Introduction to systematic reviews

Geoff Bates

Angelina Brotherhood

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CPH | CENTRE FOR PUBLIC HEALTH

LIVERPOOL JOHN MOORES UNIVERSITY

Plan for today

Time	Activity
09.30	Session One
10.40	Morning coffee break
11.00	Session Two
12.00	Lunch break
12.40	Session Three
14.10	Afternoon coffee break
14.30	Session Four
16.00	**Close**

Plan for today

Part 1: Introduction to systematic reviews

What is the purpose of systematic review and what are its main characteristics?

How does it differ from a traditional literature review and what are the advantages (and disadvantages) of doing one?

Part 2: Undertaking a systematic review – key processes

What are the main steps involved with doing a systematic review?

How can these be carried out efficiently and effectively?

Part 3: Practical challenges of systematic reviews

What are the characteristics of reviews of qualitative evidence?

What constitutes a 'good quality' review, and what information should it contain?

What are the challenges associated with doing a review of reviews?

Introductions

Contact me

Geoff Bates

Researcher in Public Health Research Synthesis

Centre for Public Health, Liverpool John Moores University, Liverpool, L3 2ET, UK

Email: g.bates@ljmu.ac.uk

Tel: +44 (0)151 231 4442

Part 1

Introduction to systematic reviews

What is a systematic review?

A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review

Cochrane Handbook for Systematic Reviews of Interventions

http://uk.cochrane.org/

Systematic reviews: a (very) brief history

- Meta-analysis is derived from the work of Glass and Smith in the late 1970s
- Initially, systematic research synthesis was adopted by medicine and health
  - First Cochrane Centre in Oxford was formed in the early 1990s with NHS funding
  - The Cochrane Collaboration has grown to become an international network of researchers undertaking systematic reviews of the effects of health care interventions
  - Encouraged by developments in computers and the internet

Systematic reviews: a (very) brief history

- Misconception that systematic reviews are of relevance only to medicine
- The Campbell Collaboration, established in the late 1990s, adapted Cochrane methodology to address broader public policy issues including social, health educational and criminological interventions
- Recently, review methodology has been adapted to include qualitative evidence

What are they used for?

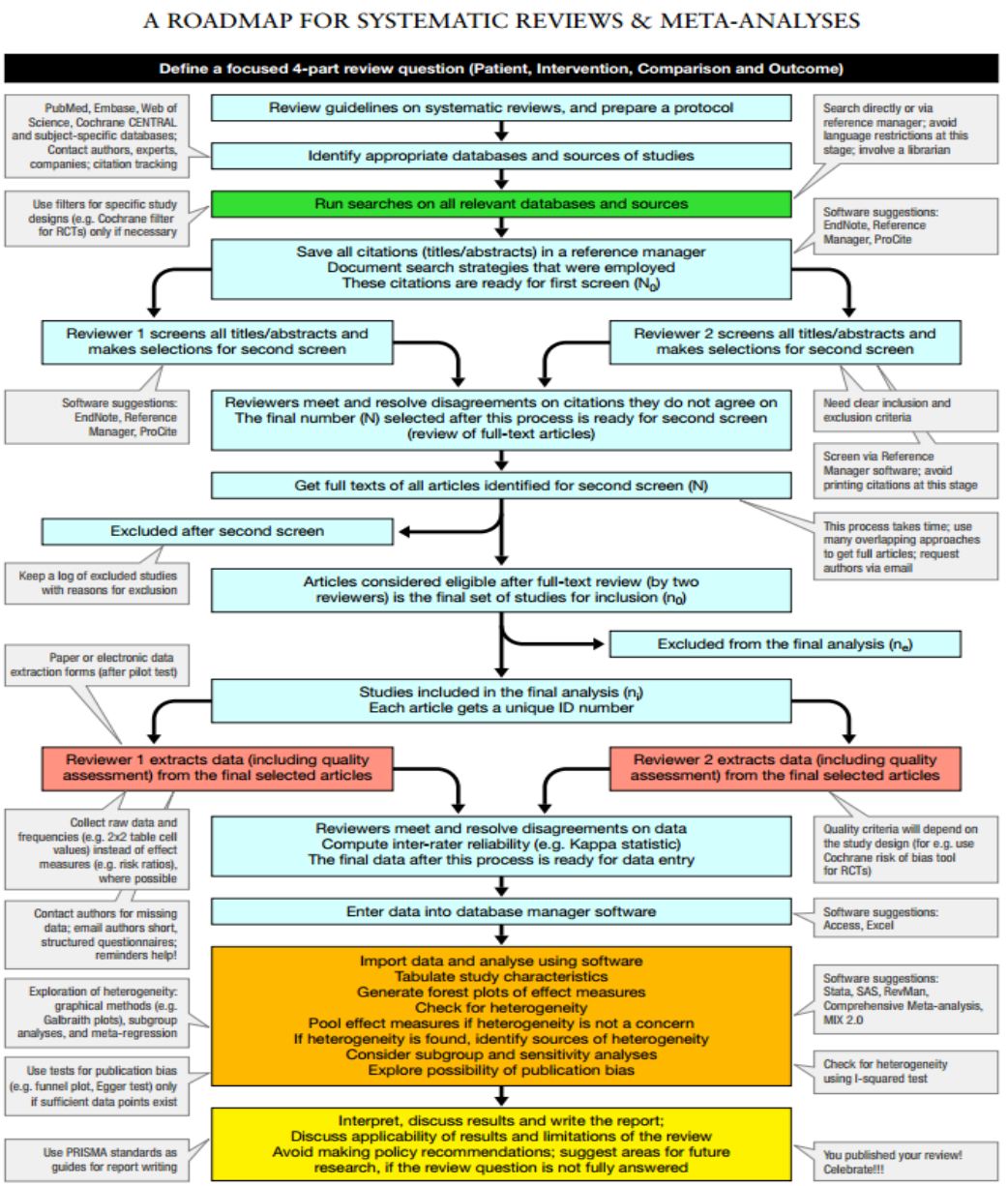
An estimated 2 million articles are published every year – how do you keep up with primary evidence?

Increased emphasis on evidence based policy and decision making

SRs are useful for:

- Examining the effectiveness of interventions
- Examining the association between a condition and outcomes
- Examining the prevalence of a disease or outcome

How do you do one?



Types of reviews

- Generally evidence reviews can be grouped into two categories: traditional literature reviews (narrative reviews) and systematic reviews

- The aims of the ‘traditional’ literature review and a systematic review are broadly the same

i.e. to identify and synthesise evidence to answer a research question

Literature reviews

Characteristics	Uses	Biases
Describes and appraises work but does not describe methods by which studies were identified and evaluated	Overviews, discussions, critiques of	

In what ways are literature reviews susceptible to bias?

I.e. why can we not always trust the findings and conclusions in a lit review?

What are the likely causes of these?

Adapted from Background to Systematic Reviews (Cochrane Collaboration)

Potential bias in literature reviews

- Is the evidence presented in literature reviews representative of all the available evidence?
- Can we be confident that the conclusions the author comes to truly represent the evidence discussed?
- How reliable therefore are the findings and conclusions?

Literature & systematic reviews: differences?

- A systematic review should identify all available research to answer the research question while more traditional literature reviews are likely to have gaps
- Two full systematic reviews on the same well defined research question should produce somewhat similar findings & conclusions
- Two narrative literature reviews however may have very different findings & conclusions

Systematic reviews - characteristics

Reduces bias associated with literature reviews:

Aims to identify ALL the evidence needed to answer a research question using systematic literature searching

- - Reports and justifies the methodology and decision making processes
- - Follows clear and consistent pre-determined criteria when selecting studies
- - Uses consistent methods to examine data and critically analyse studies

Systematic reviews - advantages

All decisions are explained and justified. The reader understands how the review has been conducted and why decisions have been made.

- SRs provide an unbiased summary of findings from a much larger body of evidence than literature reviews
- You can be confident that all (or most) relevant evidence has been included in a SR.
- Replicability – follow the methods
- Useful for identifying gaps in research

Systematic reviews – limitations/ disadvantages

Results can still be inconclusive

Studies included in a SR can still be of low quality

Time consuming process

Not all SRs are of good quality!

Typical systematic review research questions

- Questions about the effects of interventions

What is the impact of providing brief advice on managing stress to the mental wellbeing of postgraduate students?

- Questions about the associations between different conditions, theories or outcomes

What is the association between exercise and weight loss?

- Questions about the effectiveness of theories at predicting outcomes

How effective is the theory of planned behaviour at predicting behaviour change?

Part 2

Undertaking a systematic review – key processes

Typical steps in a systematic review

1. Develop your review question
2. Develop inclusion and exclusion criteria
3. Identify databases and other sources to search for studies.
4. Develop your search terms and build a search strategy to search within your chosen databases.
5. Screen firstly the titles and abstracts of your search results and then full text papers (against your inclusion criteria) to identify papers to be included in your review.
6. Collect relevant data from your included papers into tables
7. Assess the methodological quality of your included papers using a suitable measure of quality assessment.
8. The write up: synthesise the outcomes of your included papers (and undertake meta-analysis if appropriate).
9. Draw conclusions and/or recommendations based up findings.

A review example

In 2013 we were asked to undertake a review to identify the effectiveness of needle and syringe programmes for reducing negative health outcomes in people who inject image and performance enhancing drugs (IPEDs)

A very brief bit of background

- IPED users believed to be attending UK needle exchanges in increasing numbers (>2000% increase since 1990)
- People who inject anabolic steroids and other IPEDs are at risk of harms associated with sharing needles and injecting equipment e.g. hepatitis B & C, HIV
- Needle sharing amongst IPED users estimated at 10-40%
- IPEDusers are more likely to have multiple sexual partners than the general population and condom use is infrequent

As reviewers we were interested in what interventions in needle exchange settings have been demonstrated to improve health outcomes for this population.

1. Develop a research question

The research question should reflect the aims and objectives of your review

- It will help guide the whole review
- Developing a clear and well-structured question should be the first step in doing any review and will help ensure your review is focussed and efficient
- It should inform the reader on the nature and extent of the review

PICOS framework

- Used to inform the development of research questions
- Can help shape a research question and ensure that you consider exactly what you want the focus and scope of a review to be

PICOS:

Population: What population are you going to focus on?

Intervention: What is the intervention you are interested? (or: Setting, Theory etc)

Comparison: Is there anything you want to compare your interventions to?

Outcomes: Are you interested in any particular outcomes?

Study Design: Do you want to review any particular study types (e.g. RCTs)?

PICOS framework – IPED review

PICOS:

Population: people who use performance enhancing drug

Intervention: set within needle exchanges

Comparison: none

Outcomes: BBV testing uptake, BBV diagnosis, needle sharing

Study Design: controlled studies

PICOS framework – IPED review

PICOS:

Population: people who use performance enhancing drug

Intervention: set within needle exchanges

Comparison: none

Outcomes: Health outcomes, risky injection behaviours, risky sexual behaviours

Study Design: controlled studies

Question based upon PICOS

What interventions delivered in needle exchange settings are effective for reducing risky behaviours and adverse health outcomes amongst people who inject performance enhancing drugs?

Group activity: Coming up with a review question

Refer to activity sheet #1: Coming up with a review question

In your groups try and come up with some potential review questions based on the information given to you on the handout.

2. Developing inclusion and exclusion criteria

What are your criteria for including (and excluding) papers for your review?

- Should be appropriate to the research question being posed
- Helps you to decide what studies to search for, and how you are going to decide which studies to include in your review.
- Helps keep the review focused and manageable
- Should be appointed before the review starts, although may be tweaked later
- Inclusion criteria should be clearly stated in your write up: the reader should be able to understand why you have and have not included studies

Inclusion criteria: You can use PICO to help you

What interventions delivered in needle exchange settings are effective for reducing risky behaviours and adverse health outcomes amongst people who inject performance enhancing drugs?

PICO	Inclusion criteria
Population: who?	Studies that include individuals who inject performance and image enhancing drugs (steroids, melanotan, botox, human growth hormone)
Intervention: how/ where/ what?	Studies set within any service offering needle exchange e.g. drug treatment services, pharmacies, outreach services, mobile services
Outcome: what is being measured/ improved/ accomplished?	Studies that include outcomes relating to risky injection behaviours (e.g. needle sharing, needle re-use) or prevalence of blood borne viruses

Is there anything you want to exclude?

What interventions delivered in needle exchange settings are effective for reducing risky behaviours and adverse health outcomes amongst people who inject performance enhancing drugs?

PICO	Inclusion criteria
Population: who?	Anyone under 18 years of age
Intervention: how/ where/ what?	Shooting galleries/ safer injection facilities
Outcome: what is being measured/ improved/ accomplished?	Non-behavioural outcomes e.g. changes in attitudes, knowledge or intentions

Group activity: developing inclusion and exclusion criteria

Refer to activity sheet #2

In your groups, develop some inclusion and exclusion criteria for the review question:
“What interventions are effective at preventing problem gambling behaviours amongst university students”

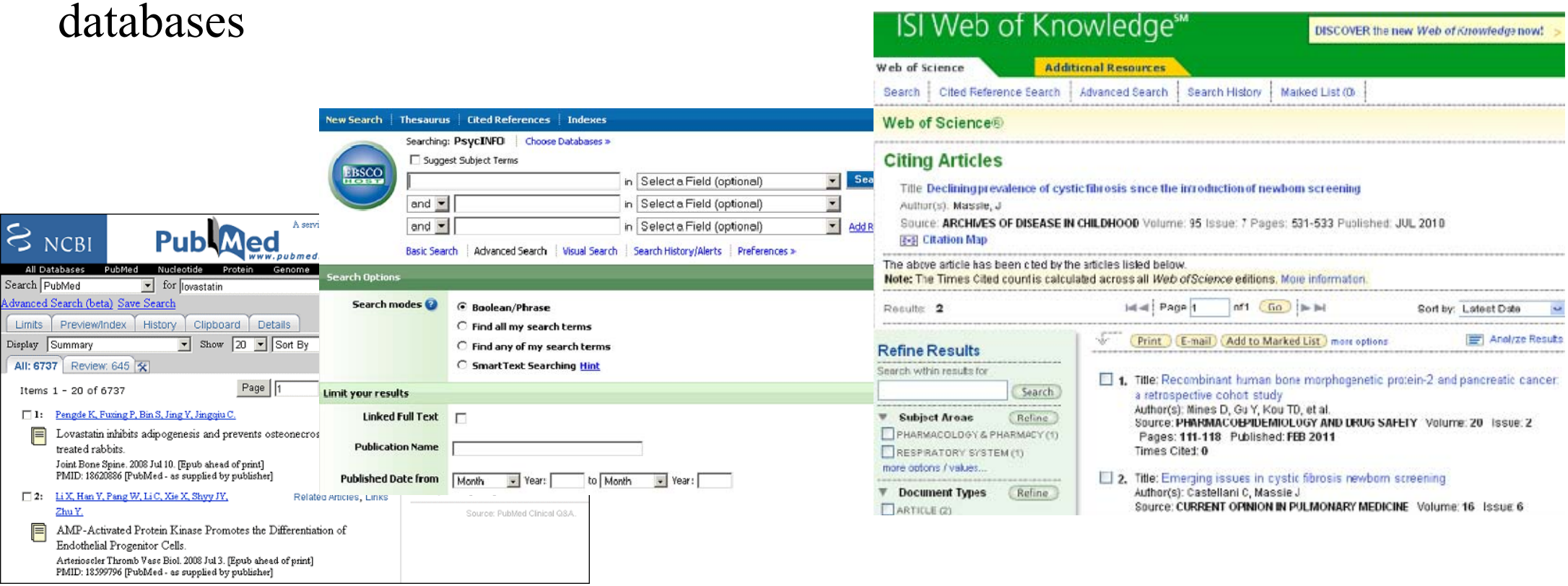
3. Identify databases and other sources to search for studies.

Systematic reviews should be based on extensive searching of bibliographic databases and other sources.

- The aim is to identify all the relevant studies to answer your research question, but not to have to spend too long finding them.
- Through your search you should be confident that you have identified all of the relevant studies for your research question.
- You should consider how to identify published studies and unpublished work/ grey literature.

Bibliographic databases

The majority of searching should take place within major bibliographic databases



Bibliographic databases

- Researchers publish the findings of their research in academic journals (e.g. Nature, the Lancet, the International Journal of Public Health)
- It would be really time consuming to look at every journal out there to find the evidence that you want
- Bibliographic databases record (mainly) articles that are published across many different journals
- One database will store records from lots of different journals so when you look in one database, you will effectively be searching across many journals at the same time

What databases should be searched?

This will depend on your research question! Identify databases that are likely to contain what you want to know.

Bibliographic databases examples

- MEDLINE
- PsychINFO
- Web of knowledge
- Sports Discus

There are lots and lots of databases and there is a lot of overlap between databases

A comprehensive search

You should search in **at least** two bibliographic databases, plus one or two supplementary sources. Report this in the write up of your review, and explain your decisions

Electronic databases x 2+	**Supplementary sources**
e.g. Social care online Medline Web of Science PsychINFO - Are there any specific databases for your topic?	• Reference lists of included papers • Past issues of key journals • Key review articles relating to topic • Key author's publications • Contacting key authors • 'Grey' literature e.g. Conference abstracts, reports

Why consider grey literature?

Is the published evidence representative of all studies carried out?

What proportion of published evaluations do you think contain positive intervention effects or significant results?

Sterling 1995: 95.6% articles in psychology journals report significant results or intervention effects. Does this reflect the amount of research that produces significant results??

"the journals are filled with the 5% of the studies that show Type I errors (rejected the null hypothesis and concludes that an effect has been found), while the file drawers back at the lab are filled with the 95% of the studies that show non-significant (e.g. p>0.05) results" (Rosenthal 1979)

How to use grey literature

Typically identified through:

- Website searching (e.g. WHO, United Nations, Government websites, charities)
- Calls for evidence

Can be used alongside evidence published in academic journals in a review. All evidence should be carefully and critically analysed to examine methodological rigour.

- A review should discuss whether grey literature was searched for and how; or if it wasn’t search for then it should justify why not.

4. Develop your search strategy to identify evidence

How do you search systematically within your bibliographic databases?

- In order to identify all the potential studies to include in your review you need to devise an appropriate *search strategy*.
- You want to identify all of your articles at the same time, and in one go. Your search strategy should enable you to do this.

Develop your search strategy to identify evidence

Systematic reviewers create complex search strategies to efficiently search for evidence. However, not all searches can be quite simple.

- The overall aim should be to identify all of the evidence available that is relevant to your research question, without having to sift through too many studies to find it.
- Typically this involves firstly the identification of key words relating to your inclusion criteria to broaden your search, and then combining your key words and using key operators in the databases to narrow it again.

Stages in developing a search strategy

1. Identify key search terms based upon your inclusion criteria (refer to the PICOS framework).

You can search within your bibliographic databases using these terms. The database will match your search terms to articles that contain them e.g. if you search “steroid” in medline it will identify articles that include the word “steroid”.

2. Development of the strategy in the bibliographic databases. This will include using the database thesaurus, combining your terms using Boolean operators: (AND and OR) and using key operators

Group activity: developing search terms

Refer to activity sheet #3

Briefly consider what you think the main search terms would be for the review "What interventions are effective at preventing problem gambling behaviours amongst university students" using the inclusion criteria identified.

Discuss these in your groups.

Building the search strategy

Appendix 1. PubMed Search Strategy

1. opioid-related disorder [mesh]
2. (((addict*[Title/Abstract]) OR disorder*[Title/Abstract]) OR abus*[Title/Abstract]) OR dependen*[Title/Abstract]
3. (((((OPIUM[Title/Abstract]) OR opiate*[Title/Abstract]) OR opioid[Title/Abstract]) OR heroin[Title/Abstract]) OR methadone[Title/Abstract]) OR morphine[Ti
4. #1 or #2 or #3
5. ((naltrexone[Title/Abstract]) OR naloxo
6. naltrexone [mesh]
7. naloxone [mesh]
8. #5 or #6 or #7
9. randomized controlled trial[pt]
10. controlled clinical trial[pt]
11. random*[tiab]
12. placebo[tiab]
13. drug therapy[mesh]
14. trial[tiab]
15. groups[tiab]
16. #9 or #10 or #11 or #12 or #13 or #14 c
17. animals [mesh] not humans [mesh]
18. #16 NOT #17
19. #4 AND #8 AND #18
20. limit 19 to 2005-2010

- Searching with database thesaurus/ mesh headings
- Combining key words with OR (alternative search terms) and AND (different concepts)
- Searching within titles and abstracts of references
- Use of truncation to search for alternative endings
- Limiting search findings e.g. human studies, date limits

Some tips

- Familiarise yourself with the databases that you want to use
- Use the ‘help’ section within databases to support the development of strategies
- Ask a librarian! Or look online – there is lots of materials available to guide you through this process

When you write up your review, describe your search strategy. Good reviews will include a sample strategy in the text, or in the appendix (more than just a few key words they have searched with)

So what next?

So at this point you have:

- Developed a research question and decided what evidence you want to identify (inclusion criteria) and omit (exclusion criteria).
- Decided where to look for your evidence and developed a search strategy
- Ran your database searches (and supplementary searches) and saved all your identified references together

5. Screening/ study selection

In all probability you will have identified a lot of references!

- Most systematic reviews will start off with 1000s of references. Your next job is to identify from this big list of references the articles that you are going to include in your review.
- This is a time consuming and somewhat tedious process – but a very important one.
- At the end of this stage you will be able to begin your review.

Screening your identified articles

Screening = comparing each article you have found to your inclusion and exclusion criteria.

Does it meet my inclusion criteria?	Yes?	Include it.
	No?	Exclude it.
	Not sure?	Include it for now.

Two typical stages

a) Title and abstract screening

If you have identified 1000s of articles then you won't have time to read the full article of all of them

- Reviewers start by reading the title and abstract of all articles and making a decision whether to INCLUDE or EXCLUDE
- All screening is undertaken by two reviewers independently.

Two typical stages

b) Full text screening

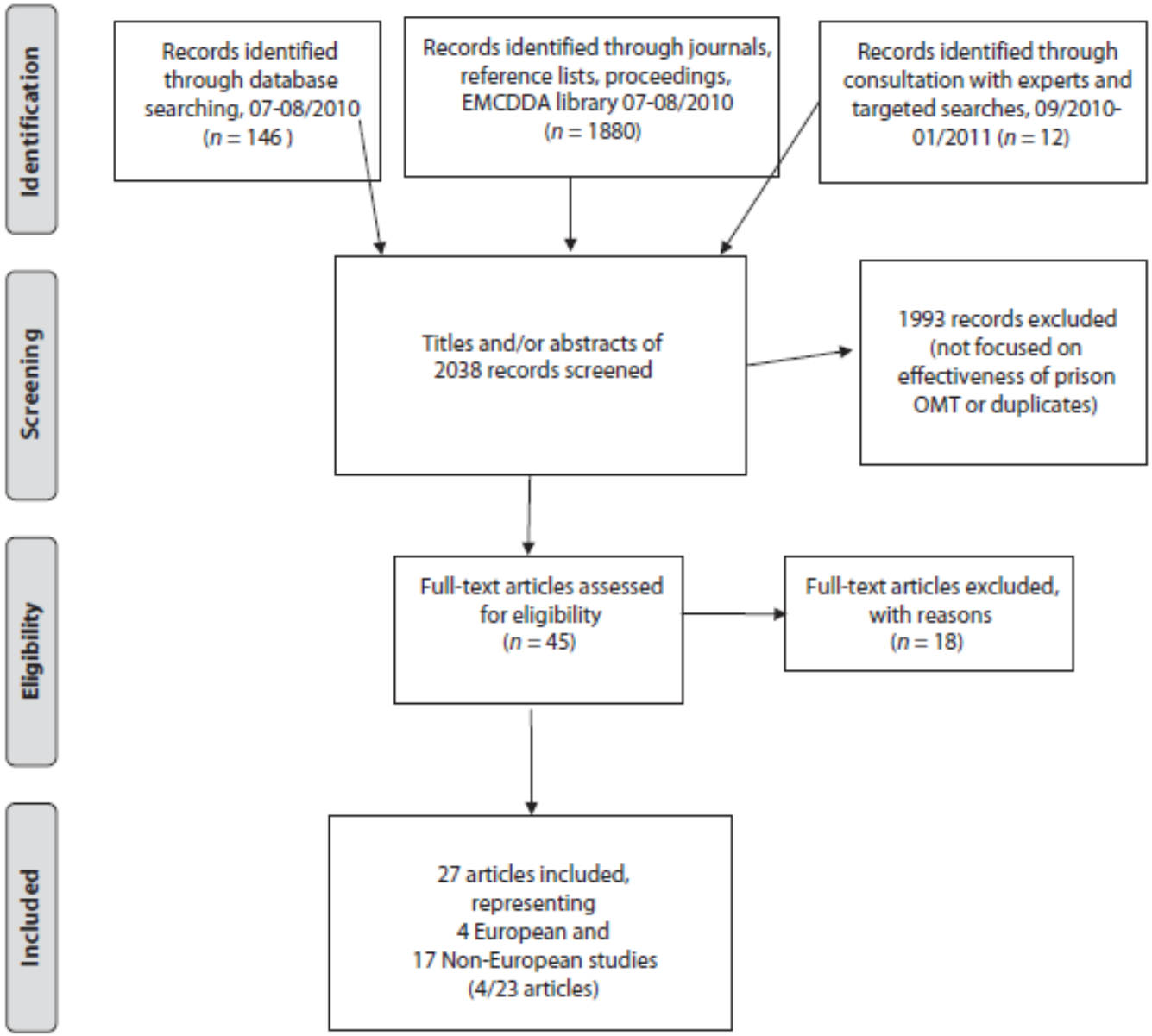
For all included studies, the full article is downloaded and reviewed again inclusion criteria.

- Reasons for excluding articles should be recorded at this stage.
- Always think: how can I justify including or excluding this article? Does it fit my inclusion criteria for this review?

Reporting the study selection process

You should report this screening process when you write up your review. This should include:

- Summary of steps undertaken and by whom
- Detail of reasons for excluding studies at the full text screening stage
- Provision of a ‘study selection flow chart’ to clearly demonstrate how you ended up with the articles included in the review



Sample study selection diagram

From: Hedrich et al, 2012. The effectiveness of opioid maintenance treatment in prison settings: a systematic review

6. Data extraction/ data collection

The process of collecting consistent information from the primary studies that you have identified.

The aim is to:

- Summarise all the key information that you (and the reader) need to make judgements about the study
- In systematic review we use pre-designed tables to record this data in. This ensures that data extraction is consistent and easy to follow.
- This will help you structure your synthesis and understand your studiesn

What happened? Who took part? What were the results?

Purpose of data collection

Data extraction forms should suit the collection and organisation of interest from your included studies.

- Data extraction should reflect the points of difference and similarity between studies that will help you compare your studies and interpret findings – you should pull out data on variables of interest that you want to compare.
- It is likely you will look at: setting/ location/ details of interventions/ population demographics/ recruitment/ sample size/ estimates of prevalence/ behaviour change etc

Sample data extraction form

Study Details	
Author/year	
objectives	
Participants (characteristics/total number)	
Setting/context	
Description of Interventions/ phenomena of interest	
Search Details	
Sources searched	
Range (years) of incl studies	
Number of studies included /	
Types of studies included	
Country of origin of incl. studies	

Appraisal	
Appraisal instruments used	
Appraisal rating	

Analysis	
Method of analysis	
Outcome assessed	
Results/Findings	
Significance/direction	

Joanna Briggs Institute Data Extraction form:
http://joannabriggs.org/assets/docs/jbc/operations/dataExtractionForms/JBC_Form_DataE_SRsRSs.pdf

Extraction tables – how to use them

You will refer to your data tables as you structure and write up your results.

You should create summary tables with key information about study characteristics and outcomes and include these in your review – either in the main body or as an appendix.

You are giving the reader enough information about the articles that you have included so that they do no need to refer to the original articles themselves.

Table 1. Summary description of primary studies in the systematic review.

Author	Country	Treatment type[a]		Group allocation	Dropouts (%)[b]		Follow-up (months)	Outcome measure
		Experimental	Control		Experimental	Control		
Hartnoll et al. (1980)	UK	HA; PS (*44*)	MA; PS (*52*)	Random	36% (ITT)	71% (ITT)	12	OR
Lobmaier et al. (2010)	Norway	NX (*23*)	MA (*21*)	Random	30% (ITT)	48% (ITT)	6	SR; OR
Löbmann and Verthein (2009)	Germany	HA; MA* (*515*)	MA* (*500*)	Random	33% (ITT)	60% (ITT)	12	SR; OR
March et al. (2006)	Spain	HA; MA* (*27*)	MA* (*23*)	Random	15% (ITT)	9% (ITT)	9	SR
Martin, Player, and Liriano (2003)	UK	DT; PS (*274*)	NT (*931*)	Non-random	(274)	(931)	12; 24	SR
McCusker and Davies (1996)	UK	HA* (*27*)	MA* (*39*)	Non-random	4% (26)	36% (25)	12; 18	SR
McSweeney (2009)	UK	DT (*242*)	NT (*252*)	Non-random	(242)	(252)	12	OR
Metrebian et al. (2001)	UK	HA (*37*)	MA (*21*)	Non-random	41% (22)	52% (10)	3; 12	SR
Naeem et al. (2007)	UK	DT; PS (*35*)	NT (*38*)	Non-random	29% (25)	29% (27)	12	SR
Perneger et al. (1998)	Switzerland	HA* (*27*)	MA* (*21*)	Random	7% (ITT)	(ITT)	6	SR
Robertson et al. (2006)	UK	HA (*108*)	MA (*110*)	Random	18% (ITT)	3% (ITT)	36	SR
Strang et al. (2000)	UK	MA* (*19*)	MA* (*18*)	Random	5% (18)	7% (15)	6	SR
van den Brink et al. (2003); study 1	Netherlands	MA; HA* (*76*)	MA* (*98*)	Random	28% (ITT)	15% (ITT)	12	SR
van den Brink et al. (2003); study 2	Netherlands	MA; HA* (*117*)	MA* (*139*)	Random	32% (ITT)	13% (ITT)	12	SR
van den Brink et al. (2003); study 3	Netherlands	MA; HA* (*119*)	MA* (*139*)	Random	31% (ITT)	13% (ITT)	12	SR

MA, methadone-assisted treatment; NX, naltrexone implants; NT, no treatment; OR, official records; ITT, intent-to-treat analysis; HA, heroin-assisted treatment; PS, psychosocial care; DT, drug testing; SR, self-report.
Note: Asterisk denotes that additional therapeutic treatment was offered.
[a]Numbers in brackets denote the original sample size in each experimental condition.
[b]Numbers in brackets denote the analysed sample size in each experimental condition; ITT denotes that the value is the same as in the 'Treatment Type' column.

From: Koehler et al, 2014. A systematic review and meta-analysis of European drug treatment programs on reoffending.

7. Quality assessment

Quality assessment refers to the process of critically analysing the studies included in the review, in a formalised and consistent manner

- The focus is on identifying whether your articles have minimised sources of bias, and whether the results reported are reliable and valid
- In systematic reviews, we use a checklist to assess studies to ensure that all articles are assessed in the same way
- This can be a useful way of identifying articles to exclude (if they don't meet determined quality standards), or to increase understanding on the nature of the evidence you are reviewing and the implications this has for your conclusions

Quality assessment checklists

- There are a range of checklists available to use
- Most checklists are similar – they ask questions about the methodological quality of the article you are reviewing, and about it's nature and how the information presented to you within it.
- There are different checklists for different types of evidence e.g. qualitative evidence, RCTs, cohort studies.
- Many checklists will have a score system attached.
- Two reviewers should independently assess the quality of included studies

What do the checklists examine?

The content will reflect the intention of the checklist. For example a checklist for critical assessment of RCTs will look at factors such as:

- Random assignment to conditions
- Blinding of study participants, assessors
- Baseline characteristics of groups
- Attrition and intention to treat
- Sample size
- Data collection methods
- Applicability to your local context

Examples of checklists

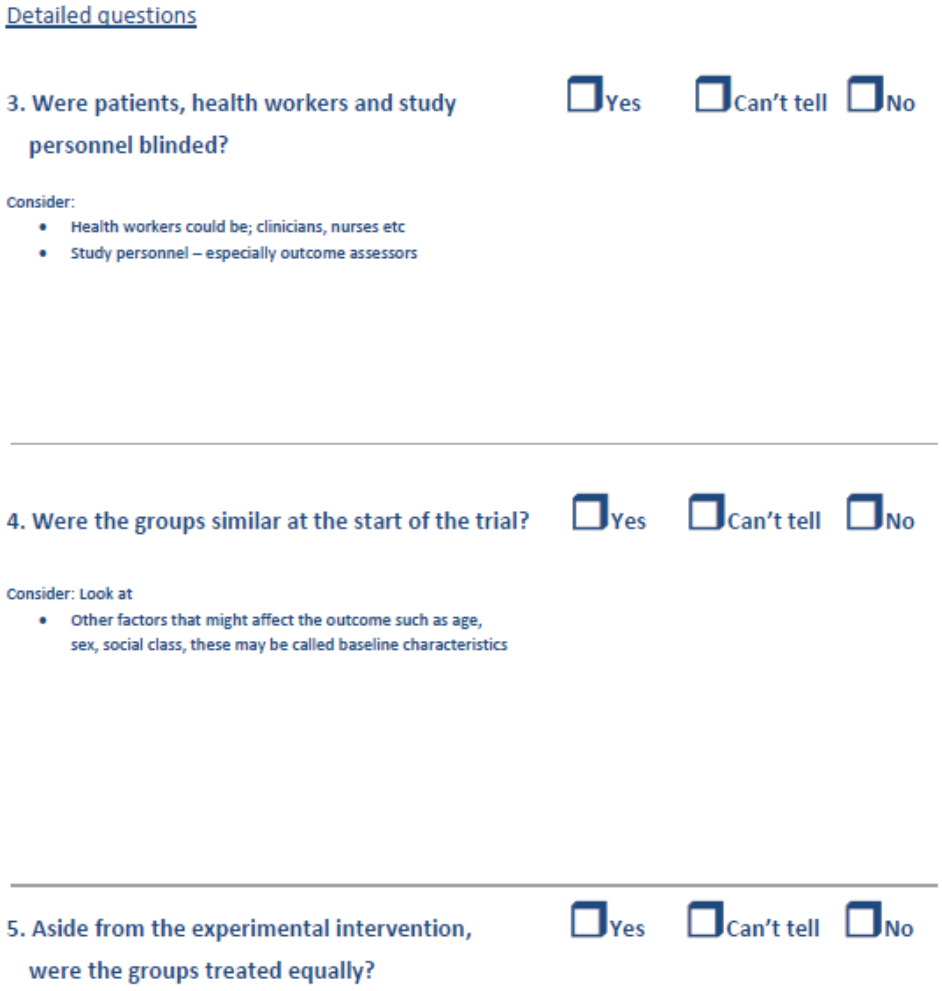
Available online e.g.

CASP: www.casp-uk.net/

JBI: http://joannabriggs.org/

Cochrane group: http://handbook.cochrane.org/

EPHPP: http://www.ephpp.ca/tools.html



Detailed questions

3. Were patients, health workers and study personnel blinded? ☐ Yes ☐ Can't tell ☐ No

Consider:
- Health workers could be; clinicians, nurses etc
- Study personnel – especially outcome assessors

4. Were the groups similar at the start of the trial? ☐ Yes ☐ Can't tell ☐ No

Consider: Look at
- Other factors that might affect the outcome such as age, sex, social class, these may be called baseline characteristics

5. Aside from the experimental intervention, were the groups treated equally? ☐ Yes ☐ Can't tell ☐ No

Undertaking quality assessment

- Think about what information you need: most of the questions will ask about factors that will be contained in the methods and results sections of articles.
- Not all questions will always apply to all articles. This depends on the nature of the tool that you select to use – it is important to select an appropriate one.
- Record the findings of your QA in your write up and describe the tool used. For example, you will see reviews describe whether each study was ‘poor’, ‘medium’ or ‘good’ quality or give the QA score from the checklist they used in their data tables.

Quality Assessment: Group Activity

Refer to Activity Sheet #4 and the accompanying hand outs.

Do not take too long reading the article! Discuss it in your group and then we will have a go at applying a typical quality assessment tool to this article.

Using the findings of quality assessment

- Can be used to exclude studies where methodological quality is low, or risk of bias judged as high
- Findings of QA should be used in the analysis and interpretation of results – how do QA findings impact upon the interpretation of your results? For example if you have mixed results, how much of this may be down to methodological differences in your studies? Or if the articles suggest a promising approach, is this undermined or strengthened by the quality of these articles?
- A summary of the quality of the studies you include should be provided highlighting the key strengths and weaknesses of the evidence base. This will help inform research recommendations

8. Synthesis – writing up your review findings

This is the process of collating, combining and summarising the findings of the individual articles included in your review

The aim here is to identify the answer to your research question.

This section usually contains a mixture of narrative synthesis and summary tables of data. It may also contain statistical synthesis e.g. meta-analysis

Narrative synthesis

The most common approach to writing up a review. Involves the systematic bringing together, organising and describing of findings.

- Relies primarily on text to summarise and explain the findings of the review
- “Tells a story” of the findings from your included studies
- Describes the relationships between studies
- Groups similar studies together and uses sub headings

What might explain results? Why are some interventions effective and some not effective?

What are the common features in studies with similar results? What might explain any variation?

Some typical steps towards a narrative synthesis

1. Group included studies together to help analysis and identification of patterns
2. Tabulate your findings (data extraction tables) including raw statistical data and direction of effects
3. Describe your studies – key features
4. Thematic analysis of concepts across included studies
5. Reflect upon the methodological quality of studies

A quick word on meta-analysis

Meta-analysis provides a statistical summary estimate of the effectiveness of one intervention/treatment against another for a given population

By combining results (and therefore increasing your sample size) you are improving statistical power

It is only appropriate to undertake MA under certain conditions – studies must be similar in factors such as population, methods and outcomes. Statistical tests for heterogeneity are available and should be used when deciding whether it is appropriate to undertake MA.

Example

Example review “Are nicotine patches associated with smoking cessation?”

- 13 studies that have looked at the impact on smoking cessation of providing nicotine patches to smokers (intervention group) compared to the impact of providing advice and information (control group)
- 13 different results/ effect sizes & confidence intervals - how can you know what the impact really is?
- If you combine all the data together then you will get one overall effect size and significance score that will answer our research question.

Reference management – a brief word

One of the biggest challenges in undertaking a SR is the large amount of evidence that will be considered

It is very important to manage references effectively!

You should provide full reference lists for studies excluded at full text screening stage as well as those you include

Using reference management software (e.g. Rev Man, Endnote) where you can store references is very useful.

Part 3

Practical challenges of systematic reviews

Summary

So far today we have gone through the steps followed in undertaking a typical systematic review. In the next part of the day we will look at two types of reviews that differ from this normal approach (although they are in fact very similar!) and look at what makes a good systematic review

Undertaking qualitative reviews

Qualitative systematic reviews

So far we have focussed exclusively on reviews of quantitative data, but what about the massive amounts of qualitative research that has been published? Can we include this in systematic reviews?

Qualitative methods are increasing in usage in evidence-based research. It focuses on individuals and it's strength is its credibility i.e. getting close to the truth through in depth research.

Group exercise: qualitative systematic reviews

Refer to activity sheet #5

In your groups consider the nature of qualitative studies and discuss the three discussion questions provided.

What did you think?

Potential differences?

Initial steps stay largely the same (you might look with different terms and in different places)

- Less comprehensive search?
- Data extraction: less emphasis on e.g. sample size.
- Quality assessment: tools used in trials don’t apply.
- Synthesis: you can’t undertake meta-analysis! Based on thematic analysis, or qualitative methodologies e.g. grounded theory

Qualitative systematic reviews - controversy

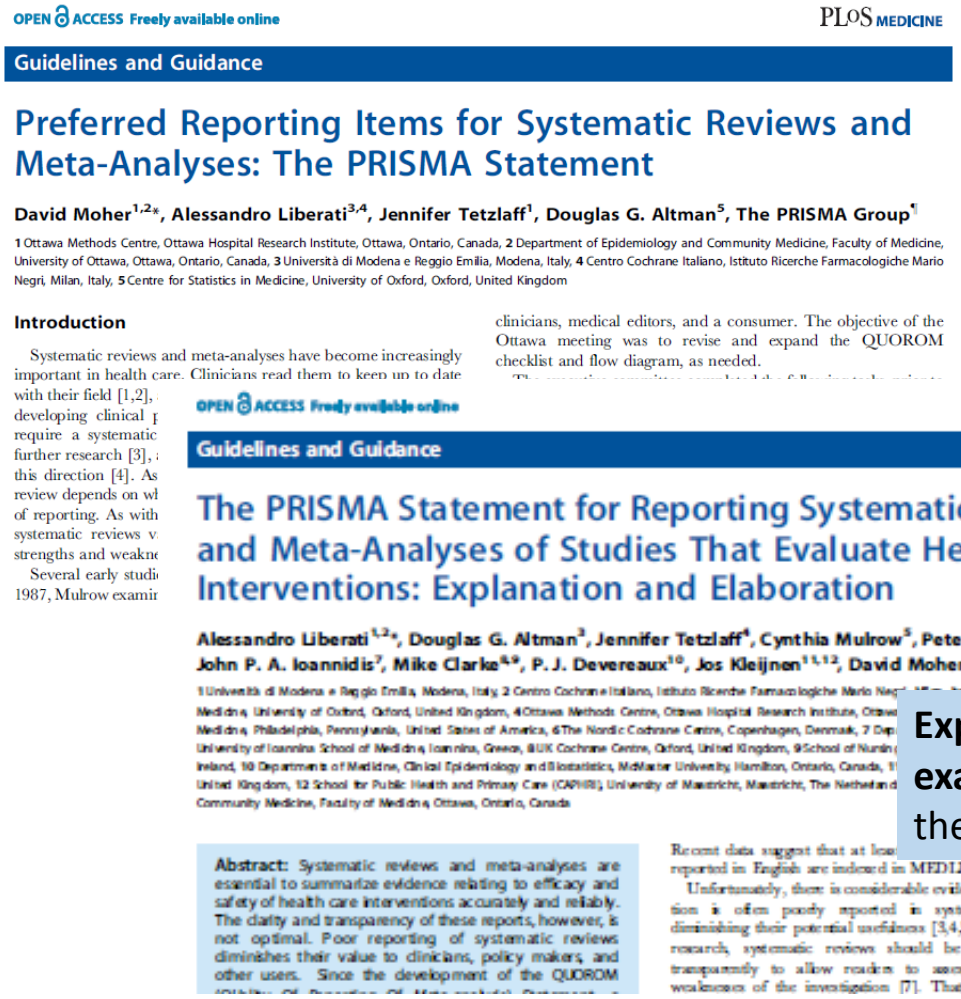
Many qualitative researchers challenge the concept of synthesising qualitative data based upon the philosophical and methodological differences between different qualitative research approaches, and the role of the researcher in qualitative the research and analysis.

What makes a good review?

Group exercise: what makes a good review?

Refer to activity sheet #6

Thinking about everything we have discussed so far today, what do you think a well-reported systematic review should look like? Briefly consider and then discuss in your groups.



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PLoS MEDICINE

Guidelines and Guidance

Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

David Moher[1,2]*, Alessandro Liberati[3,4], Jennifer Tetzlaff[1], Douglas G. Altman[5], The PRISMA Group[¶]

1 Ottawa Methods Centre, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, 2 Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada, 3 Università di Modena e Reggio Emilia, Modena, Italy, 4 Centro Cochrane Italiano, Istituto Ricerche Farmacologiche Mario Negri, Milan, Italy, 5 Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom

Introduction

Systematic reviews and meta-analyses have become increasingly important in health care. Clinicians read them to keep up to date with their field [1,2], developing clinical p require a systematic further research [3], this direction [4]. As review depends on wh of reporting. As with systematic reviews v strengths and weakne

Several early studi 1987, Mulrow examir

clinicians, medical editors, and a consumer. The objective of the Ottawa meeting was to revise and expand the QUOROM checklist and flow diagram, as needed.

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PLoS MEDICINE

Guidelines and Guidance

The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration

Alessandro Liberati[1,2]*, Douglas G. Altman[3], Jennifer Tetzlaff[4], Cynthia Mulrow[5], Peter C. Gøtzsche[6], John P. A. Ioannidis[7], Mike Clarke[8,9], P. J. Devereaux[10], Jos Kleijnen[11,12], David Moher[4,13]

1 Università di Modena e Reggio Emilia, Modena, Italy, 2 Centro Cochrane Italiano, Istituto Ricerche Farmacologiche Mario Negri, Milan, Italy, 3 Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom, 4 Ottawa Methods Centre, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, 5 University of Texas Health Science Center at San Antonio, San Antonio, Texas, United States of America, 6 The Nordic Cochrane Centre, Copenhagen, Denmark, 7 Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, 8 UK Cochrane Centre, Oxford, United Kingdom, 9 School of Nursing and Midwifery, Trinity College Dublin, Dublin, Ireland, 10 Departments of Medicine, Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada, 11 Institute of Health Sciences, University of Oxford, Oxford, United Kingdom, 12 School for Public Health and Primary Care (CAPHRI), University of Maastricht, Maastricht, The Netherlands, 13 Department of Epidemiology and Community Medicine, Faculty of Medicine, Ottawa, Ontario, Canada

Abstract: Systematic reviews and meta-analyses are essential to summarize evidence relating to efficacy and safety of health care interventions accurately and reliably. The clarity and transparency of these reports, however, is not optimal. Poor reporting of systematic reviews diminishes their value to clinicians, policy makers, and other users. Since the development of the QUOROM

Recent data suggest that at least reported in English are indexed in MEDLINE annually [3].

Unfortunately, there is considerable evidence that key information is often poorly reported in systematic reviews, thus diminishing their potential usefulness [3,4,5,6]. As is true for all research, systematic reviews should be reported fully and transparently to allow readers to assess the strengths and weaknesses of the investigation [7]. That rationale led to the

Explanations and **examples** for how to phrase these sections

PLoS Medicine, 1 July 2009 / 6 July 2009, Volume 6, Issue 7

PRISMA checklist

Table 1. Checklist of items to include when reporting a systematic review (with or without meta-analysis).

Section/Topic	#	Checklist Item	Reported on Page #
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 (PICOS).	
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., PICOS, 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	

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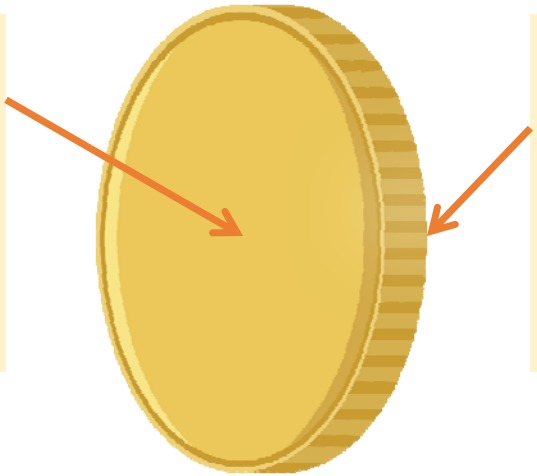
What makes a good review?

Two sides of the same coin

What should I consider **when I am writing** up a review?

(Perspective of the AUTHOR)



What do I look for in a review **written by someone else**?

(Perspective of the READER)

Systematic Reviews of *Reviews*

What is a review of reviews?

Also known as:

- Umbrella review
- Overview review
- Overview (of reviews)
- Summary/synthesis of reviews

"systematic reviews that draw together evidence **from a series of other systematic reviews**. This type of review can be useful in providing an overview of research within a particular area"

(Joanna Briggs Institute Reviewers' Manual 2014 Edition, Glossary)

Typical research aims within reviews of reviews

To summarise evidence from more than one research synthesis…

- … of **different interventions** for the same condition or problem
- … of the same intervention for the same condition or problem where **different outcomes** are addressed in different systematic reviews
- … of the same intervention for **different conditions, problems or populations**

(Cochrane Handbook for Systematic Reviews of Interventions, Chapter 22; JBI Reviewers' Manual, Methodology for JBI Umbrella Reviews)

Examples of review of reviews

- ALICE RAP, Work Package 16 “Adolescents as customers of addiction”, Deliverable 16.1, Background report 2: Review of reviews
- http://www.alicerap.eu/about-alice-rap/areas-a-workpackages/area-6-addicting-the-young.html

UNODC
United Nations Office on Drugs and Crime

- International Standards on Drug Use Prevention, United Nations Office on Drugs and Crime (UNODC)
- https://www.unodc.org/unodc/en/prevention/prevention-standards.html

When might it be useful to conduct a review of reviews?

- Broad research question
- Large number of (systematic) reviews available
- (Limited time available)

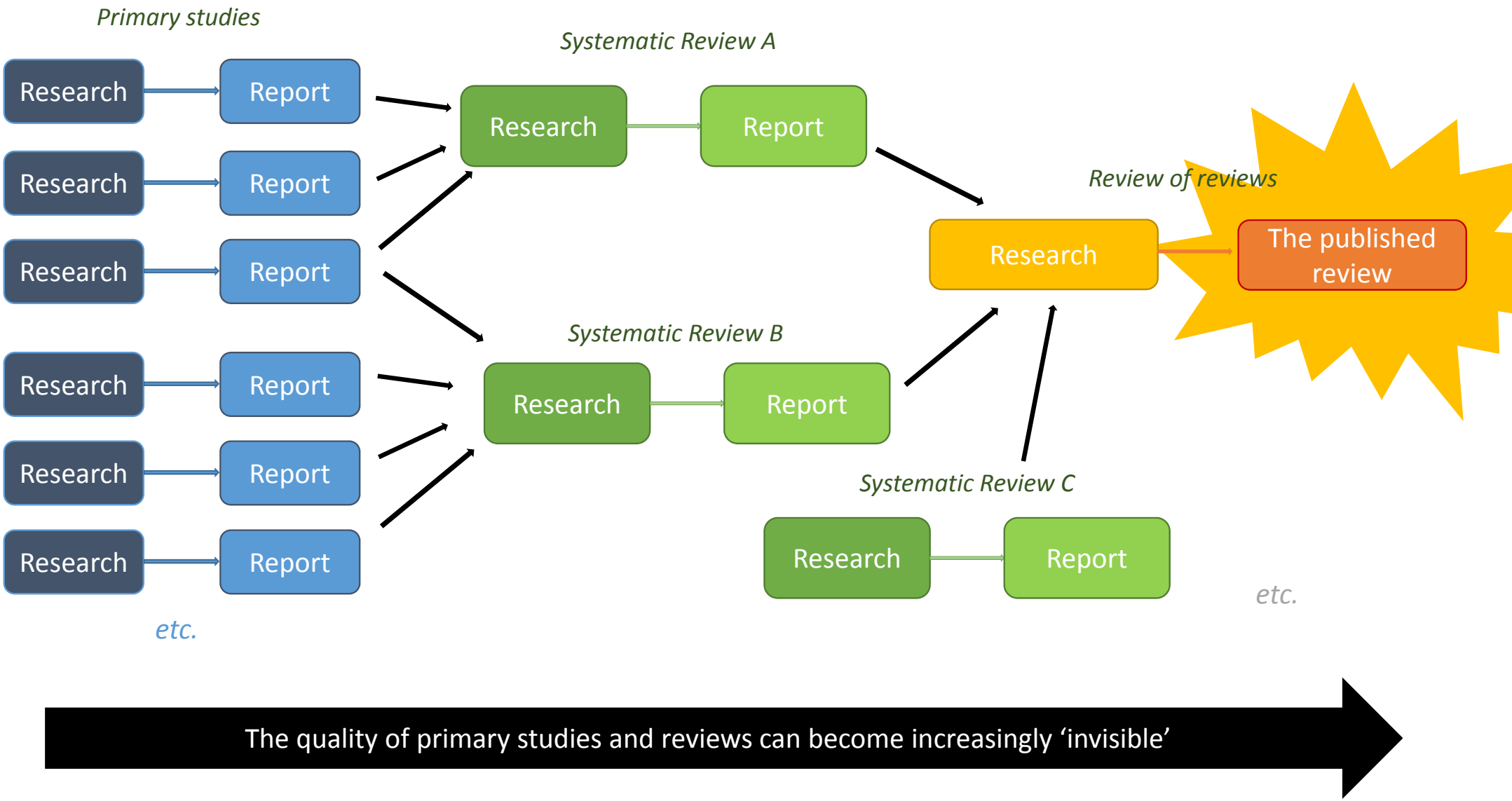
… and when might it be less useful?

- No/few primary studies
- No/few (systematic) reviews

⇒can still be useful as a *scoping review*

Similarities with a review of primary studies

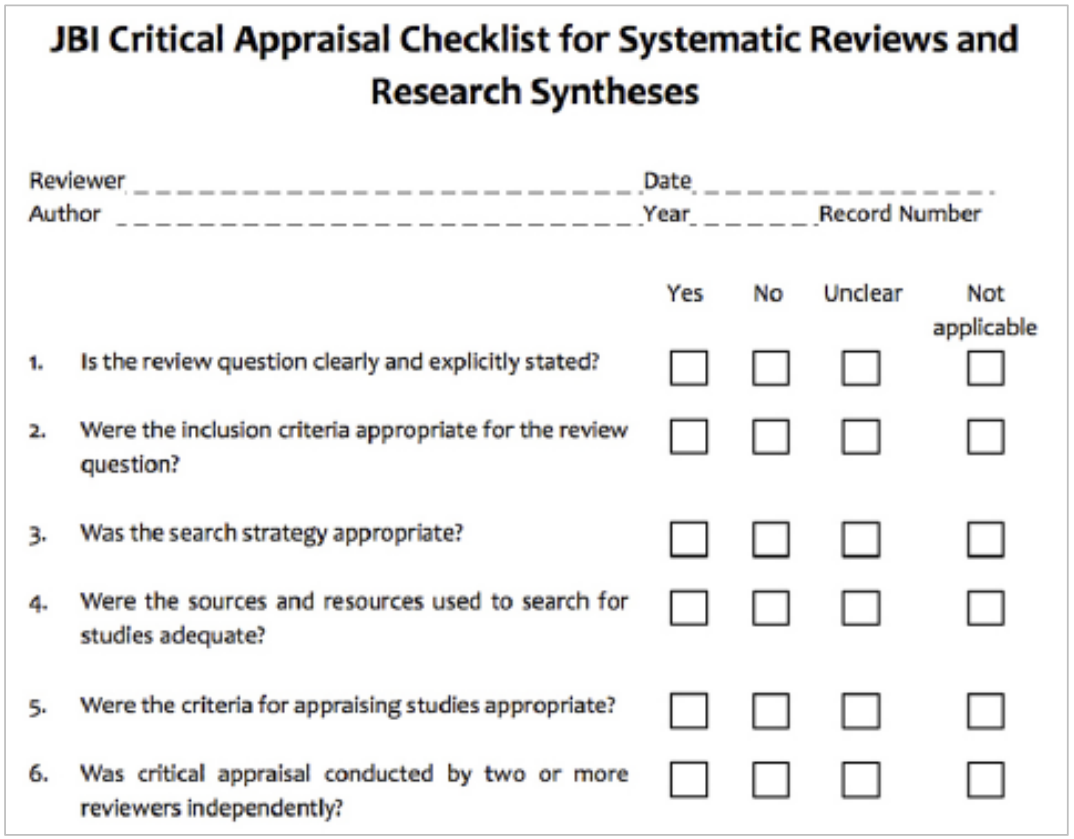
- Importance of a systematic and transparent approach
- Following the same steps
- Quality assessment equally (if not more) important!


Primary studies
Research
Report
Research
Report
Research
Report
Research
Report
Research
Report
Research
Report
etc.
Systematic Review A
Research
Report
Systematic Review B
Research
Report
Systematic Review C
Research
Report
Review of reviews
Research
The published review
etc.
The quality of primary studies and reviews can become increasingly 'invisible'

Differences between a regular review and a review of reviews

- Some differences?
  - **Broader** research question
  - Search for **reviews** rather than primary studies
    - Use pre-set filters where available; for suggested search strategy, see e.g. Montori et al. 2004)
    - Inclusion criteria at the level of the reviews and of the primary studies
  - Different **quality assessment** instruments (e.g. JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses; AMSTAR)
    - Need to consider the quality of the included reviews, as well as of the primary research included within those reviews (a high quality review may include poor quality studies)
  - **Data extraction** concerning the review and the primary research
    - More likely to limit data extraction to high quality reviews only
  - **Overlap** of primary studies
  - …

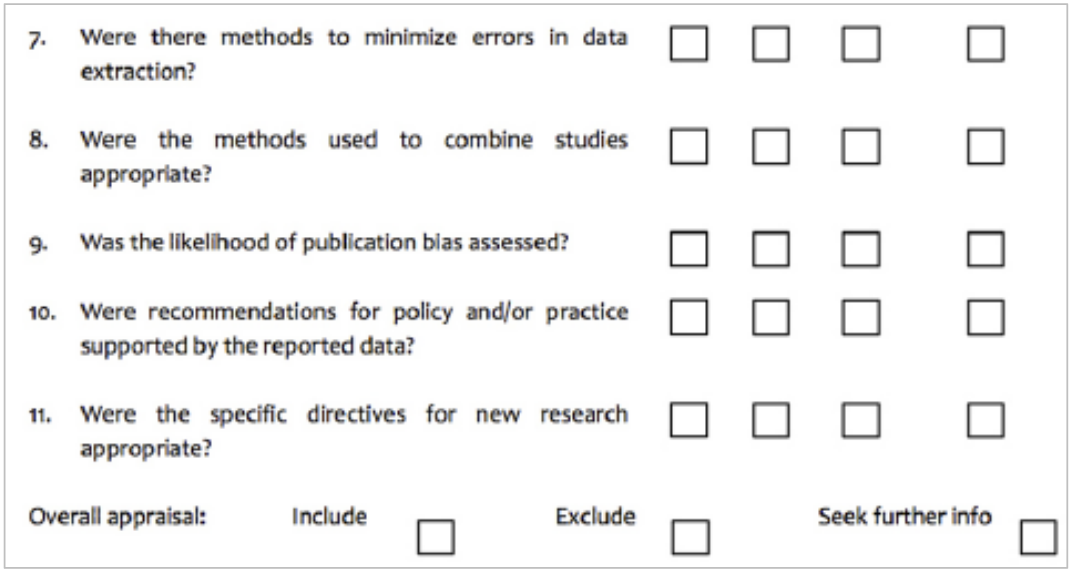
Examples of quality assessment tools for judging reviews



JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

Reviewer _____ Date _____
Author _____ Year _____ Record Number

		Yes	No	Unclear	Not applicable
1.	Is the review question clearly and explicitly stated?	☐	☐	☐	☐
2.	Were the inclusion criteria appropriate for the review question?	☐	☐	☐	☐
3.	Was the search strategy appropriate?	☐	☐	☐	☐
4.	Were the sources and resources used to search for studies adequate?	☐	☐	☐	☐
5.	Were the criteria for appraising studies appropriate?	☐	☐	☐	☐
6.	Was critical appraisal conducted by two or more reviewers independently?	☐	☐	☐	☐



7.	Were there methods to minimize errors in data extraction?	☐	☐	☐	☐
8.	Were the methods used to combine studies appropriate?	☐	☐	☐	☐
9.	Was the likelihood of publication bias assessed?	☐	☐	☐	☐
10.	Were recommendations for policy and/or practice supported by the reported data?	☐	☐	☐	☐
11.	Were the specific directives for new research appropriate?	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐

Joanna Briggs Institute Reviewers' Manual 2014, Methodology for JBI Umbrella Reviews

Examples of quality assessment tools for judging reviews

AMSTAR – a measurement tool to assess the methodological quality of systematic reviews.

≈ **1. Was an 'a priori' design provided?**

The research question and inclusion criteria should be established before the conduct of the review.

Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

≈ **2. Was there duplicate study selection and data extraction?**

There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

≈ **3. Was a comprehensive literature search performed?**

At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.

Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

http://amstar.ca/docs/AMSTARguideline.pdf

Examples of quality assessment tools for judging reviews

4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?

The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.

Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

---

5. Was a list of studies (included and excluded) provided?

A list of included and excluded studies should be provided.

Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

---

6. Were the characteristics of the included studies provided?

In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.

Note: Acceptable if not in table format as long as they are described as above.

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

Examples of quality assessment tools for judging reviews

≈ **7. Was the scientific quality of the included studies assessed and documented?**

'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.

Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

≈ **8. Was the scientific quality of the included studies used appropriately in formulating conclusions?**

The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.

Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

✓ **9. Were the methods used to combine the findings of studies appropriate?**

For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?).

- ▫ Yes
- ▫ No
- ▫ Can't answer
- ▫ Not applicable

Examples of quality assessment tools for judging reviews

10. Was the likelihood of publication bias assessed?

An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken).

Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

- ☐ Yes
- ☐ No
- ☐ Can't answer
- ☐ Not applicable

11. Was the conflict of interest included?

Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.

Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.

- ☐ Yes
- ☐ No
- ☐ Can't answer
- ☐ Not applicable

Shea *et al. BMC Medical Research Methodology* 2007 **7**:10 doi:10.1186/1471-2288-7-10

How do these criteria compare with your own Top 5?

Final group exercise! Critical assessment of a review article

Refer to activity sheet #6b and the accompanying handouts

Briefly read the review article provided and then discuss in your groups the strengths and weaknesses of the article.

Differences between a regular review and a review of reviews

- Some differences?
  - **Broader** research question
  - Search for **reviews** rather than primary studies
    - Use pre-set filters where available; for suggested search strategy, see e.g. Montori et al. 2004)
    - Inclusion criteria at the level of the reviews and of the primary studies
  - Different **quality assessment** instruments (e.g. JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses; AMSTAR)
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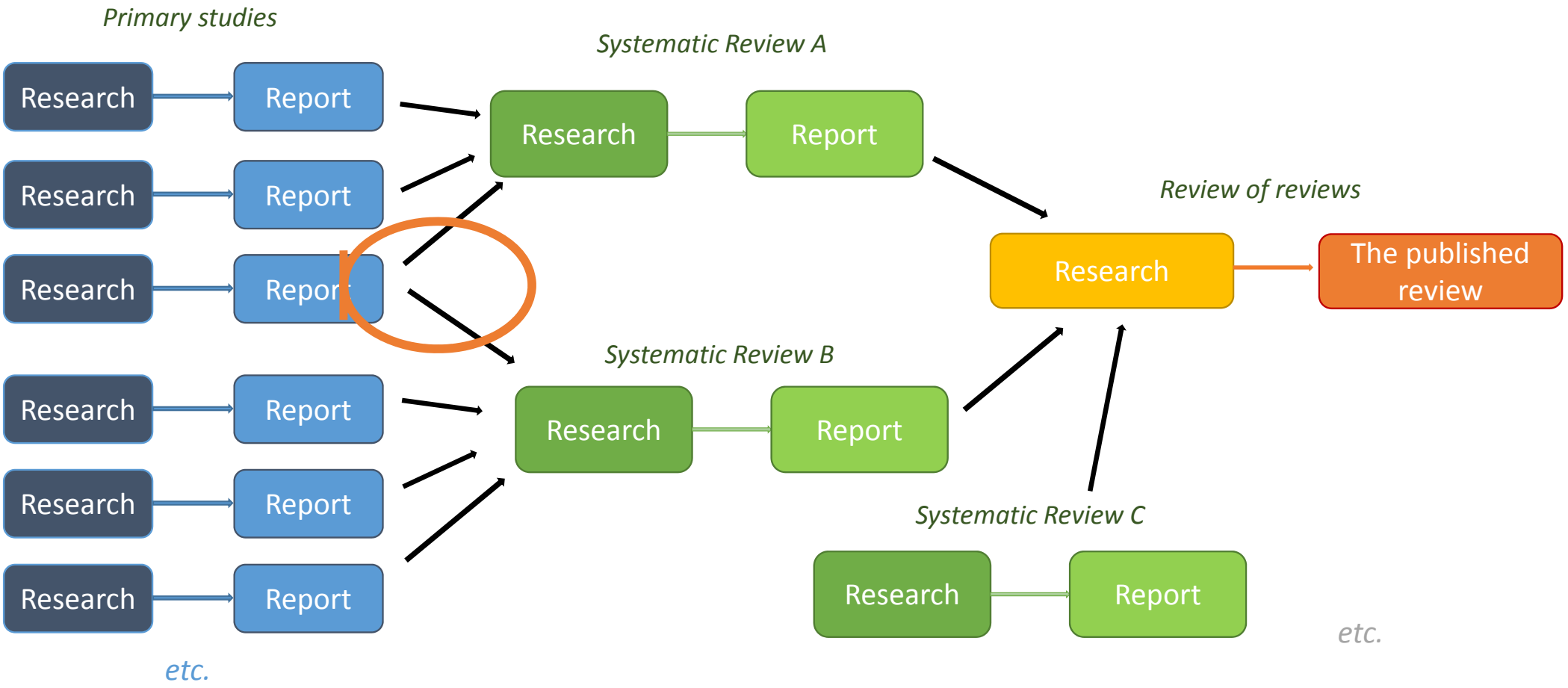
  - **Overlap** of primary studies
  - …

Overlap of primary studies



Overlap of primary studies: an example

Review author and year	Russell 20	Shoptaw 2	Smith 200	Soole 200	Stade 200	Stead 200	Stead 201	Terplan 2(	Thomas 2(	Thomas 2(	Thomas 2(	Thomas 2(	Turnbu
Multiple references per study	*											*	*
Bibliographical references of relevant primary studies													
Spoth R, Redmond C, Shin C, Greenberg M, Clair S, Feinb												1	
Spoth R, Reyes ML, Redmond C, Shin C. Assessing a publ												1	
Spoth R, Shin C, Guyll M, Redmond C, Azevedo K. Univer													
Spoth R, Trudeau L, Guyll M, Shin C, Redmond C. Univers												1	
Spoth RL, Randall GK, Trudeau L, Shin C, Redmond C. Sub												1	
Spoth RL, Randall K, Shin C, Redmond C. Randomized stu												1	
Spoth RL, Redmond C, Shin C. Randomized trial of brief f												1	
Spoth RL, Redmond C, Trudeau L, Shin C. Longitudinal su												1	
Sprunger B, Pellaux D. Skills for adolescence: experienc												1	
St Pierre TL, Kaltreider DL, Mark MM, Aikin KJ. Drug prev													
St Pierre TL, Osgood DW, Mincemoyer CC, Kaltreider DL,												1	
St Pierre TL, Osgood DW, Siennick SE, Kauh TJ, Burden FF												1	
Stanton B, Cole M, Galbraith J, et al. Randomized trial of													
Stanton B, Fang X, Li X, Fiegelman S, Galbraith J, Ricardo													
Stanton BF, Li X, Kahihuata J, Fitzgerald AM, Neumbo S,													
Starkey F, Audrey S, Holliday J, Moore L, Campbell R. Ide												1	

Example: ALICE RAP WP 16 review
Included **65** reviews
1,107 references to primary studies

- 210 refs (19%) cited by at least 2 different reviews
  - Incl. 2 references cited by 8 different reviews
- 21 reviews in which ≥ 50% of references to relevant studies had been cited by at least one other review
  - Incl. 4 reviews where **all** references to relevant studies had also been cited by at least one other review

Challenges specific to a review of reviews

- Some challenges?
  - "Age" of the primary research
  - **Your** interests don't fully match **their** interests (e.g. inclusion criteria, analysis)
  - Poor quality/detail of reporting can make your life difficult!
  - How to assess quality of primary research?
  - Can you trust the reviewers' conclusions?
  - Temptation to retrieve original publications
  - What to do if similar reviews reach different conclusions?
  - What kind of reviews to include? Any or (high quality) systematic reviews only?
  - Frustration if primary studies exist but haven't been reviewed in high quality reviews (yet)
  - Increased documentation burden
  - …

Your interests don't fully match their interests

- Example: You're interested in reviews of school-based prevention programmes for children attending secondary school
- A review includes:
  - 3 trials of school-based prevention programmes for children in secondary school
  - 5 trials of family-based prevention programmes for children in secondary school
- Should it be included? What would you do? Advantages/disadvantages?
- Possible solution: Include it if the 3 relevant trials were analysed/discussed separately
  - Advantage: you can easily extract the results that are of interest to you (no need to check the primary studies)
  - Disadvantage: if it's not the case, you're potentially excluding three relevant trials! (although they may be included elsewhere)

Example solution from ALICE RAP WP 16 review of reviews

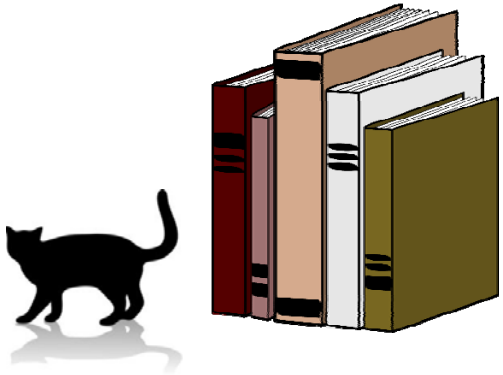
Relevance categories to aid prioritisation:

- A (all studies relevant)
- B (some studies relevant, clearly identified + analysed separately)
- C (some studies relevant but would require additional work, possibly looking up the original publications)

Poor quality/detail of reporting can make your life difficult!

- Example: You're interested in reviews of violence prevention programmes among young adults aged 18-24 years
- A review includes:
  - 3 trials of violence prevention programmes – only average age: 18.4, 23.2, 24.1 years
  - 2 trials of violence prevention programmes – among "bar patrons"
- Should it be included? What would you do? Advantages/disadvantages?
- Option: Include it because it is *likely* to be relevant to your population of interest (and note this limitation in your report)
- If age not reported, the situation would be different … limit data extraction only to high quality reviews with adequate detail of reporting?

Potentially an uncomfortable trade-off



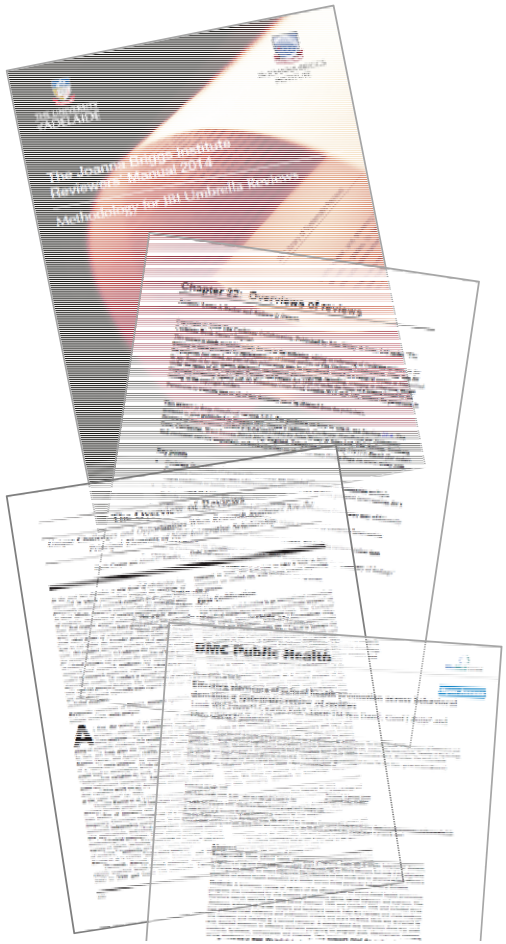
Limit yourself to high quality reviews clearly in line with your research interest, but potentially miss out on relevant studies

Be more inclusive and comprehensive, but spend more time and money

A few words of advice

- ✓ Decide in advance **what is important** to you (and **what is feasible**)
- ✓ Think about the **different levels of data** (i.e. your review, the included reviews, the included primary studies) when defining inclusion criteria, assessing quality, extracting data, etc.
- ✓ It's **easier to 'lump' than to 'split'** - consider not only what your funder is interested in but also what evidence is actually likely to be available
- ✓ Anticipate potential challenges and **set up rules** in advance for how you will handle them

Additional guidance



- The Joanna Briggs Institute Reviewers' Manual 2014, Methodology for JBI Umbrella Reviews: http://joannabriggs.org/assets/docs/sumari/ReviewersManual-Methodology-JBI_Umbrella%20Reviews-2014.pdf
- Cochrane Handbook for Systematic Reviews of Interventions, Chapter 22, Overviews of reviews: http://handbook.cochrane.org/chapter_22/22_overviews_of_reviews.htm

- Methodological journal articles
- Existing reviews of reviews! (especially project reports)

Why you should care *even if you don't intend to conduct such a review*

Understanding the challenges and processes involved

will help you to appraise potential weaknesses and strengths

of published/submitted articles

Some useful links

Cochrane methods handbook: http://handbook.cochrane.org/

Joanna Briggs Institute handbook: http://joannabriggs.org/assets/docs/sumari/ReviewersManual-2014.pdf

Joanna Briggs Institute methods for umbrella reviews: http://handbook.cochrane.org/

CASP critical analysis tools: http://www.casp-uk.net/#!casp-tools-checklists/c18f8

EPHPP quality assessment tools: http://www.ephpp.ca/tools.html

PRISMA (reporting systematic review guidelines): http://www.prisma-statement.org/