrenia-like psychoses (e.g. schizoaffective psychosis and schizoaffective disorders), irrespective of the diagnostic criteria used. There is no clear evidence that the schizophrenia-like psychoses are caused by fundamentally different disease processes or require different treatment approaches (Carpenter 1994).

Types of interventions

1. Antipsychotic(s) any dose or form of administration.
2. ‘Typical’ antipsychotic drugs such as haloperidol or chlorpromazine, any dose or form of administration.

Types of outcome measures

We grouped outcomes into short term (up to 12 weeks), medium term (13 to 26 weeks) and long term (over 26 weeks).

Primary outcomes

1. Global state
2. Relapse

Secondary outcomes

1. Death - suicide and natural causes
2. Global state
3. No clinically important change in global state (as defined by individual studies)
4. Average endpoint global state score
5. Average change in global state scores

Service outcomes
SEARCH STRATEGY:
What will you search? Who will you contact?

• What bibliographic databases? At the very least: Pubmed and Cochrane (CENTRAL).

• What subject specific databases? What regional databases? Only if you need to.

• Will you contact pharmaceutical companies? Will you contact authors of research trials, and/or study sponsors of unpublished data? Trial Registries?

• What other types of Grey Literature will you investigate?
  • What is Grey Literature?
  • The Fourth International Conference on Grey Literature (GL '99) in Washington, DC, in October 1999 defined grey literature as follows: "That which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers."
SEARCH STRATEGY:

How will you Search?

• What are your search terms? Limits, filters: What is your date range? Remember to use term harvesting and adjust search strategy with additional terms (synonyms) as you examine relevant articles. Make sure you document your search with dates.

• Good article on effective search strategies:
  • https://journals.library.ualberta.ca/eblip/index.php/EBLIP/article/view/7402/6436

• Define your filters: Don’t just rely on filters that are designed by indexers based on subject headings alone. You might miss some relevant articles. Add your own Keyword filters. Here is a good example of a search string using RCT filters:
  • (clinical[Title/Abstract] AND trial[Title/Abstract]) OR (clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])

• Make sure you document your search with a specific description that includes the date of retrieval, years covered, database name, database host, search terms, filters.
Search methods for identification of studies

Electronic searches
1. Update search
   We searched The Cochrane Schizophrenia Group Trials Register (November 2007) using the phrase:
   "(aniprazole" or "ability" or "ability in title, abstract, index terms of REFERENCE) or (aniprazole in interventions of STUDY)
   This register is compiled by systematic searches of major databases, hand searches and conference proceedings (see Group Module).
2. Previous electronic searches
   We searched The Cochrane Schizophrenia Group Trials Register (May 2007) using the phrase:
   "(aniprazole" or "ability" or "ability in title, abstract, index terms of REFERENCE) or (aniprazole in interventions of STUDY)

Searching other resources
1. Reference searching
   We inspected the references of all identified studies for more trials.
2. Personal contact
   We contacted the first author of each included study for information regarding unpublished trials.
3. Drug companies
   We contacted the manufacturers of aniprazole (Bristol-Myers Squibb) for additional data.
4. We searched The US Food and Drugs Administration website - http://www.fda.gov using the word "aniprazole" and also "ability".

Data collection and analysis
[For definitions of terms used in this, and other sections, please refer to the Glossary.]
1. Selection of trials
   Citation information downloaded from electronic sources included details of author, institution or journal of publication. We independently inspected all reports. We resolved any disagreement by discussion, and where doubt remained, we acquired the full article for further inspection. Once the full articles were obtained, we independently decided whether the studies met the review criteria. If disagreement could not be resolved by discussion, we sought further information and these trials were added to the list of those awaiting assessment.

2. Assessment of methodological quality
   We assessed the methodological quality of included studies using the criteria described in the Cochrane Handbook (Higgins 2005), which is based on the degree of allocation concealment. Poor concealment has been associated with overestimation of treatment effect (Schulz 1995). Category A includes studies in which allocation has been randomised and concealment is explicit. Category B studies are those which have randomised allocation but in which concealment is not explicit. Category C studies are those in which allocation has neither been randomised nor concealed. Only trials that are stated to be randomised (Categories A or B) of the handbook were included in this review. The categories are defined below:
Data collection and analysis

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2. Assessment of methodological quality

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A. Low risk of bias (adequate allocation concealment)
B. Moderate risk of bias (some doubt about the results)
C. High risk of bias (inadequate allocation concealment).

We assessed the methodological quality of included trials in this review using the Jadad Scale (Jadad 1996). The Jadad Scale measures a wider range of factors that impact on the quality of a trial. The scale includes three items:

1. Was the study described as randomised?
2. Was the study described as double-blind?
3. Was there a description of withdrawals and drop outs?

Each item receives one point if the answer is positive. In addition, a point can be deducted if either the randomisation or the blinding/masking procedures described are inadequate. For this review we used a cut-off of two points on the Jadad scale to check the assessment made by the handbook criteria. However, the Jadad Scale was not used to exclude trials.

3. Data collection

JB independently extracted data from selected trials, and HGE re-extracted data from two different samples (10%). Where disputes arose we attempted to resolve these by discussion. When this was not possible and further information was necessary to resolve the dilemma, we did not enter data but added the trial to the list of those awaiting assessment.
Search methods for identification of studies

Electronic searches

In January 2014 we searched the following electronic databases to identify reports of relevant RCTs:

- The Cochrane Wounds Group Specialised Register (searched 23 January 2014);
- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2013, Issue 12);
- Ovid MEDLINE (1946 to January Week 3 2014);
- Ovid MEDLINE (In-Process & Other Non-Indexed Citations, January 22, 2014);
- Ovid Embase (1974 to 2014 January 22);
- EBSCO CINAHL (1982 to 23 January 2014);

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) using the following exploded MeSH headings and keywords:

#1 MeSH descriptor: [Face] explode all trees 2314
#2 MeSH descriptor: [Facial Injuries] explode all trees 334
#3 MeSH descriptor: [Ear] explode all trees 917
#4 (face or facial or nose or mouth or "ear" or ears or "lip" or lips):ti,ab,kw 23013
#5 (#1 or #2 or #3 or #4) 24156
#6 MeSH descriptor: [Surgery, Plastic] explode all trees 104
#7 (plastic next surg* or (reconstructive next surg*)):ti,ab,kw 1179
#8 (#6 or #7) 1229
#9 (#5 and #8) 223
#10 ((facial near/surgery) or (craniofacial near/surgery) or (face next lift*) or face-lift* or facelift*):ti,ab,kw 205
#11 (#9 or #10) 393

Cochrane Database of Systematic Reviews:

**Perioperative corticosteroids for preventing complications following facial plastic surgery**

02 June 2014
We searched the Cochrane Central Register of Controlled Trials (CENTRAL) using the following exploded MeSH headings and keywords:

#1 MeSH descriptor: [Face] explode all trees 2314
#2 MeSH descriptor: [Facial Injuries] explode all trees 334
#3 MeSH descriptor: [Ear] explode all trees 917
#4 ([face or facial] or [nose] or [mouth] or ["ear"] or [ears] or ["lip"] or [lips])ti,ab,kw 23013
#5 ([#1 or #2 or #3 or #4]) 24155
#6 MeSH descriptor: [Surgery, Plastic] explode all trees 104
#7 ([plastic next surg*] or [reconstructive next surg*])ti,ab,kw 11179
#8 ([#5 or #7]) 1229
#9 ([(#5 and #8)] 225
#10 ([facial next/surgery] or [craniofacial next/surgery] or [face next lifted*] or [face-lift*] or [facelift*])ti,ab,kw 205
#11 ([#9 or #10]) 363
#12 MeSH descriptor: [Adrenal Cortex Hormones] explode all trees 11158
#13 ([corticosteroid*] or [corticoid*] or [glucocorticoid*] or [steroid*])ti,ab,kw 26630
#14 (dexamethasone or methylprednisolone)ti,ab,kw 6897
#15 ([#12 or #13 or #14]) 35747
#16 (n11 and n15) 20

Search strategies for Ovid MEDLINE, Ovid Embase and EBSCO CINAHL can be found in Appendix 1. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision) (Lefebvre 2011). We combined the Embase search with the Ovid Embase filter developed by the UK Cochrane Centre (Lefebvre 2011). We combined the CINAHL search with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2014). There were no restrictions on the basis of date or language of publication.

We searched the Current Controlled Trials website (http://www.controlled-trials.com/ctf) for any reports of ongoing trials (last search 29 January 2014).

Searching other resources

We scrutinized reference lists of any identified relevant studies for additional citations. We contacted specialists in the field and tried to contact the authors of the included trials for any possible unpublished data, but with no success.
DIG DEEP:
Begin a Comprehensive Search

• Digging for gold. The quality of the review depends on the quality of the studies that have been examined, evaluated, and summarized.

• Look for all relevant published and unpublished studies to reduce bias.

• Be prepared to sacrifice precision because you want a large amount of results that may contain useless studies from which to choose.

• The deeper you go, the more you will uncover. You will get a lot of useful documents, but a lot of useless records as well. Then you need to weed it down to the best.
SEARCH BIBLIOGRAPHIC DATABASES

- Pubmed: Also includes data and papers from conferences.
- Cochrane Central Register of Controlled Trials (CENTRAL): Includes published articles from Embase and Pubmed, but also other unpublished sources including all Cochrane Review Groups' Specialized Registers and the hand-search results register.

GREY LITERATURE

- Don’t forget these databases that also include data and papers from conferences:
  - WorldCat
    - Thesis/Dissertation
  - BIOSIS previews (via WOS)
    - This is an expansive index to life sciences and biomedical research from journals, meetings, books, and patents. The database covers pre-clinical and experimental research, methods and instrumentation, animal studies, and more.
  - WOS Core Collection. Filter to “Proceedings Paper” or “Meeting Abstract.”
WHY GREY LIT?

• To Find:
  • Updated studies and current studies
  • Missing data from published studies
  • Current National Academy of Medicine systematic review standards call for grey lit inclusion (Standard 3.2)

• 3.2.1
  • “Search grey literature databases, clinical trial registries, and other sources of unpublished information about studies.”

• 3.2.2
  • “Invite researchers to clarify information about study eligibility, study characteristics, and risk of bias.”
MORE GREY LITERATURE

• Clinical Trial Registries
  • ClinicalTrials.gov
  • WHO International Clinical Trials Registry Platform – http://apps.who.int/trialsearch/
• FDA Pharmaceutical or Medical Devices (Updated Daily)
  • US Food and Drug Administration (FDA) - http://www.fda.gov/Drugs/default.htm
  • US Food and Drug Administration (FDA) – http://www.fda.gov/MedicalDevices/default.htm
  • National Drug Code directory (FDA)- https://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm

• Technical Reports
  • Government agencies issue reports.
  • Universities or pharmaceutical companies
  • Advocacy groups
    • “What organizations are interested in your topic?”
• Specialists in a Field, Authors of Research Trials, or Study Sponsors
  • For any unpublished data on your topic
• Additional Resource to Guide You
  • Grey Literature report – http://www.greylit.org/home
  • AllTrials.net
SEARCH SUBJECT SPECIFIC DATABASES

• Specialized databases if needed, such as ERIC for education.
• Agri-Food Public Health
  • AGRICOLA
  • BIOSIS
SCREENING:
Based on Your Inclusion/Exclusion Criteria

• Usually conducted in two passes. Need to have at least two independent reviewers with a third person available for conflicts.

• First Pass:
  • Review title/abstract (try to read just the abstract to save time).
  • Check for possible source of bias with the author, or journal itself.

• Second Pass:
  • Review full-text if it is a keeper after the first pass. Kick out if it doesn’t match all of your criteria.

• Select: Protocol specifies decision criteria. Does it meet those needs? Does it address the question?

• Document your search and give reasons for exclusion. Include the date. Follow the PRISMA Flow document (next slide).

• Rayyan is a free web-tool that dramatically speeds up the process of sorting, screening and selecting studies.
Comprehensive search

1. Review Title/Abstract

2. Read Full Text

PRISMA 2009 Flow Diagram

- Records identified through database searching
  \( (n = \) )
- Additional records identified through other sources
  \( (n = \) )
- Records after duplicates removed
  \( (n = \) )
- Records screened
  \( (n = \) )
- Full-text articles assessed for eligibility
  \( (n = \) )
- Studies included in qualitative synthesis
  \( (n = \) )
- Studies included in quantitative synthesis (meta-analysis)
  \( (n = \) )
- Records excluded
  \( (n = \) )
- Full-text articles excluded, with reasons
  \( (n = \) )

Critically appraise your selection
Articles identified through database searching  
\( n = 210 \)

Articles included after screening for title  
\( n = 78 \)

Articles excluded based on title  
\( n = 132 \)  
Reasons for exclusion: not reporting on hybrid ablation, language other than English or veterinary studies.

Articles included after screening for abstract  
\( n = 45 \)

Articles excluded based on abstract  
\( n = 33 \)  
Reasons for exclusion: not reporting on hybrid ablation (but e.g. on pharmacological hybrid therapy), case reports, comments on other articles or letters to the editor.

Full-text articles excluded  
\( n = 12 \)  
Reasons for exclusion: Only short description of what hybrid ablation is, no abstract available and full text appeared letter or case report.

Articles included after screening Full-text  
\( n = 33 \) (including 9 review articles)

Included articles  
\( n = 35 \) (including 10 review articles)

Additional articles identified after scanning of reference lists of selected papers  
\( n = 2 \)

(Vroomen & Pison, 2016)
APPRAISAL AND SELECTION

Evaluation and appraisal of each study/article in the literature review is essential to retrieve the highest value of evidence before inclusion.

- Excellent resource to guide you in choosing the best studies:
  - https://casp-uk.net/

- Assess the quality of the studies.
  - **Two or more researchers** should work independently to avoid bias in selection.
  - Go deep, go close to uncover any bias in the study itself. Who is the researcher? What are his or her associations.

  - Medicine’s Financial Contamination: Disclosure rules may seem arcane, but money corrupts medical research
  - Top Cancer Researcher Fails to Disclose Corporate Financial Ties in Major Research Journals
• Look closely, carefully, and critically. Otherwise mistakes and bias happen that can affect health care.
  • Last year the *NEJM* issued a correction on a 1980 letter to the editor. The reason for the correction is reported here in *The Atlantic*.
    • The article describes how a letter to the editor of the *NEJM* from a Harvard Graduate Student describing the rare risk of addiction to opioids on patients in a controlled hospital setting morphed and grew legs. It was routinely cited incorrectly as evidence by researchers in many scholarly journals and consumer magazines. It was inaccurately called an “extensive study” and even a “landmark study.” Drug companies even used it to say opioid addiction was unlikely.
    • This event was also described in the book *Dreamland: the tale of America’s opiate epidemic*. 

APPRAISAL
Equal distribution of the studies. Each dot is a study. Likely no publication bias.
DATA MANAGEMENT

Clear record keeping is essential. Remember you will be collaborating with others, so they need to understand what you have done. Must be reproducible.

• Where to document:
  • Web based options such as Google Drive offers sharing and collaboration features, such as Google Docs and Google Sheets.

• What to document:
  • Search process, search details, the date of when you searched, number of records retrieved, progress notes, search terms, filters, explanations/annotations about why you chose those terms, a narrative supplement explaining decisions impacting search results, reasons for exclusions, etc.
  • http://prisma-statement.org/documents/PRISMA%202009%20flow%20diagram.pdf
CITATION MANAGEMENT

• Use Bibliographic Reference Software such as Endnote or RefWorks
  • Offers sharing and collaboration features which allows all members of the team to appraise and weed.
  • Can cite while you write.
  • Saves citations and abstracts in folders and subfolders with access to the articles.
• You can export your references as a .cmv file and import into spreadsheet software such as:
  • Excel
  • Google Sheets
DATA EXTRACTION, ANALYSIS AND SUMMARY

• What data will be extracted from the studies that were selected for inclusion?

• What software will be used?
  • Review Manager 5 (RevMan 5)
    • RevMan facilitates preparation of protocols and full reviews, including text, characteristics of studies, comparison tables, and study data. It can perform meta-analysis of the data entered and present the results graphically.
    • It is free.

• How will it be summarized in order to describe the results?
  • Meta-Analysis (Forest Plot)
  • Narrative Analysis
DATA EXTRACTION, ANALYSIS AND SUMMARY

• With a Meta-Analysis
  • This involves using statistical analysis to consolidate data or results from the research studies into a single quantitative answer or summary from which conclusions are drawn.

• Without a Meta-Analysis
  • Results from qualitative data or quantitative data are analyzed and summarized with a conclusive narrative without being statistically combined.
### How to read a forest plot?

<table>
<thead>
<tr>
<th>Study IDs</th>
<th>Intervention group n/N</th>
<th>Control group n/N</th>
<th>Relative risk (fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative risk (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rowling JK 2000¹</td>
<td>1/131</td>
<td>2/133</td>
<td>17.8</td>
<td>0.50</td>
<td>(0.05 - 5.49)</td>
</tr>
<tr>
<td>Albus D 2003²</td>
<td>7/279</td>
<td>9/290</td>
<td>77.7</td>
<td>0.84</td>
<td>(0.36 - 1.93)</td>
</tr>
<tr>
<td>Hermione G 2005³</td>
<td>3/102</td>
<td>1/101</td>
<td>4.5</td>
<td>3.00</td>
<td>(0.12 - 72.77)</td>
</tr>
<tr>
<td>Total</td>
<td>512</td>
<td>542</td>
<td>100.0</td>
<td>0.87</td>
<td>(0.41 - 1.87)</td>
</tr>
</tbody>
</table>

Test for heterogeneity Chi-square = 0.79, df = 2, p = 0.67, I² = 0.0% ³
Test for overall effect z = 0.35, p = 0.7 ³

¹ N = total number in group, n = number in group with the outcome.
² Outcome of interest in picture and in number. Fixed effect model used for meta-analysis.
³ Influence of studies on overall meta-analysis.
⁴ Overall effect.
⁵ Heterogeneity (I²) = 0%. So, we use fixed effect model.
⁶ p value indicating level of statistical significance

[https://uk.cochrane.org/news/how-read-forest-plot](https://uk.cochrane.org/news/how-read-forest-plot)
WHERE DO I PUBLISH?

• Contact the publisher
  • They may have their own criteria.

• Check out our Scholarly Communications LibGuide
  • This is an excellent resource that will help you evaluate journals from which to choose.
RESOURCES

- PRISMA (preferred reporting items for systematic reviews and meta-analyses consists of a 27-item checklist)
  - And a four-phase flow diagram, that will guide you in your documentation process for searching and inclusion/exclusion
- Here is a very detailed outline from the National Academy of Medicine: Finding What Works in Health Care, Standards for Systematic Reviews
  - Standard 2.2 and 3.2
    - As you look at this detailed outline notice the emphasis on reducing bias, both as it pertains to study selection and within the team itself. Transparency and impartiality is key.
- Does one already exist?
  - Cochrane Database of Systematic Reviews:
  - PROSPERO: International prospective register of systematic reviews
    - https://www.crd.york.ac.uk/PROSPERO/
- Register your Protocol:
  - http://www.crd.york.ac.uk/PROSPERO/
- Guidelines on How to Register and Report your Findings:
  - http://www.equator-network.org/
  - http://collections.plos.org/reporting-guidelines
  - https://effectivehealthcare.ahrq.gov/research-methods/
RESOURCES

• Here is an excellent article that can help you organize your topic:
  • Formulating the evidence-based practice question: A review of the frameworks
  • https://journals.library.ualberta.ca/eblip/index.php/EBLIP/article/view/9741/8144

• CASP: Excellent resources on guiding you in critically appraising studies. Quality assessment tool.
  • https://casp-uk.net/

• Rayyan: is a free web based too that speeds up the collaborative screening process and selecting studies.
  • https://rayyan.qcri.org/welcome