Systematic reviews in public health

Geoffrey Setswe MPH, DrPH

DrPH Seminar, University of Limpopo

School of Public Health

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Concepts

- A **systematic review** is an overview of *primary studies* that used *explicit* and *reproducible* methods

- A **meta-analysis** is a mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis in the same way

- Although meta-analysis can increase the *precision* of a result, it is important to ensure that the methods used for the review were *valid* and *reliable*

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What is a Cochrane Review?

- People in the CC hunt through electronic databases and health care journals, looking for clinical trials of all health care treatments and interventions.

- They sort out which are good reliable studies, and summarise results in a Cochrane review. The reviews are published and CD-ROM four times a year.

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Aim of a systematic review

- The aim of a systematic review is to systematically and thoroughly assess the best possible scientific evidence about the effects of a health care intervention.

- Everything about the review should aim to minimise the possibility of ending in a biased conclusion.

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Misconceptions about systematic reviews

- Systematic reviews can include only RCT's;

- They are of value only for assessing the effectiveness of health care interventions;

- They must adopt a biomedical model;

- They have to entail some form of statistical synthesis

- Systematic reviews are of no relevance to the real world

- Systematic reviews are simply "bigger," and glorified literature searches

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Advantages of systematic reviews

• Explicit methods limit bias in identifying and rejecting studies

• Conclusions are more reliable and accurate because of methods used

•Large amounts of information can be assimilated quickly by healthcare providers, researchers, and policymakers

• Delay between research discoveries and implementation of effective diagnostic and therapeutic strategies may be reduced

• Results of different studies can be formally compared to establish generalisability of findings and consistency (lack of heterogeneity) of results

• Reasons for heterogeneity (inconsistency in results across studies) can be identified and new hypotheses generated about particular subgroups

•Quantitative systematic reviews (meta-analyses) increase the precision of the overall result

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Methodology for a systematic review

State objectives of the review of RCTs and outline eligibility criteria

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Search for trials that seem to meet eligibility criteria

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Tabulate characteristics of each trial identified and assess its methodological quality

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Apply eligibility criteria, and justify any exclusions

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Assemble the most complete dataset feasible, with assistance from investigators, if possible

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Analyse results of eligible RCTs, using statistical synthesis of data (meta-analysis) if appropriate and possible

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Compare alternative analyses if appropriate and possible

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Prepare a critical summary of the review, stating aims, describing materials and methods, and reporting results
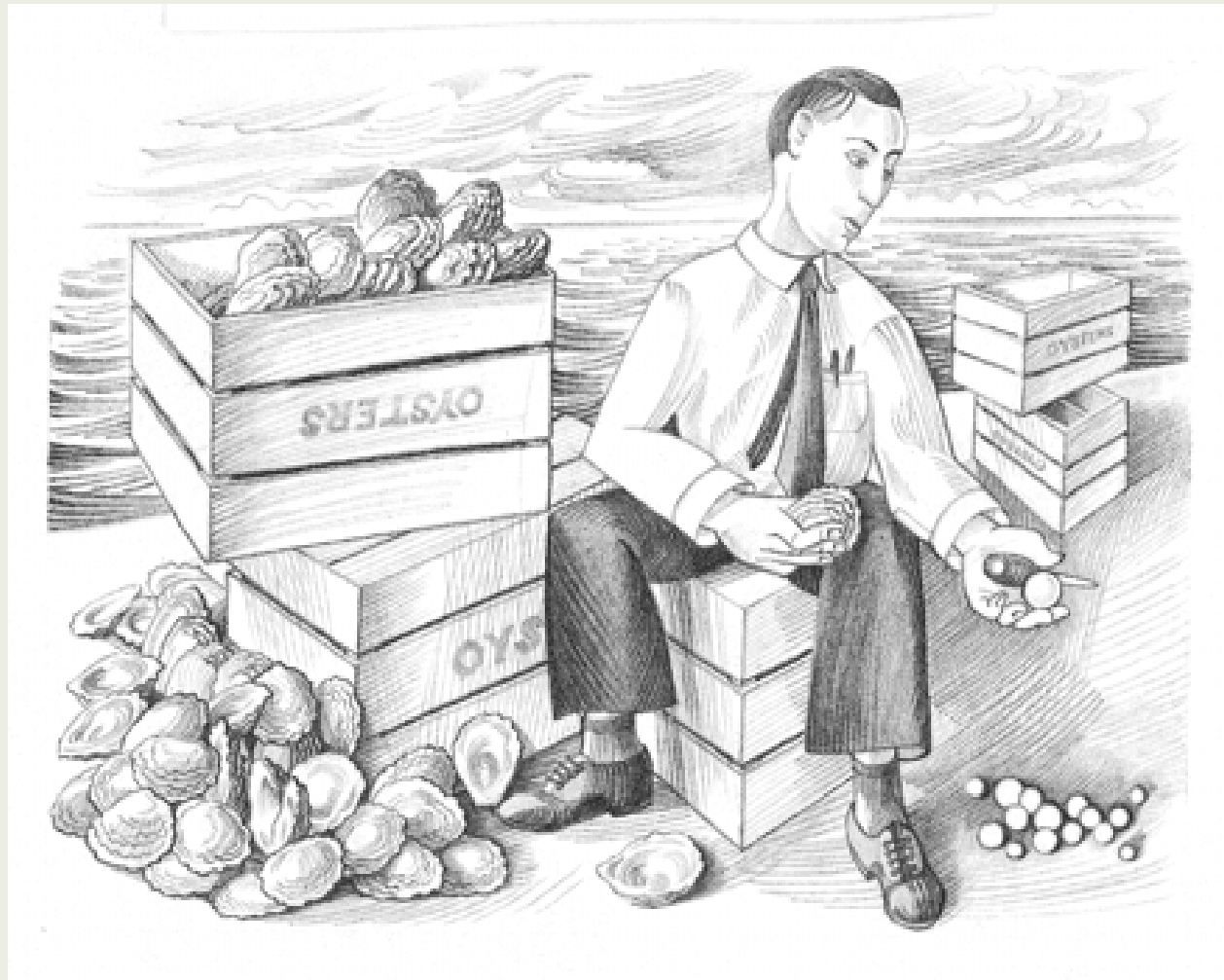
Checklist of data sources for a Systematic review

- Medline database
- Cochrane controlled clinical trials register
- Other medical and paramedical databases
- Foreign language literature
- "Grey literature" (theses, internal reports, non-peer reviewed journals, pharmaceutical industry files)
- References (and references of references, etc) listed in primary sources
- Other unpublished sources known to experts in the field (seek by personal communication)
- Raw data from published trials (seek by personal communication)

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Assigning weight to trials in a systematic review

Each trial should be evaluated in terms of its:

- Methodological **quality**—the extent to which the design and conduct are likely to have prevented systematic errors (bias)
- **Precision**—a measure of the likelihood of random errors (usually depicted as the width of the confidence interval around the result)
- **External validity**—the extent to which the results are generalisable or applicable to a particular target population
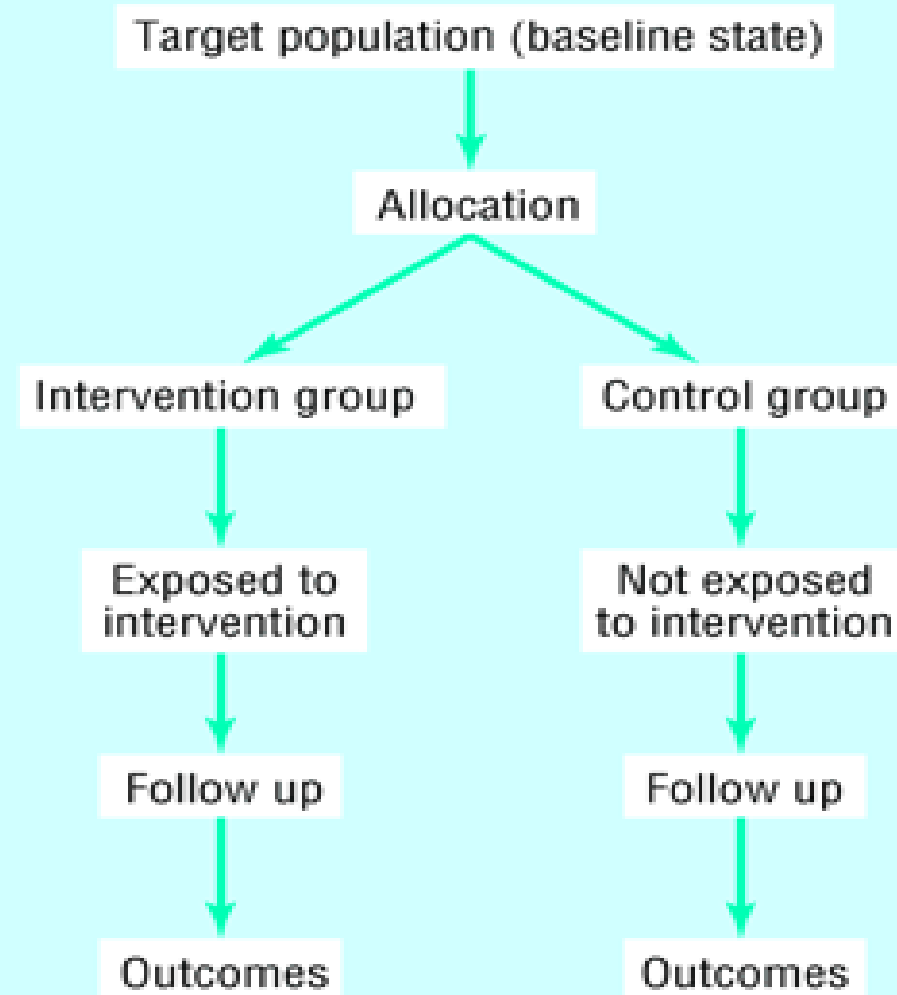
Assessing methodological quality of published papers

Essential questions to ask about the methods section of a published paper are:

1. Was the study **original**?

2. **Whom** is the study about?

3. Was the **design** of the study **sensible?**

4. Was **systematic bias avoided** or minimised?

5. Was the study large enough, and continued for long enough, to make the **results credible?**

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Sources of bias to check for in a RCT

Selection bias (systematic differences in the comparison groups attributable to incomplete randomisation)

Performance bias (systematic differences in the care provided, apart from the intervention being evaluated)

Exclusion bias (systematic differences in withdrawals from the trial)

Detection bias (systematic differences in outcome assessment)

Target population (baseline state)

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Allocation

Intervention group   Control group

Exposed to intervention   Not exposed to intervention

Follow up   Follow up

Outcomes   Outcomes

Group Exercise

Read the RCT on male circumcision (MC) and work in groups to review the following characteristics:

Group 1: Methods
- How was randomization done?
- Was blinding done? Yes No Unclear
- If Yes, was it Provider, Participants, Assessor?
- Calculate loss to follow-up (overall; treatment/control)

Group 2: Participants
- Inclusion criteria (e.g gender, HIV status; age)
- Exclusion criteria
- Numbers in treatment group
- Numbers in control group

Group 3: Outcomes
- Mortality, infections, etc
- How was assessment done

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Examples of systematic reviews

Review question	Methods	Authors' conclusions
Does spending more money on schools improve educational outcomes?	Meta-analysis of effect sizes from 38 publications[w1]	Systematic positive relation between resources and student outcomes
Do women or men make better leaders?	Review of organisational and laboratory experimental studies of relative effectiveness of women and men in leadership and managerial roles[w2]	Aggregated over organisational and laboratory experimental studies in sample, male and female leaders were equally effective

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How to Conduct a Cochrane HIV/AIDS Systematic Review

Before getting started, read through
o *Completing a review with the Cochrane HIV/AIDS Group* and the
o *Cochrane Collaboration Open Learning Material for Reviewers*

o Identify a *focused 4-part review topic (Patient, Intervention, Comparison, Outcome)*
o Complete a *Systematic Review Registration Form*
o Submit form to *Editorial Base*

o Wait for title approval and registration ID from editorial base after submission
o Identify co-reviewer(s) or work with editorial base to identify co-reviewers

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Download latest version of *Review Manager (RevMan)* software a
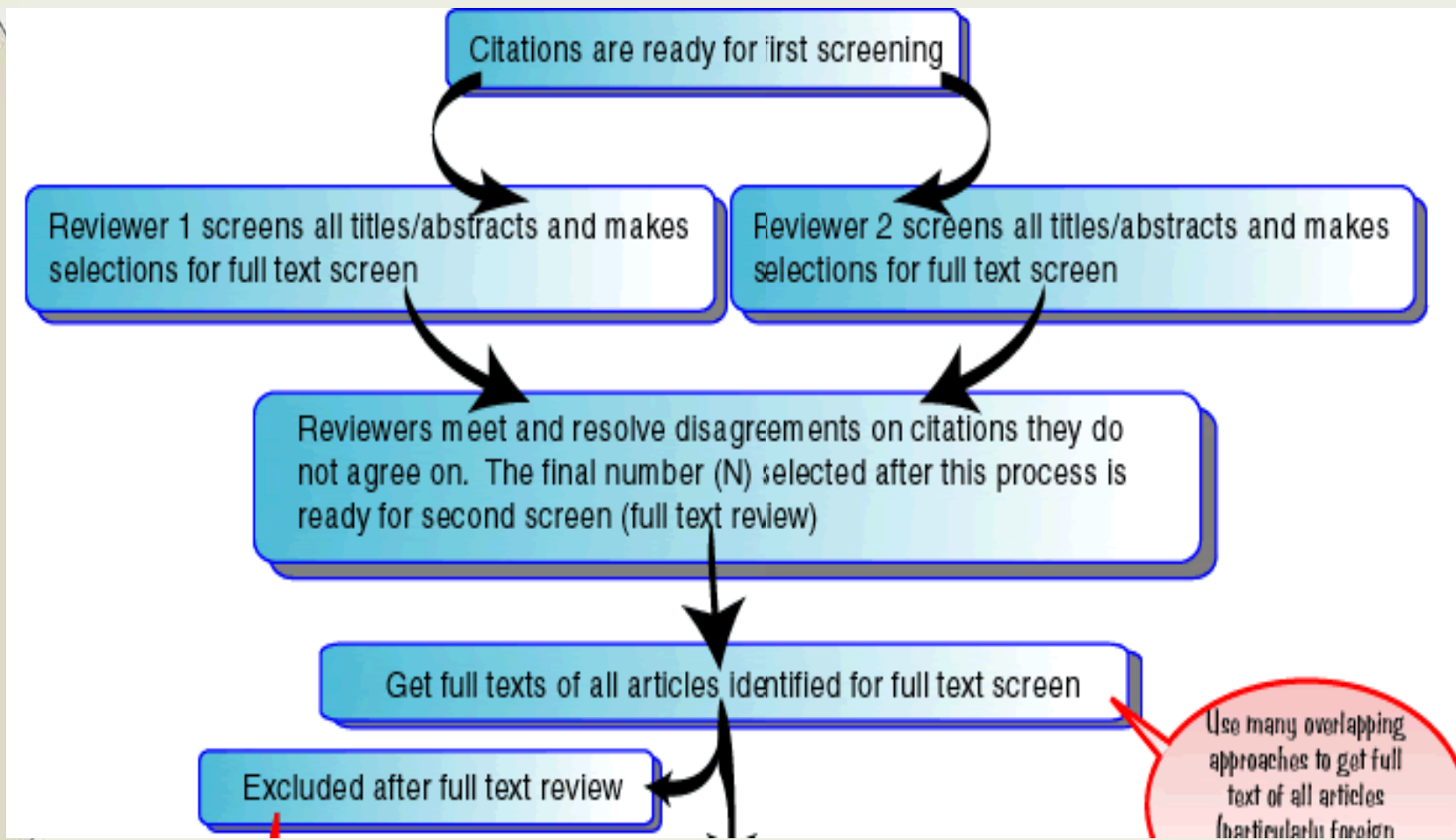Reviewer's Handbook

Identify appropriate databases/sources to search including: *Pubmed*, *Embase*, *AIDSTRIALS*, *AIDSDRUGS*, *Cochrane Library*, *LILACS*, *Web of Science*, *BIOSIS*, and the *York Checklist of Databases*

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Consult *'Classification of Study Designs'* to determine the types of studies to be included in review. Read *Editorial Guidelines on the Inclusion and Appraisal of Experimental and Observational Studies*.

Prepare a Protocol in RevMan and submit to the **Editorial Base** for peer review

Conduct database searches, check bibliographies of identified studies for new studies, contact authors and experts for additional studies

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Articles considered eligible after full text review is the final set of studies for inclusion

(handsearching foreign journals); this takes time and effort.

Excluded from the final analysis

Keep a log of excluded studies (at this stage on) with reasons for exclusion - enter in 'Table of 'Excluded Studies' in RevMan

Included in the final analysis
Each article gets a unique ID number

Contact authors for missing data

Reviewer 1 extracts data (including quality assessment) from the final selected articles

Reviewer 2 extracts data (including quality assessment) from the final selected articles

Reviewers meet and resolve disagreements on data
Compute inter-reliability - see *website for computing Kappa statistics*

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See sample data extraction forms based on study design. For other forms & checklists, go to www.medepi.org/meta

See quality assessment checklist based on study design: Interventional Study, Cohort, Case Control

o Enter data into RevMan
o Tabulate study characteriss and quality information
o Look for Heterogeneity
o Pool data if appropriate
o Explore possibility of publition bias

Use additional guidlines for completing review: QUORUM (for RCT data) and MOOSE (for observational data)

Complete all sections of RevMan and submit final review to **Editorial Base** for peer review

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Reference

Egger M, Smith GD and Altman DG (2001) Systematic reviews in health care: Meta-analysis in context

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