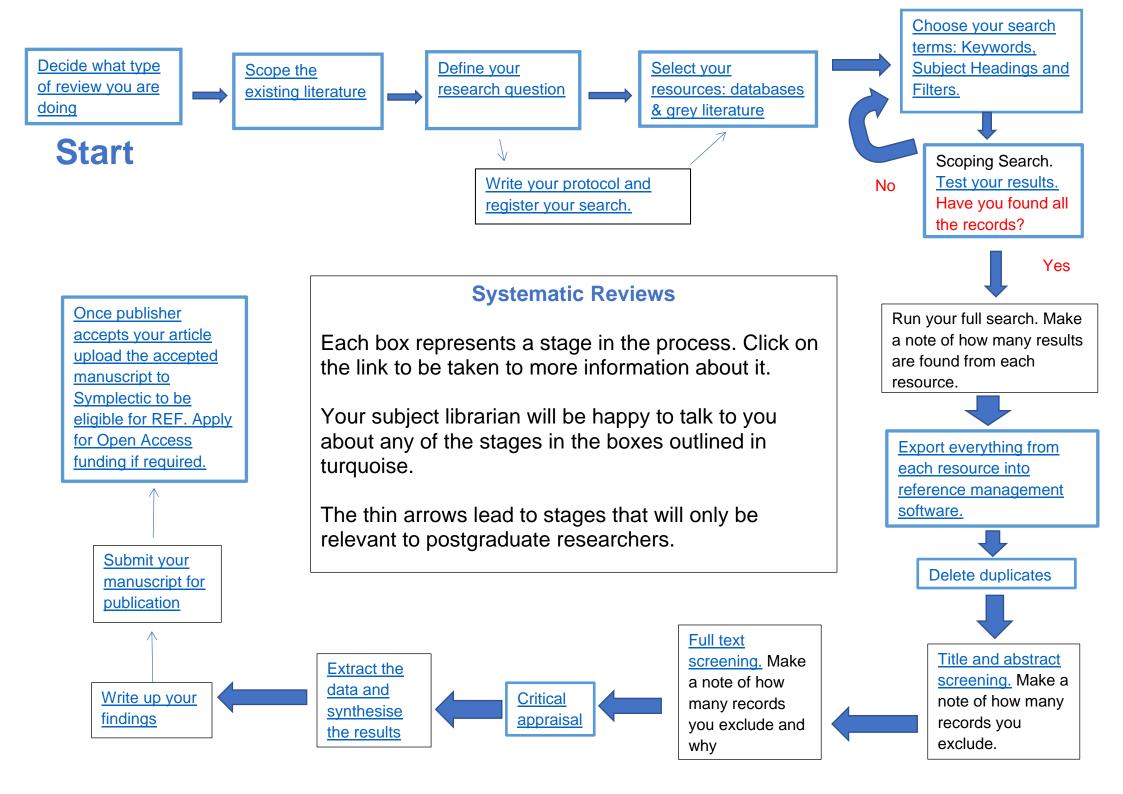
Imperial College London

Systematic Review Flowchart

The process of planning and completing a medical systematic review

Imperial College London Library Services 2022





1. Decide what type of review you are doing.

A proper systematic review looks at absolutely every resource to find all the information to answer a very narrow research question.

	Systematic Review	Literature Review
Definition	High-level overview of primary research on a focused question that identifies, selects, synthesizes, and appraises all high quality research evidence relevant to that question.	Qualitatively summarizes evidence on a topic using informal or subjective methods to collect and interpret studies.
Goals	Answer a focused clinical question Eliminate bias	Provide summary or overview of topic
Question	Clearly defined and answerable clinical question Recommend using PICO as a guide	Can be a general topic or a specific question
Components	Pre-specified eligibility criteria Systematic search strategy Assessment of the validity of findings Interpretation and presentation of results Reference list	Introduction Methods Discussion Conclusion Reference list
Number of Authors	Three or more	One or more
Timeline	Months to years Average eighteen months	Weeks to months
Requirements	Thorough knowledge of topic Perform searches of all relevant databases Statistical analysis resources (for meta-analysis)	Understanding of topic Perform searches of one or more databases
Value	Connects practicing clinicians to high quality evidence Supports evidence-based practice	Provides summary of literature on a topic

What's In A Name?: the difference between a systematic review and a literature review and why it matters. (1)

The table above (1) shows the extra level of complexity needed to complete a systematic review including needing multiple authors to help avoid bias in screening and use of statistical analysis resources to enable meta-analysis of all the relevant results. Basically, a systematic review needs to:

- Have found all the data available to answer the focussed research question.
- Have aimed to minimise bias by using explicit, systematic methods that are documented in advance with a protocol and then recorded in the review using. the PRISMA flowchart (2). [continued...]

• The undertaking of the review should be transparently recorded, including publishing the search strategies, so that the results can be verified or reproduced.

<u>This University of Pittsburgh webpage</u> gives more details of what is involved in a systematic review, including the timeline suggested by the Cochrane Handbook (3).

Often when people say they have completed a systematic review they just mean that they have searched more than one database systematically. Although this isn't a 'proper' systematic review, there is still academic value in doing this. It means that they have made a thorough search strategy, which can be reproduced by other researchers, and used this in several databases to find many resources that provide the evidence to support their argument.

This article by Grant and Booth provides a good description of the different types of review that can be written. (4)

If you are going to be doing a 'proper' systematic review then it may be worth you completing this free CourseEra online course from John Hopkins University. (5) It takes approximately 14 hours to complete and covers how to formulate an answerable research question, define inclusion and exclusion criteria, search for the evidence, extract data, assess the risk of bias in clinical trials, and perform a meta-analysis.

You may also find it useful to look at our <u>reading list</u> where we collect links to useful handbooks, articles and books that explain the process of doing a systematic review.

There is also a Microsoft Teams site which aims to be a Community of Practice for those engaging in systematic reviews to get advice and support from others involved in the same process. The site is being developed as a pilot scheme by the Imperial College London Medicine Liaison Librarians but we are hoping to attract people from across the College, and its collaborators, who have experience of systematic reviews, as well as those who are new to the process. The Librarians can offer support and advice, especially about the searching part of the process, but are not experts in other areas such as meta-analysis and statistics. The aim of this site is to provide a community space for researchers to receive and offer support to each other as systematic reviews are conducted. To join, click on 'join or create a team' on the main Imperial College London Teams page and search for 'systematic.' Alternatively, please email lib-med-liaison@imperial.ac.uk and ask to be added.

If you have any questions about this stage of the process your subject librarian will be happy to help. Our <u>subject support page</u> lists the medical librarian for each campus (6) or book a research consultation at a time convenient for you using our <u>online booking</u> <u>form</u>. (7)

2. Scope the existing literature

As you start to think about the research question that you're going to ask, you should take a general scoping look at the current literature that has been written. This will enable you to see any possible gaps in the research as well as ensure that your question has not already been answered by someone else. It will also help to ensure that you understand the area that you are researching.

We have written these pages (8) to be a good resource for tips about starting your search. We also have a number of tutorials and guides available on our subject support page to help you search our databases (6).

<u>PubReminer</u> (9) is a useful tool. It will run your simple search through PubMed and show you the resulting abstracts as well as generating frequency tables. These tables will show you the journals in which your query is published the most, the authors which are most active in the field of your query, the most commonly used words in the titles and abstracts and also the MeSH.

The Yale MeSH analyser (10) is another useful tool. Enter up to 20 PMIDs (the unique identifying number PubMed gives to each of its articles) of relevant articles and it will create a grid that shows the subject headings assigned to them by PubMed. Their blog explains how "You can then easily scan the grid and identify appropriate MesH terms, term variants, indexing consistency, and the reasons why some articles are retrieved and others are not, a common frustration for expert searchers. This inevitably leads to fresh iterations of the search strategy to include new terms." (11) The grid also shows the author-assigned keywords which can offer you some ideas of extra keywords to use in your search.

Ovid automatically does phrase searching e.g. heart attack will only find those two words together in that order. Therefore, if you are doing a quick keyword search for two completely different concepts put AND between them (e.g. exercise AND neurodegenerative so that the database knows to search for these anywhere in the title/ abstract/ keywords etc. and that they don't have to be near each other).

There is more information about searching keywords and subject headings in <u>Section Six</u> of this flowchart as well as <u>Appendix Three</u> and <u>Appendix Four</u>.

Remember that you only need to be doing simple searching at this stage because you are just coming up with ideas.

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3. Define your research question.

Systematic reviews need to answer a specific question. If you begin searching without defining your question, your search will take much longer as you will have to read lots of irrelevant results. You will also risk bias because your ideas might be influenced by what you find.

It may be that you decide to do a scoping review instead. They are still just as valid and you still need search comprehensively and systematically to search for all the data to answer the research question. However, you will analyse the results differently. The difference is that they exist to give an overview of the area rather than answering a specific research question. For example, a systematic review might ask 'ls x or y more effective at curing z?' while a scoping review might be 'what barriers affect x when used to cure z?' If you are not sure what type of review you are doing then you might find this article useful at explaining the difference (12).

The most common way of defining health questions is by using PICO. It is a useful way to ensure that you have asked a specific question that is relevant to the patient or problem. It also identifies the key concepts that will need to be in articles so they can be found in your search.

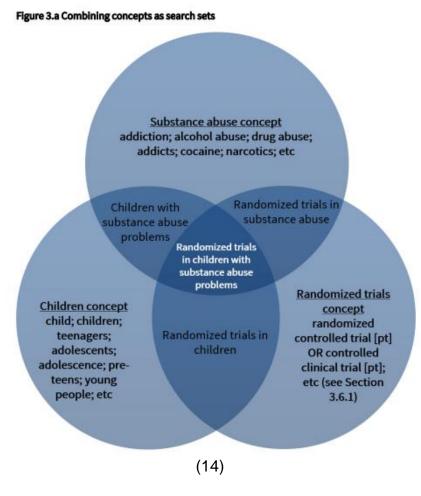
More information about the need for a specific question, frameworks including PICO and a template to help you break down a search into its concepts can be found on this <u>King's College London page</u> (13)

When deciding if your question is suitable for a systematic review you need to consider:

- If the systematic review has been done before. Links to systematic review databases are available in the '<u>literature searching</u>' page of the Medicine subject support pages (6). If it has, then has enough research been published since that review or are there enough improvements to be made to that original review to justify your review?
- Is there enough research that has been written for you to be able to analyse? If not, do you need to broaden your question?
- More commonly, has too much research been written about this topic? If your search is already bringing back lots of results then you will need to focus your question further. We generally advise that you shouldn't be finding more than 1000 results per database.

Your research question will now have identified the core concepts that you are going to be searching for. While developing your search strategy you should make sure that you keep each of the concepts that you are searching for distinct. These will then be combined using Boolean (AND/ OR) to ensure that you are not searching through too many irrelevant results. [continued..]

The Technical Supplement to Chapter Four of the Cochrane Handbook includes this useful diagram for visualising your search strategy



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4. Write your protocol and register your research.

A protocol should be prepared before a review is started and then used as a guide to carry out the review. It describes the rationale, hypothesis, and planned methods of the systematic review. The Prisma group have this statement and checklist to help the development and reporting of protocols (2).

This guide by the Centre for Reviews and Dissemination at York University advises researchers how to write their protocol (15)

At this stage it is useful to register your systematic review. This means that other researchers will not waste their time answering similar questions. Many journals also check a review was registered as a mark of quality as it ensures that it didn't deviate from its pre-defined criteria. This should be done via Prospero (16)
Information about proposing and registering a new Cochrane Review is available here (17)

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Return to the flowchart

5. Select your resources: databases and grey literature

A full systematic review should look at every resource available- both published articles which are found in databases and also grey literature. You should search what you can considering the scope, time and resources available. The Cochrane Handbook explains in <u>Section 4.2.2. Minimizing Bias</u> why you should not just search one database (18).

Databases.

Bibliographic databases are the best resources to use to search for journal articles because they allow advanced, structured searches. You can easily import to reference management software and also save your results so they can be adapted as you discover new search terms. The medicine subject support <u>resources page</u> (6)_lists the databases we subscribe to at Imperial College that we believe will be most useful to those involved in medical research. These include those that are only dealing with health topics (such as the ones provided by Ovid) as well as Scopus and Web of Science that search journals which cover a broad range of subjects. This can be useful if you are researching a non-clinical question that could be covered by non-medical journals such as technology in health, economic policies etc.

If you are researching an area that isn't just health related, you can also check the <u>subject support</u> pages for those topics to see if the librarians recommend any other specialist databases (6)

We also have a number of tutorials and guides available on our <u>subject support page</u> to help you search our databases (6). If you encounter any problems accessing them please contact <u>your Librarian</u>.

Grey Literature

Grey Literature has been defined as "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." (19) Basically it covers anything that isn't a published article such as a conference paper, health report or unpublished clinical trial etc. Ideally you should include grey literature to ensure that you have used all the data currently available to guide your results. It also helps your review avoid publication bias.

This <u>libguide by Kings College London</u> has more information about grey literature (20)

The <u>Cochrane Handbook</u> says that <u>ClinicalTrials.Gov</u> and the <u>WHO International Clinical Trials Registry Platform (ICTRP)</u> are the most important trial registers to search (18). You can find more information about these, and other trial registers, in Appendix One.

You may also want to search for preprints. These are scientific manuscripts that have been uploaded to a public server for others to read for free. Initially they are posted without peer-review but they may get feedback or reviews and may eventually be published in a peer-reviewed journal. A quick way to do this is by searching <u>Europe PMC</u> as it covers the main biomedical preprint servers.

The awkward thing about grey literature is that there isn't a systematic way of searching for it. You will find some examples in the references of the articles your database search has found and your supervisor, or experts in the field, may be able to recommend others. You should also think about possible organisations and websites that might include useful data. See Appendix One for a list of some sources of grey literature.

You can also do a simple search for grey literature on Google by including filetype:pdf or filetype:doc as part of your search. This means that your results will only include pdfs or Word documents. Don't rely on popular documents that are high up in the search results. Important documents can be easily retrieved via Google but some grey literature may be hidden within results, down several pages or not visible at all due to a relative lack of popularity.

PRISMA 2020 requires that systematic reviews report search strategies and number of records identified for all websites and registers, so you need to keep track of how and where you have searched for grey literature. More detail and examples of this can be found in the PRISMA-S extension (21).

Remember, when you find grey literature resources, they have not been peer reviewed so make sure that you critically appraise them. One of the most popular ways to do this is using the <u>AACODS checklist</u> (Authority, Accuracy, Coverage, Objectivity, Date, Significance) (22)

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Return to the flowchart

6. Choose your search terms: Keywords, Subject Headings and Filters.

Imperial College made video tutorials that explain how to create an effective search strategy using keywords and MeSH in Ovid and other databases. These are available via the <u>Tutorials, Guides & Skills page</u> of our subject support page (6). If you encounter any problems accessing the tutorials please contact <u>your Librarian</u>.

As you start planning your search look in the <u>Cochrane Library</u> (16) to see if any of the concepts you are going to be researching have already been covered by a Cochrane Review. The appendices of these reviews include the search strategies used and so you can see what terms were used and 'borrow' as appropriate. If you re-use part of a Cochrane search ensure that you reference it appropriately.

You should use both keywords and subject headings in your search. You will use the same keywords across each database although some aspects may be altered to reflect how that database works. You will use the appropriate subject headings for each database. See Appendix Two for some tips to help you alter your search strategy across different databases.

A useful tool to help you translate your search across different platforms is the <u>Polyglot Search Translator</u>. Copy and paste a PubMed or Ovid Medline search into the box and then scroll down to see what the search would look like in another database. Please note that Polyglot only shows changes to syntax/command language – it can not check for different subject headings so you will still need to manually check for these in each database.

Keywords

Keywords are the simplest way to search a database. Type them into the search box and the database will see if that combination of letters can be found anywhere in the title/ abstract/ keywords of an article. However, if a researcher has used a different word which has the same meaning (e.g. a plural, abbreviation, different spelling or synonym) then the database won't find it. As a result, you need to think of all possibilities.

See Appendix Three for more information about keywords.

Subject Headings

Librarians index articles for health databases by tagging them with subject headings that relate to the content. It means that all the indexed articles about heart attacks can be quickly found regardless of which words were used to describe them because they've all been indexed with the same subject heading. For example, the subject heading used in Medline to cover the topic is 'myocardial infarction.' It also means that the subject heading will find relevant articles where the terms are not used in the title or abstract even though they are the subject of the research.

The subject headings used in the Medline database are called MeSH, which stands for Medical Subject Headings. MeSH descriptors are organised into 16 categories: A for anatomic terms, B for organisms, C for diseases, D for drugs and chemicals, etc. Each of the categories are called 'trees.' Each category is further divided into subcategories. Within each subcategory, descriptors are arrayed hierarchically from most general to most specific in up to thirteen hierarchical levels.

Organising MeSH in this way means that you can choose to broaden or narrow your search by altering the hierarchical level of your subject headings so that you're not retrieving too many or too few results.

When searching MeSH you sometimes have the choice of exploding or focussing the subject headings. 'Explode' means that you are including in your search all articles that were indexed with the more specific subject headings. 'Focus' means that you restrict the term to articles that the indexer thought were the focus of what the article was about. This is not generally advised for systematic reviews since you are aiming to find all the available data on the topic.

You can be even more specific by choosing a subheading of a MeSH e.g. neoplasms/ physiology. However, this can be too narrowing so we recommend that you choose them all.

See Appendix Four for more information about searching using subject headings in different databases.

Filters

Filters are different from some of the filters/limits you can select in databases when viewing or running your search strategy. While these may help you narrow or focus your results when doing a quick or causal search, they are not reliable enough for systematic literature searching. As they generally rely on subject headings only, they will likely cause you to miss new, as yet un-indexed articles.

Filters are tested search term combinations designed by librarians and researchers. They usually involve a combination of keywords and subject headings and indexing terms and can be added to your final search strategy to help identify specific methodologies or study types. For instance, you can a use a filter to exclude any results that are not RCTs or are tests on animals rather than humans. You add your chosen filter at the end of your search strategy if desired.

Search filters are also available for other types of study designs such Diagnostic Studies, Qualitative Studies and Systematic Reviews. Because different databases have different subject headings, specialised versions of filters have been designed for each database. For instance, the filter to find RCTs in Ovid Medline is slightly different from the filter for RCTs in Ovid Embase, so you must use a filter that has been designed for each database you are using.

Kings College Library has a helpful guide on finding relevant filters for your search and adding them to your search strategy. (23)

See Appendix Five for more information about filters and for the filters in Embase & Medline for human studies and RCTS.

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Return to the flowchart

7. Test your results.

The <u>Prisma flow diagram</u> (2)shows how the results of your search strategy will be refined until you have excluded all articles that are irrelevant and know which studies you are going to analyse. The flow diagram was updated in 2020 and there are now different templates depending on the sources used to identify the studies and whether the review is new or updated.

Before you get to the stage of screening your results in your reference management software, you want to be confident that you are not going to find any extra relevant studies later in the process that weren't found by your search strategy. If this is the case, you will have to get rid of everything in your reference management software, rewrite your search strategy so it would have found the relevant article, export everything again and then restart your screening.

The easiest way to do this is scan your results for around ten articles in your results that sound like they are relevant. Look through the references for these. If there are any relevant articles listed here would the keywords and MeSH in your search strategy have found them? If not, alter your search strategy so it does.

You can also search relevant titles on Scopus or Web of Science as they give information about which articles have cited the ones that you are interested. Search the list of these and check whether your search strategy would have found any appropriate ones.

This <u>blog post by Amanda Wanner</u> (an information specialist at the University of Plymouth) gives a more scientific way of using EndNote to test your gold standard of results to ensure the search strategy would have found them. (24)

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Return to the flowchart

8. Export everything from each resource into reference management software.

Once you are confident that your search has found all relevant articles, it is time to move your results into reference management software. This will get rid of duplicates, help you organise your results and ensure that they are correctly cited when you write your review.

To help you work out which software package is best for you, Imperial College has written this comparison of some of the most popular options (25)

We support EndNote (26) and RefWorks (27). We can also offer advice on Mendeley and Zotero.

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Return to the flowchart.

9. Delete duplicate search results

Once you have exported your search results into your chosen Reference Management software, you will need to remove duplicate article records.

Most Reference Management software includes a feature to help you remove duplicate records. Note that these do not always work perfectly, some duplicates will be missed which you will need to remove manually.

Keep a record of the number of articles you had before and after removing the duplicates, you will need to report on this when writing up.

If you are using **RefWorks**, see this guide by Library of Rush University Medical Centre for guidance on removing duplicates (28)

If you are using **Endnote**, remove duplicates using the following steps:

- Click 'Library menu and choose 'Find Duplicates'
- Click 'Cancel' to see the duplicates in list form
- Make sure that the highlighted references on the duplicates list are in blue (you may need to slightly move the webpage's bottom or side bar to make this happen)
- Click 'delete'

There is also guidance on pages 9-10 of the <u>Imperial College Library EndNote x20 Workbook</u> (29)

If you are using **Mendeley**, this <u>Mendeley support webpage</u> provides a step by step guide for removing duplicates.(30)

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Return to the flowchart

10. Title and Abstract Screening

You are now ready to screen your articles to select which ones you will use in your systematic review. Each article should be reviewed to see if it meets the inclusion criteria that was set out in the protocol. Advice on developing the inclusion criteria can be seen in <u>section 1.2.2.3 of the guide</u> by the Centre for Reviews and Dissemination at York University: (13)

The screening of a systematic review is normally carried out in two stages, and by at least two people. It is important to keep a record of the number of articles you exclude at each stage as you will need to report on this when writing up. An example of the screening process is outlined in Section 4.6 of the Cochrane Handbook. (18) [continued...]

Imperial College subscribes to Covidence. This is the same software that Cochrane reviewers use. The key steps supported by Covidence include citation screening, full text review, Risk of Bias assessment, extraction of study characteristics and outcomes. It makes it much easier to screen your results with other reviewers. Members of the College can get extra details and join here (31) Extra help and support for using it is provided by Covidence here (32)

Further advice on carrying out both screening stages can be seen in <u>section 1.3.2 of the guide</u> by the Centre for Reviews and Dissemination at York University (13).

The first stage involves reviewing the title and abstract of each article to see if it meets the inclusion criteria. You must record the number of articles you decide to exclude but you do not need to record the reasons why. It is usual to exclude most of your results in this stage of the process because the broadness of your search strategy meant a large number of articles included in the results will be obviously irrelevant.

Return to the flowchart

11. Full Text Screening

The second stage of screening involves reviewing the full text of the articles you have remaining after completing the first stage. You will need to check each article to determine if it meets the inclusion criteria.

If you are using Endnote you can make use of the Find full text feature to retrieve the full text of your articles. The instructions for this are on pages 10 and 20 of our Endnote x20 Workbook (29). The Find full text feature won't find all the articles, but it should find a large majority of them. If you are off campus then you may find it useful to connect to our VPN if possible. You can also search for individual articles through Imperial LibrarySearch (33)

If you don't find all the articles through Library Search, check if there are Open Access versions available, there are various services you can use to check this. Examples of these include <u>Unpaywall</u> for Chrome browsers (34) and the <u>Open Access Button</u> that you can also download for Chrome or copy and paste details of the article in the search box on the webpage (35).

If there are articles that you are still unable to find, place a Document Delivery request with the Library, details are here (36). Staff, students of Imperial College and affiliated NHS users get free and unlimited Document Delivery requests. Click on the 'order a book or article' link above the search box in <u>LibrarySearch</u> to place your request(s).

Once you have found the full text of your articles, you may wish to attach them as PDFs to the article records in your Reference Management software. [continued..]

If you are using **RefWorks**, see page p4 of the <u>Imperial College Library RefWorks quick guide</u> for guidance on attaching PDFs to article records (37).

If you are using **Endnote** see page 6 of the <u>Imperial College Library Endnote Workbook (29).</u>

If you are using **Mendeley** highlight the citation to which you wish to add a document and scroll down the Details tab (right column) to the files section and click on 'add files.'

If you are using Covidence then you can use the bulk PDF import tool to upload all your pdfs at once so you can then easily screen the articles within the software. The details about how to do this are included in Covidence's help pages (32).

The details of each article you exclude must be recorded along with the reason for the exclusion.

Return to the flowchart

12. Critical appraisal

The next step is to assess the quality of your selected articles. There are various checklists you can use for this, for a list of examples see the Critical appraisal tab on the <u>resources page</u> of our subject support page (6).

Further information on the process can be found in section <u>1.3.4.4. of the guide</u> by the Centre for Reviews and Dissemination at York University (13) and on <u>Thomas Jefferson University's libguide</u> (38).

This article by the Cochrane Collaboration describes a tool they developed for assessing risk of bias in random trials (39).

You will need to record the details of any articles you decide to exclude after carrying out a critical appraisal, along with the reasons why the decision was made. You will need to report on this when writing up.

Return to the flowchart

13. Extract the data and synthesise the results

You are now ready to carry out the data extraction and synthesise the results.

Cochrane offers tools to support the management and analysis of data for Cochrane Reviews. These are available here (40). If you are carrying out a meta-analysis or network meta-analysis then chapters ten and eleven of the Cochrane Library handbook provide useful guidance (18).

Section 1.3.5 of the guide by the Centre for Reviews and Dissemination at York University provides <u>information on synthesising</u> <u>both quantitative and qualitative data</u> (15)

If you are working with qualitative data, this article also contains some useful tips (41)

Return to the flowchart

14. Write up your findings

The structure of your systematic review will largely depend upon the requirements of the journal or organisation you are publishing with, however there are various online guides available to help you structure your write up. One example is <u>this following section</u> of the guide by the Centre for Reviews and Dissemination at York University (15) while <u>chapter three of the Cochrane Handbook</u> details how to report the review (18).

<u>Prisma</u> (2) provides a checklist which can be used to structure the write up of a systematic review, plus a flowchart which can be used to record the number of articles that were included and excluded at each stage.

Return to the flowchart

15. Submit your manuscript for publication

This guide, by the University of Illinois at Chicago, provides some useful tips to help you decide which publication to submit your manuscript to. (42)

Another way to help you choose which journal to submit to is to type the title and/or abstract of your review into <u>Jane</u> (43). The website will then compare your document to millions of documents in PubMed to find the best matching journals, authors or articles.

If you have any questions about this stage of the process your subject librarian will be happy to help. Our <u>subject support page</u> lists the medical librarian for each campus (6) or book a research consultation at a time convenient for you using our <u>online booking</u> <u>form</u>. (7)

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16. Upload the article to Symplectic and apply for Open Access funding

To be eligible for the Research Excellence Framework (REF), the Higher Education Funding Council (HEFCE) requires that manuscripts are deposited in a repository within three months of acceptance. For further details on the REF see their webpage (44)

We advise that you deposit your work in Spiral (Imperial institutional repository) as soon as it is accepted for publication. To do this you need to upload your work via Symplectic. Our webpage gives further information (45).

When you upload your manuscript to Symplectic you will have the option to apply for funding to pay open access fees and article processing charges (APCs). Our webpages give further information (46).

Our Open Access pages give further guidance on being eligible for the REF, applying for funding, depositing in Spiral and complying with the polices of your research funders' and Imperial (47).

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Return to the flowchart

References to all the sources we have linked to can be found in Appendix Six

Appendix One: Sources of Grey Literature.

Trials Registers.

- https://sites.google.com/a/york.ac.uk/yhectrialsregisters. This resource links to registers around the world and, usefully, tells you how to search them.
- https://clinicaltrials.gov/ ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. One of the registers that you're required to search if you're doing a Cochrane review.
- http://www.who.int/ictrp/en/ WHO International Clinical Trials Registry Platform. Aims to facilitate the prospective registration of all clinical trials, and the public accessibility of that information. One of the registers that you're required to search if you're doing a Cochrane review.
- https://www.cochranelibrary.com/central CENTRAL. Available through the Cochrane Library as a source of reports of randomized and quasi-randomized controlled trials. Most records are taken from bibliographic databases (mainly PubMed and Embase), but records are also derived from other published and unpublished sources, including CINAHL, ClinicalTrials.gov and the WHO's International Clinical Trials Registry Platform.)
- https://bepartofresearch.nihr.ac.uk/ UK trials since Brexit. Pre-Brexit trials will still be on the EU Register (link below) but they won't be updated.
- https://www.clinicaltrialsregister.eu/ctr-search/search EU Clinical Trials Register. The EU Clinical Trials Register contains information on interventional clinical trials on medicines conducted in the European Union (EU), or the European Economic Area (EEA) which started after 1 May 2004.
- http://www.anzctr.org.au/Default.aspx Australian New Zealand Clinical Trials Registry
- http://www.isrctn.com/ The ISRCTN register contains clinical trials from around the world, including from 1 January 2022, all CTIMPs in the UK, that are submitted to the HRA using the IRAS combined review service. ISRCTN accepts all studies involving human subjects or populations with outcome measures assessing effects on human health and well-being, including studies in healthcare, social care, education, workplace safety and economic development.
- https://en.wikipedia.org/wiki/List_of_clinical_trial_registries Wikipedia list of registers for clinical trials by country.

Repositories:

- https://core.ac.uk/ CORE's mission is to aggregate all open access research outputs from repositories and journals worldwide and make them available to the public. It is now the world's largest collection of open access research papers.
- http://www.opendoar.org/ provides a quality-assured listing of open access repositories around the world. Maintained by the University of Nottingham and Lund University.

- https://www.oclc.org/en/oaister.html OAIster is a union catalogue of over 50 million records of open access digital resources.
- https://www.base-search.net/ BASE is one of the world's biggest search engines especially for academic web resources.
 BASE provides more than 240 million documents from more than 8,000 sources. You can access the full texts of about 60% of the indexed documents for free (Open Access).

Theses

- http://ethos.bl.uk/ EThOS aims to provide a national record of all doctoral theses awarded by UK Higher Education institutions & free access to the full text of as many theses as possible
- http://search.ndltd.org/index.php Search the 6,194,628 electronic theses and dissertations contained in the NDLTD (Networked Digital Library of Theses and Dissertations) archive
- https://oatd.org/ Open Access Theses and Dissertations. Metadata comes from over 1100 colleges, universities, and research institutions. OATD currently indexes 6,129,263 theses and dissertations.
- https://library-search.imperial.ac.uk/permalink/44IMP_INST/mek6kh/alma9955933401001591 ProQuest Dissertations and Theses. Paid for by Imperial College so you'll need to be logged in or using a College computer.

Websites

- https://www.plos.org/ A nonprofit open-access science, technology, and medicine publisher with a library of open-access journals and other scientific literature published under an open-content license.
- http://www.nesta.org.uk/ Nesta is an independent charity that works to increase the innovation capacity of the UK and regularly publishes research papers. It looks at citizen engagement in public services, digital arts & media, future thinking, government innovation, health & aging, impact investment, innovation policy, new models for inclusive economic growth and opportunities for young people.

Health Information

- https://www.digital.nhs.uk/ provider of high-quality information, data and IT systems for health and social care. Catalogue contains the official statistical publications HSCIC produces about health and care in England. It also contains results from surveys, audits, reports and other statistics
- https://www.tripdatabase.com/ As well as research evidence, you can also search across other content types including images, videos, patient information leaflets, educational courses and news.
- http://cash.libraryservices.nhs.uk/database/ The Current Awareness Service for Health (CASH) is run by a team of library managers and information professionals with years of experience in delivering current awareness services.

- https://mednar.com/mednar/desktop/en/search.html U.S. based Mednar is a free, medically-focused deep web search engine. A search occurs in real-time, retrieving relevant medical information as if you were going to each individual website yourself.
- http://www.dc.nihr.ac.uk/ The Dissemination Centre critically appraises the latest health research from both within the NIHR and other research organisations to identify the most reliable, relevant and significant findings
- https://www.kingsfund.org.uk/ The King's Fund's Information and Knowledge Services provide a unique and free source of information on health and social care management and policy, systems, services and leadership; they do not cover clinical issues and treatments.
- http://www.nuffieldtrust.org.uk/ The Nuffield Trust is an independent health charity. They aim to improve the quality of health care in the UK by providing evidence-based research and policy analysis and informing and generating debate
- http://www.health.org.uk/ "We make links between the knowledge we gain from working with those delivering health and health care and our research and analysis."
- https://www.cadth.ca/grey-matters-practical-tool-searching-health-related-grey-literature-0 Grey Matters: Word Checklist to download. You can then go through the document checking off each link as you search it. It links to a number of grey literature resources and aims to be comprehensive when covering Canadian and international health technology assessment agencies.
- https://www.who.int/ World Health Organisation- the website includes its publications as well as health data & statistics.

Appendix Two:

How to adapt a search across different databases.

Once you are happy with your search strategy you will need to adapt it for other databases. You will need to search all the appropriate databases to ensure that you are finding all the information to answer your research question.

This section will first explain the wildcards and phrasing you can use across each database and will then show several searches for the same research question.

You will use the same keywords across each of the databases. However, sometimes you might have to phrase things slightly differently. Only the health databases use subject headings, so you won't be able to search for them in Web of Science or Scopus. The subject headings will change across the databases. Even if you are using the same database platform e.g. Ovid for both Medline and Embase then you will need to check what the different subject headings are for that particular database. Enter the keywords and see which relevant subject headings that database recommends. You may find it useful to also refer to Appendices Three and Four that offer more explanations of keywords and subject headings.

Cochrane

- use quotation marks to find phrases. E.g. "mobile phone" will only find those two words together in that order.
- Proximity Searching: Use Near/n to find those two words near each other. For example, return near/3 hospital will find those two words within up to three words of each other.
- ? represents a missing character e.g. wom?n will find women or woman.

Ebsco databases (including CINAHL)

- use quotation marks to find phrases. E.g. "mobile phone" will only find those two words together in that order.
- Proximity searching: Write liver N1 fail* to find those two words together in either order or with one word in between, write liver N2 fail* to find those two words together in either order or up to two words in between etc
- # can replace 0 or 1 character within a word e.g. wom#n will find women or woman. Behavio#r will find both behaviour and behavior.

Ovid databases (such as Embase.)

- automatically does phrase searching e.g. heart attack will only find those two words together in that order.
- Proximity Searching: Child* adj1 cancer* will find those two words together in either order (so could find childhood cancer or cancerous children.) Child* adj2 cancer* will find those two words together in either order and also those two words with another word in between (so could find childhood skin cancers, cancer in children, childhood cancer etc.) Child* adj3 cancer* will find those two words together in either order and also those two words with up to two other words in between etc.
- The databases won't suggest subject headings if you have used adj and may be confused by truncation for your keywords. So you might find it useful to search for a general phrase to get the correct subject headings and then add the truncation and proximity searching.
- ? can replace 0 or 1 character within a word e.g. wom?n will find women or woman. Behavio?r will find both behaviour and behavior.
- *n will add extra characters up to the number n e.g. leg*1 will find legs or lego but not legend.

PubMed.

- use quotation marks to find phrases. E.g. "mobile phone" will only find those two words together in that order.
- Proximity searching: Use N in the same way as you would in Cinahl.

Scopus.

- No subject headings.
- Double quotes " " will search for fuzzy phrases- It will search for both singular and plurals (with some exceptions) and wildcards can be used. "heart-attack" will search for heart-attack, heart attack, heart attacks, and so on

- Curly brackets { } will search for a specific phrase. It limits the search to only the specified character string, and symbols can be used. {heart attack} will only search for heart attack but not heart attacks or heart-attack.
- Proximity Searching: use W/ in the same way as you would use N in Cinahl.
- You can use the asterisk at the start and in the middle of words as well as at the end e.g. *medical will find biomedical as well as medical. And bio*engineering will find biochemicalengineering as well as bioengineering (as examples)
- ? represents a missing character e.g. wom?n will find women or woman. You can use it multiple times e.g. buckt??th will find bucktooth or buckteeth.
- Scopus automatically searches both US and UK spellings.

Web of Science.

- No subject headings.
- use quotation marks to find phrases. E.g. "mobile phone" will only find those two words together in that order.
- Proximity searching. Use Near/ in the same way as you would use N in Cinahl.
- You can use the asterisk at the start and in the middle of words as well as at the end e.g. *medical will find biomedical as well as medical. And bio*engineering will find biochemicalengineering as well as bioengineering (as examples)
- ? represents 1 missing character e.g. wom?n will find women or woman.
- # represents 0 missing character e.g. Behavio#r will find both behaviour and behavior.

Some examples of how a search for the question 'how does broken sleep affect the academic performance of medical students?' would be adapted for the other databases are:

Ovid Medline	Embase (Ovid)	Scopus
Exp Sleep Wake Disorders/	Exp sleep disorder/	1. TITLE-ABS-KEY depriv* w/1
2. Insomnia*.mp3. Depriv* adj2 sleep*.mp	2. Sleep deprivation/3. Depriv* adj2 sleep*.mp	sleep* 2. TITLE-ABS-KEY insomnia*
4. Fragment* adj2 sleep*.mp	4. Insomnia*.mp	3. TITLE-ABS-KEY fragment* w/1
5. Insufficient sleep.mp	5. Fragment* adj2 sleep*.mp	sleep
6. 1 or 2 or 3 or 4 or 5	6. Insufficient sleep.mp	4. TITLE-ABS-KEY (insufficient
7. Exp Educational Measurement/	7. 1 or 2 or 3 or 4 or 5 or 6	sleep}
8. Academic adj2 perform*.mp	8. Exp academic achievement/	5. 1 or 2 or 4 or 4
9. Success adj3 exam*.mp	Academic adj2 perform*.mp	

10. Academic adj3 achiev*.mp	10. Success adj3 exam*.mp	6. TITLE-ABS-KEY academic w/1
11. Education adj2 perform*.mp	11. Academic adj3 achiev*.mp	perform*
12.7 or 8 or 9 or 10 or 11	12. Education adj2 perform*.mp	7. TITLE-ABS-KEY success w/2
13. Students, Medical/	13.8 or 9 or 10 or 11 or 12	exam*
14. Medical student*.mp	14. Exp medical student/	8. TITLE-ABS-KEY academic w/2
15. Medic* undergraduate*.mp	15. Medical student*.mp	achiev*
16. Medicine adj2 student*.mp	16. Medic* undergraduate*.mp	9. TITLE-ABS-KEY education w/1
17.13 or 14 or 15 or 16	17. Medicine adj2 student*.mp	perform*
18.6 and 12 and 17	18.14 or 15 or 16 or 17	10.6 or 7 or 8 or 9
	19.7 and 13 and 19	11.TITLE-ABS-KEY "medical student"
		12.TITLE-ABS-KEY "medical
		undergraduate"
		13. TITLE-ABS-KEY medicine w/1
		student*
		14.11 or 12 or 13
		15.5 and 10 and 14

Appendix Three: Tips for using keywords.

Synonyms:

Think of all the possible words that can be used to describe your concept e.g. heart attacks can also be called cardiovascular strokes, myocardial infarctions and myocardial infarcts. Look at MeSH to see synonyms for the concept you are looking for. In PubMed these are listed in the 'used for' section of the page, in Ovid click on the 'scope' column of the MeSH. Check you have also considered possible plurals and abbreviations for these words.

Use wildcards:

• Using an asterisk * will tell the database that the word has been truncated and so it will search for any possible combination of letters that could be added to the stem. E.g. diabet* will find diabetes and diabetic.

• Using a question mark? tells the database that there could be an additional or a different letter in that word. This is very useful when searching for words that have different American to British spellings e.g. p?ediatrician will find paediatrician and pediatrician. Organi?ation will find organization and organisation.

Narrow/ broaden your search down by looking for words that are near each other.

- In PubMed: use quotation marks to find phrases. E.g. childhood cancer will only find those two words together in that order.
- In Ovid databases: Ovid automatically does phrase searching e.g. heart attack will only find those two words together in that order. It can be useful to use adjacency to find words that are near each other and so likely to be linked. Child* adj1 cancer* will find those two words together in either order (so could find childhood cancer or cancerous children.) Child* adj2 cancer* will find those two words together in either order and also those two words with another word in between (so could find childhood skin cancers, cancer in children, childhood cancer etc.) Child* adj3 cancer* will find those two words together in either order and also those two words with up to two other words in between etc.
- In Cinahl: Write liver N1 fail* to find those two words together in either order or with one word in between, write liver N2 fail* to find those two words together in either order or up to two words in between etc.
- In Scopus: Use curly brackets to search for a specific phrase. use W/ in the same way as you would use N in Cinahl
- In Web of Science: use Near/ in the same way as you would use N in Cinahl.

Focus the search by only looking for those words in certain places.

- In PubMed and Cinahl: click on the 'advanced' link under the search box. You can then choose from the drop down menu next to this search box which fields you would like to search. The most commonly used one is Title/ Abstract.
- In Ovid databases: the default search is .mp which stands for multipurpose. Limit the search by typing .ti,ab,kw. after the word to tell the database you only want to search for that word in the title, abstract or keyword sections. You can also use .ti,ab. to just search these fields [.tw does the same so you may sometimes see this in other people's search strategies.]
- In Scopus and Web of Science the drop down menu is next to the main search box so you can easily choose which fields you would like to search.

Appendix Four:

How to search for Subject Headings in different databases.

• In PubMed (Medline): scroll to the bottom of the homepage and choose 'MeSH' from the NCBI Literature Resources section. PubMed automatically explodes its terms. If you do not want it to do this then tick 'Do not include MeSH terms found below this term in the MeSH hierarchy' below the list of subheadings. To focus the search tick 'Restrict to MeSH Major Topic.' You can see the organisation of the tree towards the bottom of the page.

PubMed MeSH tutorial: https://www.nlm.nih.gov/bsd/disted/meshtutorial/introduction/

• In Ovid: only search one database at a time. This is because although all Ovid databases look the same they have slightly different trees. When you search a single database you have the option below the search box of 'match term to subject heading.' As you search for your keyword, Ovid will suggest which subject headings it thinks would be most appropriate. For each line you can click the 'scope' column to confirm the definition of the subject heading and see which other keywords have been linked with that heading. Click on the name of the subject heading to see where it is in the tree. Click in the 'explode' or 'focus' columns if you would like to do either of these.

When looking at other people's Ovid search strategies:

Diabetes Mellitus/ the subject heading of diabetes mellitus has been searched

Exp Diabetes Mellitus/ they exploded the subject heading of diabetes mellitus

*Diabetes Mellitus/ they focussed the subject heading of diabetes mellitus

Exp Diabetes Mellitus/hi [history] they exploded the subject headings of diabetes mellitus and chose the history subheading

- In Cinahl: the 'suggest subject terms' box above the search box should be ticked. Cinahl will then suggest possible subject headings. As you tick an option a column will open on the right so that you can choose a subheading if you would like. You can only tick the explode column if your subject heading has a plus sign (+) next to it as this is what indicates that there are narrower terms. If you want that subject heading to be the focus of the articles then tick the 'major concept' column. You may find this three minute video about using MeSH in Cinahl useful: https://vimeo.com/355572790
- Scopus and Web of Science do not have Subject Headings as they cover many different subject areas.

Appendix Five:

The filters below are to find RCTs within Medline and Embase and for human studies. You can see that while each filter is trying to identify the same types of articles they are different to take into account the different databases' search interfaces and indexing of subject headings and publication types. Make sure you use a filter that has been designed for each database you are using. Please get in touch with your librarian if you have any questions about finding, using, or adapting search filters.

Human Studies filter for Ovid Medline

- 1. [Final search strategy result]
- 2. exp animals/ not humans.sh
- 3. 1 not 2

Human Studies filter for Ovid Embase.

- 1. [Final search strategy result]
- 2. (exp animal/ or nonhuman/) not exp human/
- 3. 1 not 2

There are several filters that can be used for RCTs. The below are taken from SIGN's (Scottish Intercollegiate Guidelines Network) search filters webpage that also has details for other platforms as well as filters for different types of studies (48).

Filter for RCTs in Ovid Medline	Filter for RCTs in Ovid Embase	
1 Randomized Controlled Trials as Topic/	1 Clinical Trial/	
2 randomized controlled trial/	2 Randomized Controlled Trial/	
3 Random Allocation/	3 controlled clinical trial/	
4 Double Blind Method/	4 multicenter study/	
5 Single Blind Method/	5 Phase 3 clinical trial/	
6 clinical trial/	6 Phase 4 clinical trial/	
7 clinical trial, phase i.pt	7 exp RANDOMIZATION/	
8 clinical trial, phase ii.pt	8 Single Blind Procedure/	
9 clinical trial, phase iii.pt	9 Double Blind Procedure/	
10 clinical trial, phase iv.pt	10 Crossover Procedure/	
11 controlled clinical trial.pt	11 PLACEBO/	
12 randomized controlled trial.pt	12 randomi?ed controlled trial\$.tw.	
13 multicenter study.pt	13 rct.tw.	
14 clinical trial.pt	14 (random\$ adj2 allocat\$).tw.	
15 exp Clinical Trials as topic/	15 single blind\$.tw.	
16 or/1-15	16 double blind\$.tw.	
17 (clinical adj trial\$).tw	17 ((treble or triple) adj blind\$).tw.	
18 ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).tw	18 placebo\$.tw.	
19 PLACEBOS/	19 Prospective Study/	
20 placebo\$.tw	20 or/1-19	
21 randomly allocated.tw	21 Case Study/	
22 (allocated adj2 random\$).tw	22 case report.tw.	
23 or/17-22	23 abstract report/ or letter/	
24 16 or 23	24 Conference proceeding.pt.	
25 case report.tw	25 Conference abstract.pt.	
26 letter/	26 Editorial.pt.	
27 historical article/	27 Letter.pt.	
28 or/25-27	28 Note.pt.	
29 24 not 28	29 or/21-28	
	30 20 not 29	

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