Dissertation Module: Research Skills Program
Topic 2: Literature Review

The Literature Review – Introduction

Each properly conducted research project starts with a thorough and systematic literature review (Topic 1, Figure 2). It is important to conduct a comprehensive literature review at the beginning for a number of reasons:

- Scientific research needs to be seen in the context of similar studies and needs to be based on a sound theoretical framework. When you develop your research idea, you need to read up on the literature in order to understand the context of your research and the theory and thinking behind it.
- It is imperative to see whether identical or similar studies have been conducted previously, as the answer to your research question might already be known. If similar studies were previously conducted and problems were identified, it may be necessary for you to modify your methods or to rethink your question.
- If the literature review reveals an apparent lack of knowledge in the research area, you have justification to go ahead with your study. If very few studies have previously dealt with your research question and the answer is still largely unknown, then you have identified a knowledge gap that you can endeavour to fill.

Please appreciate the difference between the usual introductory section of a journal article or for example your initial one-page background brief and a systematic literature review. The former (two) allow the authors to choose from the available literature to make a point and guide the reader to the study or topic at hand; the latter is a systematic review of all literature investigating the research topic of interest. A systematic literature review aims to provide an exhaustive critical assessment of the available literature. Such a review should be conducted so that another independent researcher is able to reproduce the conclusions drawn. Sometimes, but not always, systematic reviews combine the quantitative results from the selected studies in so-called meta-analyses that apply special statistical techniques.

The Process of Conducting a Literature Review on 1 Page

- Develop a research question/hypothesis
  - Construct a searchable research question using PICOT
- Develop a search strategy
  - Identify key concepts of search
  - Translate key terms, where possible, into MeSH terms
  - Relate terms logically into search sets, as appropriate
  - Identify possible exclusion data (if needed)
  - Identify relevant limits (e.g. date, age, region, etc)
  - Utilise Boolean search in part or as whole, as needed
  - Write down your search strategy – step 1 - in a paragraph or as appropriate
- Conduct a literature search:
  - Identify suitable and accessible sources for searching:
    - Medical literature databases
    - Appropriate non-medical literature databases
    - Clinical evidence databases
    - Clinical evidence search engines
    - Grey literature
    - Specific relevant journals
    - Other sources
  - Vary search strategy to each database/source, as needed
  - Use MeSH or non-Mesh searching or a combination, as needed
  - Use filters (limits, evidence filters, etc) as required
  - Save and list searches and search strategies, by source
  - Write down your search strategy – step 2- in a paragraph or as appropriate
- Sort citations:
  - Exclude duplicates
  - Divide results into full-text and non-full-text
  - Exclude non-relevant papers (but say why)
  - Prioritise remaining papers (and say why)
  - Organise citations, using traditional citation rules via, if possible, citation manager application
  - Group remaining papers into meaningful sub-topics
  - Create a flow-chart which summarises the result of your literature search
- Read / critically review each paper:
  - Identify evidence type (where relevant)
  - Identify any bias or other factors that may undermine efficacy of paper
  - Extrapolate any statistics from paper relevant to search
  - Create tables (by identified sub-topics) including all articles in your review (cite first author, year, country, type of study, sample size, main results, and critical comments – as appropriate).
- Write up the literature review:
  - Summarise papers critically, quoting above sub-sections as needed
  - Synthesise evidence, if relevant, by type, source and conclusions
  - If required and appropriate conduct meta-analysis
  - Identify any gaps in evidence, where relevant
  - Identify, where relevant, how evidence informs practice
  - Write up your results of your literature review in form of a manuscript for publication
  - Create a presentation of the results of your literature review

Research questions for literature reviews

As stated in Topic 1: Systematic literature reviews require you to state a very specific, searchable research question. The principles behind the statement of a research question for a literature review (your first assignment) and a research project (your second assignment) are very similar; although the research hypothesis for a project will require a falsifiable statement (statement of the expected result) while the literature review does not.

The Cochrane Handbook for Systematic Reviews of Interventions (handbook.cochrane.org) explains in detail all the factors which require consideration when stating a searchable research question for a literature review (Higgins and Green, 2011). Although this handbook is for interventions studies only, many rules can be applied to reviews that include studies with other designs. Part 2, chapter 5 of the handbook outlines important eligibility criteria for studies to be selected, including: types of participants (population), types of interventions (if applicable), types of outcome measures, and the design of the studies. In chapter 5.6 the handbook also discusses advantages and disadvantages of a broad versus a narrow scope of review questions with instructive examples. Following these criteria will help you formulating a searchable research question.

As with operational research hypotheses, PICOT can be used for stating a research topic in a searchable manner, as it forces us to name the key elements of interest. Hence, phrasing a research question in PICOT format is a good start for a systematic literature review. More recently, the alternative SPIDER format was introduced for searching for qualitative and mixed-method literature (Cooke et al. 2012). SPIDER stands for Sample, Phenomenon of Interest, Design, Evaluation, and Research type, and was shown to identify a more manageable number of qualitative research articles when compared with the PICOT format (Cooke et al. 2012).

There is no point in starting a literature review if you have not yet decided on your searchable research question. That is, you need to have a clear idea of your research topic. The falsifiable operational research hypothesis for the project proposal might be shaped by the literature review.

So within your Dissertation the research topic which you have stated in your one-page proposal might be altered to a searchable research question for your systematic literature review. The results of the review should then inform the research question of your research proposal.

Practical tips on conducting a literature review

A review of the literature is the process of *collecting*, *classifying*, and *evaluating* what other researchers have previously written about the specific topic stated in the searchable research question. Three skills are necessary to conduct a literature review (based on Taylor 2008):

1. *Information seeking*: the ability to scan the literature efficiently and systematically using manual and computerised methods to identify a set of potentially useful articles, books, and websites.

2. *Critical appraisal*: the ability to apply principles of analysis and evaluation to identify those studies that are unbiased and valid.

3. *Writing*: the ability to write the literature review in a concise manner. Do use dictionary and grammar books when you read and write; in particular if English is your second language.

Information seeking - Where to look for literature?

Information relevant to research in the health sciences may be found in the medical, allied health, social, educational, anthropological, and psychological sciences. You might need to search through journals, books, and government documents at the library. However, these days most journals are available online. Fortunately, with the internet, literature searches have become much easier and quicker as there are a number of major databases available, virtually at neutral cost. One of the biggest databases of medical literature in the broadest sense is MEDLINE. MEDLINE is a service of the United States National Library of Medicine and the National Institutes of Health and is searchable by using PubMed. MEDLINE is the United States National Library of Medicine's bibliographic database and includes journals on medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the preclinical sciences. In July 2014, PubMed covered over 24 million citations for the biomedical literature. However, PubMed is not the single sufficient search basis. You may not find papers that were published in the last three months. Also, some topics may require conducting a search with specialised databases.

Another large database is CINAHL (Cumulative Index to Nursing and Allied Health Literature), which focuses on nursing and allied health literature, including full-text versions of more than 70 journals. CINAHL online covers the nursing and allied health literature from 1981 to the present. Current Contents Search is the online version of *Current Contents* publications. It reproduces the tables of contents for current issues of thousands of journals in the sciences, social sciences, and arts and humanities. Current Contents is a database from the Institute for Scientific Information, which is part of Thomson Reuters Web of Knowledge. There are numerous other bibliographic databases, such as EMBASE and PsycINFO, which can help identify published literature in the health sciences. Some websites, such as www.doaj.org and http://highwire.stanford.edu/lists/freeart.dtl, have specialised in open access journals and freely available online full-text articles. Finally, you should also consider using Google and Google Scholar, although these should not be your

sole sources. The strength of Google and Google Scholar is that they also cover grey literature.

One of the most influential databases, which has been developing during the last two decades, is the Cochrane Collaboration's Cochrane library. The *Cochrane Collaboration* is an international, independent, not-for-profit organisation of almost 27 000 contributors from more than 120 countries. The collaboration was established in 1993 and is named after Archie Cochrane (1909–88), a British epidemiologist and energetic promoter of using randomised controlled trials for assessing healthcare interventions. Contributors to the Cochrane Collaboration work together in teams on one specific topic of their interest to produce a systematic assessment of healthcare interventions. The Cochrane Collaboration publishes systematic literature reviews that are very influential because they are at the top of the hierarchy of available evidence in the health sciences. The reviews are available online. In addition, the Cochrane Collaboration has also been developing a register of reports of controlled trials called CENTRAL. CENTRAL is freely available through the Cochrane Library (www.thecochranelibrary.com).

In addition there a numerous regional electronic bibliographic databases, for example, the African Index Medicus (indexmedicus.afro.who.int), IndMed (indmed.nic.in), LILACS for latin America and the Caribbean, and IMSEAR for south-east Asia. There are subject-specific databases such as TRIP which stands for Turning Research into Practice which focuses on evidence-based healthcare (tripdatabase.com). In addition there are databases for dissertations and theses as well as for grey literature. You may also want to see whether you are eligible to use the HINARI. Then you may be waived for the charge to access some papers. An exhaustive list of databases available is presented in the Cochrane Handbook (handbook.cochrane.org)(Higgins and Green, 2011), part 2, chapter 6. Which sources of literature are most relevant to a specific literature review is entirely dependent on the research question. So please choose the databases which you will search carefully.

After stating a searchable research question, the first main step in a literature review is finding all the previous articles, books, and other information that are relevant for your literature review, using the sources mentioned above.

You might start searching the available databases online or visit libraries to check books and hard copies of journals. Always use several databases, so to be sure that you have identified all relevant articles. Naturally, there will be doubling up between different databases which will need to be checked in the next step of the selection process. Certain citation managers can help in filtering out duplicated papers. It is also important to check the references of already selected manuscripts, as they inevitably refer to previous work in the same area. This kind of *snowballing* search is important but sometimes difficult to control. We note this because, as with everything else in research, literature reviews should be reproducible.

Designing a search strategy

The eligibility criteria for studies, or in other words the searchable research question, will inform the search strategy. The eligibility criteria should specify the types of study designs, types of participants, types of interventions (if applicable), and types of outcomes. Further

criteria might include geographic (e.g. Chinese literature for Chinese herbal medicine studies), language, or time period limitations. These latter limitations need to be carefully justified.

Searches for systematic reviews aim to be extensive as they aim for including all relevant studies. Hence you might end up with a large number of studies initially. If there seems to be masses of literature relevant to your research, you should carefully rethink your search strategy. You might be searching too broadly and you may need to refine your search by adding more search terms.

MEDLINE and EMBASE and many other databases can be searched using standardised subject terms which were assigned by indexers. In MEDLINE these standardised subject terms are called MeSH, in EMBASE they are called EMTREE. These standardised subject terms are useful as they help to find articles which may use different words for describing the same set of circumstances. Please check this out for the databases you use for your search. In MEDLINE, try using key words from the list of Medical Subject Headings (MeSH) <www.nlm.ncbi.nih.gov/mesh>. MeSH is maintained by the United States National Library of Medicine and contains more than 27 000 subject headings organised in 16 categories that form treelike structures. The more narrowly you can define your research question, the more easily you will be able to select the relevant sections of the available literature. An example of a first literature search is given in Box 1.

To learn more about MeSH terms and how to use them effectively, go to the PubMed website and check out their online training using animated tutorials at: www.ncbi.nlm.nih.gov/mesh.

Box 1 Example of a first search for literature

Assume you would like to conduct a literature review on nutritional aspects in refugee populations, with a particular focus on women's health.

If you enter 'refugee' as a search term into the PubMed search engine, more than 9451 hits appear. It is obviously impossible to deal with this number of publications in any meaningful way. By adding 'nutrition' to your search, more than 434 articles are selected. This seems more feasible and might be a starting point for actually reading abstracts for further selection of the manuscripts that are really relevant to your topic.

Boolean operators: AND and OR

In Box 1 the search terms "refugee" and "nutrition" were combined using the logic operator AND which implies that only records are identified which relate to both "refugee" and "nutrition" simultaneously. If we had instead used the Boolean operator OR we have at least 338,424 hits because this search will retrieve all articles related to "refugees", or to "nutrition", or to both.

You should use Boolean operators to define your search strategy. The Cochrane Handbook (part 2, chapter 6) shows some examples of search strategies using Boolean operators in Boxes 6.4.e and f.

Managing articles and references

The results of a literature review can be rather overwhelming, especially if the planned study is in a well-researched area. Therefore, it is advisable to do the following:

- Sort the material by subtopics. For example, in Box 1 the researcher was interested in nutrition in refugee camps. If the focus is women's health, then subtopics might include children/teenagers/women of childbearing age/older adults. If the focus is on the experience in different countries, then subtopics might include Asia/Africa/South America. This obviously depends on the aims of the search, as stated in the research question.
- Write comprehensive abstracts of the literature identified as you read to prevent the need for frequent re-reading.
- Keep an up-to-date list of the literature you have identified. Many researchers use reference manager software, such as EndNote or Reference Manager, to help keep track of the literature. This approach is highly recommended.

However, if you cannot find much literature at all about your research topic, and you are sure that you have explored all avenues, then there are a few possible explanations:

- You could be at the cutting edge of something new in your discipline and it is not surprising that there is little information available.
- Your search could be too narrow and you may not have accessed relevant literature in a closely related field. You may use other keywords to perform another search or the relevant bibliographic databases are yet to be found.
- There is nothing in the literature because it is not a worthwhile area of research. It is important to consider this option carefully.

Documenting the search process

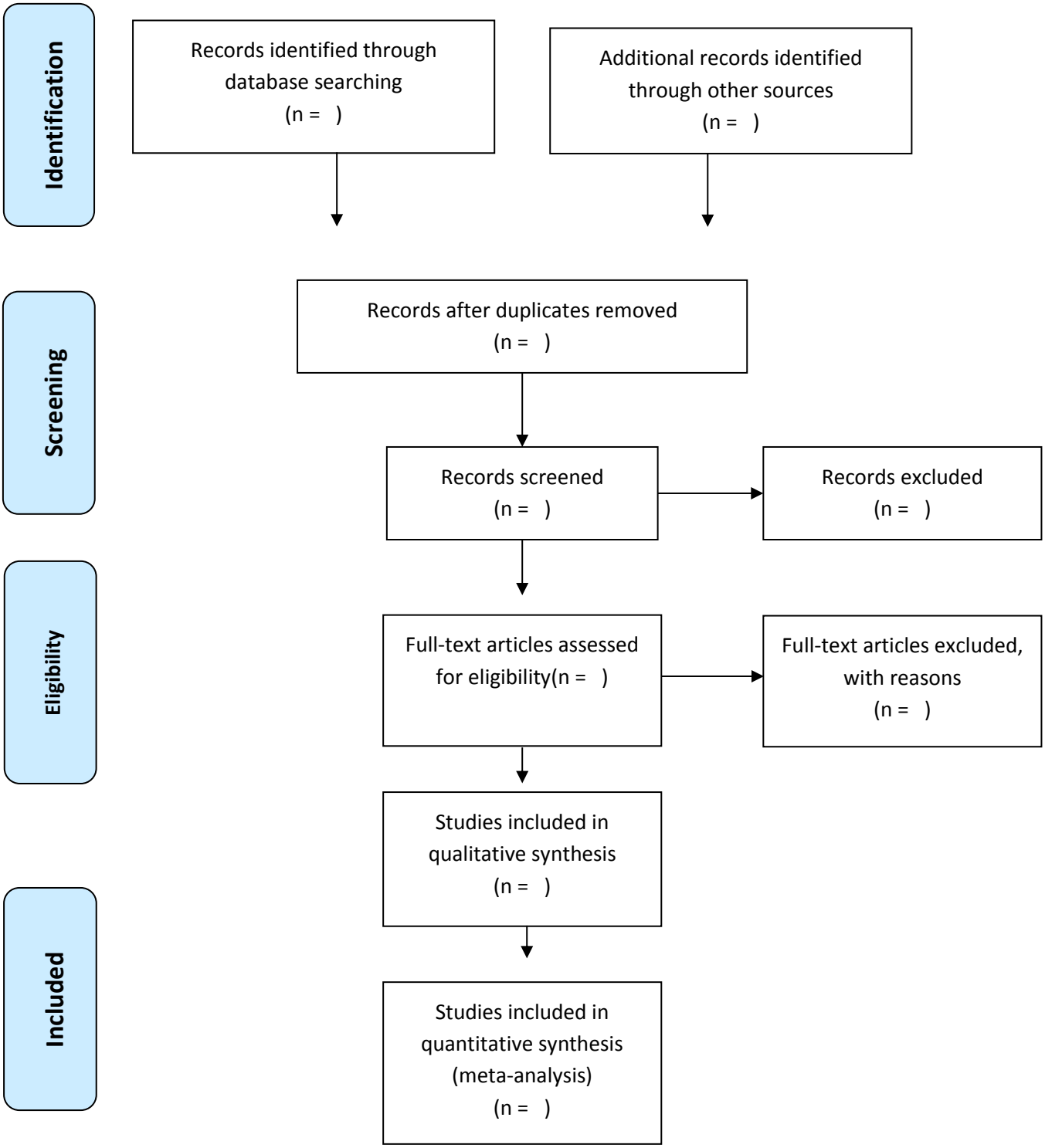
The search process needs to be documented in enough detail throughout the process to ensure that it can be reported correctly in the review, so that all searches from all databases used are reproducible by other researchers.

When conducting searches for a literature review, you need to keep a written record of how, when, and where you searched and what search terms you used. This record is called the **search protocol** and documents your search for future reference. In this sense, your literature review should be systematic. The search protocol should be sufficiently detailed so that if somebody else repeated the literature search using your protocol, the result would be very similar.

Researchers who conduct literature reviews today will often follow the PRISMA statement (Moher et al. 2009). PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. PRISMA asks researchers writing a literature review to prepare a flow chart of the search process (Figure 1). In order to be able to create such a flow chart one needs to know the number of unique records identified by each search; the number of

records excluded after preliminary screening of titles and abstracts; and the number of records retrieved in full text. Reasons for the exclusion of full text articles should be provided.

Figure 1: PRISMA flow diagram (Moher et al. 2009)



Critical appraisal

The next major step in your literature review is a *critical appraisal* of the literature you have identified. Your readers will need more than just a descriptive list of articles and books. Unfortunately, not all published literature is of high quality and it is often left to readers to make up their own minds.

To critically appraise a manuscript one should consider the various *perspectives* that potentially influenced the choice of methodology, as well as the results and conclusions. Although 'unbiased' scientific research is valued, the truth is that nobody is entirely free from outside influences.

A journal article rarely presents a systematic overview of the available literature, but rather a selected collection of articles that the authors can carefully pick to suit their reasoning.

The essential component of critically appraising the published literature is to analyse the literature you have identified in a judgmental manner. Box 2 lists questions that you should ask when reading the literature.

Box 2 Questions to ask when critically appraising literature for a literature review

1 Did the authors clearly formulate a research question?

2 Was the relevance of the research question discussed?

3 What was the authors' research perspective? Is this perspective similar to your framework?

4 Did the authors evaluate the most important literature relevant to the research question?

5 Was an appropriate study design chosen to address the research question?

6 How good was the design of the study? This includes judging the study design in the overall hierarchy of evidence and deciding how well the particular study was conducted. Was the sample size adequate? Was the statistical analysis adequate? Were design features applied to minimise bias? What potential bias occurred and how was it managed and discussed? Were the conclusions based on the results of the study?

7 How did the authors structure their argument? Could this argument be deconstructed?

8 Does this literature contribute to my understanding of the problem being studied? What were the strengths and limitations of the study?

9 How does this piece of literature fit into my research?

Source: Based on Taylor 2008

The Hierarchy of Evidence

Traditionally, the different study designs are ordered with respect to how valid and reliable their results are considered. This is, of course, assuming that a particular study was conducted without flaws. The hierarchy of evidence is therefore important when critically appraising articles. As we will introduce and discuss the strengths and weaknesses of the different study designs later in this skills program, it is difficult for you to fully appreciate the *hierarchy of evidence* at this point in your studies. However, when you conduct a literature review, it is important to be aware that different study designs provide different weights of evidence. Several researchers have developed hierarchies of evidence for research studies. See, for example, the Oxford Centre for Evidence-Based Medicine's (2009) levels of evidence for clinical studies, which are available online as a Microsoft Word document. In Table 1 we present a hierarchy for research studies in the health sciences.

A word of caution is needed here. It is extremely difficult to state a generally valid hierarchy of evidence across all the different study designs without taking the specifics of the research question into account. Bear in mind that many questions cannot be addressed by randomised controlled trials and, therefore, require designs that are considered of lesser 'quality'. For example, if you wish to identify risk factors for a disease, such as smoking as a risk factor for coronary artery disease, then a randomised controlled trial cannot be conducted because it would be unethical to randomise people into smokers and non-smokers. Moreover, when studying a rare disease or outcome, your limited resources might be better spent on an 'inferior' design with appropriate sample size than on an underpowered trial with an insufficient number of events. The best study design is useless if the conduct of the study is flawed. Table 1 is one possible "hierarchy of evidence". Other hierarchies have been developed which try including the type of research question. For example, see the following website from the Oxford Centre for Evidence-based Medicine: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/ which provides a hierarchy of evidence of study designs stratified by research topic including treatment, diagnosis, and prognosis.

Table 1: Hierarchy of evidence

Weight of evidence	Study design	Information
Excellent	Systematic review and meta-analysis of randomised controlled trials (RCTs)	Summary information based on several studies; filtered information
Very good	Randomised controlled trial	Single study; unfiltered information
Good	Non-randomised experimental studies: Before and after studies Quasi-experimental	Single study; unfiltered information

Weight of evidence	Study design	Information
	studies	
Moderate	Cohort study Case–control study Cross-sectional study Descriptive studies	Single study; unfiltered information
Poor	Case reports and case series Expert opinion Personal communication	Single study; unfiltered information

Source: Based on Evans 2003; Guyatt et al. 1995

As you can see from Table 1, the Cochrane Collaboration is aiming to achieve the highest level of available evidence with systematic reviews of randomised controlled trials. As already noted above, in a systematic review, *all* available information is used, including all published and, if possible, all unpublished studies. The information of each study, including authors, year published, sample size(s), and study design and participants characteristics, are painstakingly listed in tables. Sometimes, but not always, a meta-analysis is performed. A *meta-analysis* is the use of statistical tools to summarise the results of several studies to reach an overall conclusion about all available evidence. Thus systematic reviews are comprehensive reviews of all the available information on a specific topic.

The Cochrane Collaboration's open learning material website provides a step-by-step approach on how to conduct systematic reviews and meta-analyses. However, be aware that the quality of a systematic review is naturally based on the quality of the original studies summarised. If a systematic review is based on well-conducted randomised controlled trials, then the conclusions of the review will provide excellent evidence. However, if a systematic review is based on studies that rank lower in the hierarchy of evidence or if substantial bias is identified, then, the conclusions from the review will have to be considered cautiously.

How to Read a Scientific Publication

There have been numerous tools developed to help us read and critically appraise the scientific literature. In the early 1990s David L. Sackett and his evidence-based medicine working group started the ball rolling with a series of publications called "The users' guide to medical literature" in the Journal of the American Medical Association (Oxman, A.D., et al., 1993; Guyatt, G.H., 1993; Guyatt, G.H., 1994). Sackett and his colleagues brought "evidence-based" medicine into the limelight and nowadays evidence-based practice is a cornerstone of all disciplines of the health sciences.

Of the books on evidence-based practice we can certainly commend Trisha Greenhalgh's book "How to read a paper" (2006) but would especially like to draw your attention to the Critical Appraisal Skills Programme (CASP) which developed a series of appraisal tools for different study designs. CASP is the brainchild of the UK based Solutions for Public Health, a non-profit NHS public health organisation. CASP tools are now available for randomised

controlled trials, cohort studies, case-control studies, qualitative research, systematic reviews, economic evaluation studies, and diagnostic test studies (see example for randomised controlled trials in Appendix). Each tool typically provides a list of about 10 to 12 questions which are relevant when reading a publication of the specified study type. The Cochrane Handbook, part 2, chapter 8, provides another support tool on how to critically assess the selected papers.

There are numerous other tools available to help with critical appraisal of the literature, the most notable being for experimental studies, such as the PEDro scale. This scale is widely used by physiotherapists and based on the Delphi list of criteria for the quality of RCTs published by Verhagen and colleagues in 1998. PEDro is available online at: http://www.pedro.org.au/wp-content/uploads/PEDro_scale.pdf. Also in 1998, Downs and Black suggested a 27 item appraisal tool intended for both randomised and non-randomised trials.

Please note: Critically appraising a publication is the only way to assess the evidence provided by the manuscript. However, finding things that are wrongs in a published article does not necessarily imply that the study was superfluous or that the authors are "bad" scientists.
No research study is ever perfect!
Always remember that the overwhelming majority of researchers are trying to conduct their studies in the very best way possible but are limited by resource availability and often by unforeseeable problems and complexities involved in conducting research.

Writing

Finally, we provide some tips on the style of writing that is appropriate for a literature review. In contrast to the introduction or discussion sections of a journal article, a literature review should include *all* relevant and appropriate information identified by the search. As a consequence, the writing style of a literature review also differs slightly. While the introduction and discussion sections of manuscripts tend to be more journalistic, literature reviews are written more like results sections. They present the identified literature—preferably in tables—and summarise the major findings in a strictly factual manner.

The literature review should be organised according to a guiding concept. For example, in Box 1 we introduced a search for refugee and nutrition and later stated that subtopics might be women's health or experiences in different countries. If the intention is to conduct a literature review on the nutritional needs of displaced people with a focus on women's health, one would most likely sort the literature according to life-span categories: infants/children/teenagers/women of childbearing age/older women/men. The identified literature should be sorted and collated within the identified categories.

Tabulation is a helpful tool to gain an overview of the published literature. While you read the manuscripts, extract any important information from the text and put it into a table. Summary of finding tables are suggested by the Cochrane Handbook (part 2, chapter 11) and this approach is also very similar to the matrix method for literature reviews suggested by Garrard (2007). Table 2 provides an example of tabulating a literature review.

Table 2: Example of two entries from a table created for a literature review on nutritional women's health in refugee situations.

First author and year	Country	Study question	Study design	Sample size	Main finding	Critical comments
Jayatissa, R. 2006	Sri Lankan camps after tsunami	Nutritional status of children and pregnant women	Cross-sectional, cluster sampling	Children: 878 Pregnant women: 168	Children: 35% underweight 20% stunted 16% wasted Pregnant women: 37% underweight	Well designed
Rossi, L. 2005	Armenia	Nutritional status of children and mothers	Cross-sectional, cluster sampling	Children: 3390 Mothers: 2649	Children: 12% stunted, 4% wasted Mothers: 4% underweight 33% overweight	Well designed; large study

Summary tables such as Table 2 may become quite extensive but should be included in every literature review. This forces the authors of the literature review to be disciplined in their approach and shows the reader which studies were considered in the review.

The objective of a literature review is not just to list all relevant articles but to demonstrate the intellectual ability to recognise relevant information, and to organise, synthesise, and evaluate it according to the guiding concept. The reader of a literature review not only wants to know what literature exists, but also, and more importantly, requires informed evaluation of the literature. You can use Table 1 to make an initial assessment of the level of evidence provided by the articles but then you need to further critically appraise every article selected using for example, CASP.

It is usually a bad sign if every paragraph of a literature review begins with the names of authors followed by a list of their research findings. In addition, please do not discuss the literature like row 1 of the summary table is this and row 2 is that. Instead, you are expected to organise your review into useful, informative sections that present themes or identify trends that relate to the research questions that interest you. You might:

- evaluate and synthesise results into a summary of what is and is not known
- identify controversy if it is apparent in the literature
- develop questions for further research—for your own research.

Remember that a literature review will ideally guide the reader to your research topic. For example, if you are a PhD student and you can identify gaps in the current literature and show that your own proposed research questions would fill some of these gaps, then you have at least, in part, convinced the reader of the significance of your own research project.

Researchers who conduct literature reviews today will often follow the PRISMA statement when writing up their results (Moher et al. 2009). PRISMA suggests to first create a flow-chart of selected articles (Figure 1 above). It includes further a 27-item checklist that spells out all the details required for writing up the literature review (Table 3). When writing up a literature review you are required to outline detailed information on these 27 items (e.g. about the sources of information searched and the search strategies used) so that another independent person could repeat the search and find the same publications. Please consider Table 3 when writing your literature review assignment.

Table 3: PRISMA checklist for reporting a systematic literature review (Moher et al 2009).

SECTION/TOPIC	#	CHECKLIST ITEM
TITLE		
Title	**1**	Identify the report as a systematic review, meta-analysis, or both.
ABSTRACT		
Structured summary	**2**	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
INTRODUCTION		
Rationale	**3**	Describe the rationale for the review in the context of what is already known.
Objectives	**4**	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOT).
METHODS		
Protocol and registration	**5**	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
Eligibility criteria	**6**	Specify study characteristics (e.g., PICOT, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	**7**	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	**8**	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	**9**	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
Data collection process	**10**	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	**11**	List and define all variables for which data were sought (e.g., PICOT, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	**12**	Describe methods used for assessing risk of bias of individual studies (including specification of whether this

		was done at the study or outcome level), and how this information is to be used in any data synthesis.
Summary measures	**13**	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	**14**	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I_2) for each meta-analysis.
Risk of bias across studies	**15**	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	**16**	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
RESULTS		
Study selection	**17**	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram (Figure 1 below).
Study characteristics	**18**	For each study, present characteristics for which data were extracted (e.g., study size, PICOT, follow-up period) and provide the citations.
Risk of bias within studies	**19**	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
Results of individual studies	**20**	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	**21**	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	**22**	Present results of any assessment of risk of bias across studies (see Item 15).
Additional analysis	**23**	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
DISCUSSION		
Summary of evidence	**24**	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
Limitations	**25**	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	**26**	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
FUNDING		
Funding	**27**	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

Systematic literature reviews can be registered. If you are working within the Cochrane Collaboration, your systematic literature review is registered with Cochrane and your review protocol is published, protecting your topic while the review is being conducted. You can also register your review with PROSPERO, an international database of prospectively registered systematic reviews, hosted by the University of York's Centre for Reviews and Dissemination (University of York and National Institute for Health Research 2013).

Registration of reviews and prospective publication of review protocols is an important tool for increasing transparency of the review process and reducing publication bias.

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