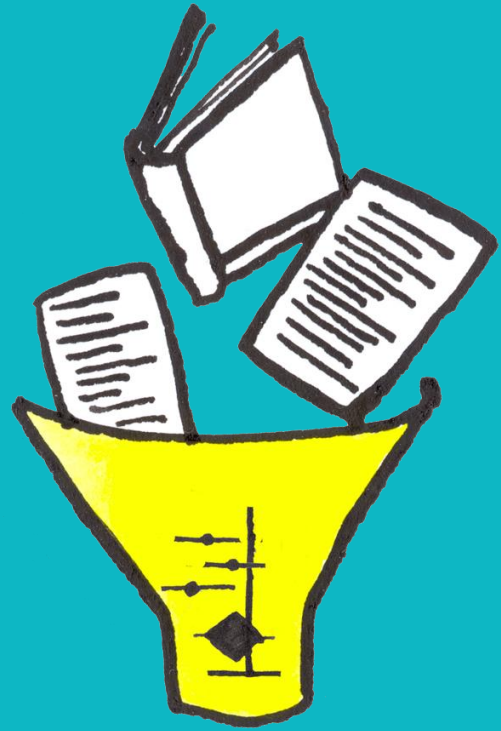


INTRODUCTION TO SYSTEMATIC REVIEW & META-ANALYSIS



LEARNING OBJECTIVES

- ▶ Describe the steps in conducting a systematic review
- ▶ Develop an answerable question using the “Participants Interventions Comparisons Outcomes” (PICO) framework
- ▶ Describe the process used to collect and extract data from reports of clinical trials
- ▶ Describe methods to critically assess the risk of bias of clinical trials
- ▶ Describe and interpret the results of meta-analyses

*You can have data without
information, but you cannot
have information without data*

”

Daniel Keys Moran

SYSTEMATIC REVIEW



Systematic Review uses explicit methods to Identify, Select, Appraise and Synthesise results from similar but separate studies

WHY TO DO SYSTEMATIC REVIEW?

- ▶ Sheer volume of literature : Millions of articles published in thousands of journals each year.
- ▶ Practitioners and Researchers are busy: Saving time doing exhaustive literature researches
- ▶ Subjective summaries may misrepresent results
- ▶ It aims to answer specific questions, reduce uncertainties and identify outstanding questions

IMPORTANCE OF SYSTEMATIC REVIEW

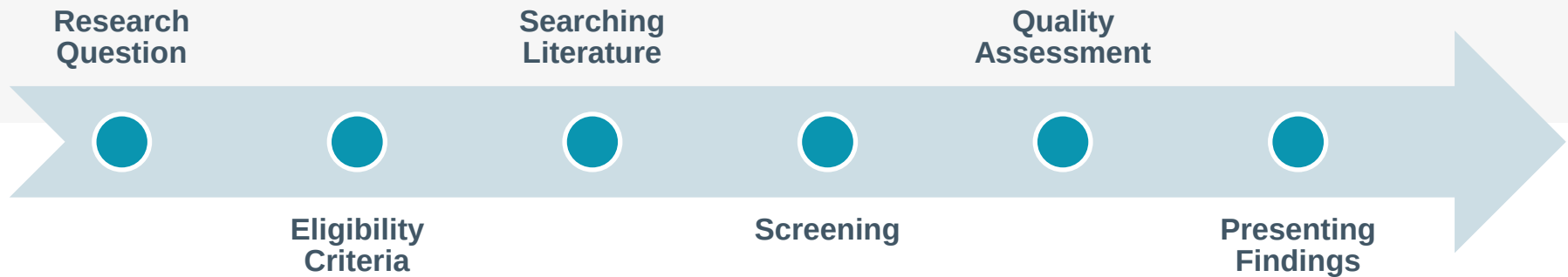
- ▶ Summarizes Knowledge
- ▶ Less Bias : Transparent and Reproducible
- ▶ More Power
- ▶ Source for Evidence-based Practices

WHAT IS THE DIFFERENCE BETWEEN A SYSTEMATIC REVIEW AND TRADITIONAL LITERATURE REVIEW ?

Systematic Review v/s Literature Review

	SYSTEMATIC REVIEW	LITERATURE REVIEW
EVIDENCE	HIGH EVIDENCE	LOW EVIDENCE
METHOD	SYSTEMATIC STEPS ACCORDING TO A DETAILED PROTOCOL	EXPERT OPINION “NO PROTOCOL AND NO SYSTEMATIC STEPS”
BIAS	LOW	HIGH
REPRODUCIBILITY	YES	NOT REPRODUCIBLE
SCOPE	NARROW SCOPE	WIDE SCOPE

STEPS IN CONDUCTING SYSTEMATIC REVIEW



1. FORMULATING THE RESEARCH QUESTION

- ▶ Specific “Narrow Scope”: Each type of question requires a different type of research
- ▶ Components of a “well-structured: & “answerable” question: PICO
 - ▶ P: Population or Patient
 - ▶ I : Intervention/Exposure
 - ▶ C: Comparison group/s
 - ▶ O: Outcome
- ▶ Supported by clear eligibility criteria

2. DEFINE ELIGIBILITY CRITERIA

- ▶ Criteria based on which you decide to include some studies and exclude some studies



Inclusion
Criteria



Exclusion
Criteria

MAJOR DOMAINS OF ELIGIBILITY CRITERIA

- ▶ POPULATION : Age Range? Minimum Sample Size? Gender? Definition of Condition? Disease stage?
- ▶ Intervention : Form of drug? Mode of administration? Dose? Etc.
- ▶ Comparison Group/s : Placebo ? Or standard therapy? Or no treatment?
- ▶ Outcome : Efficacy measured on (../../....), Safety “reporting adverse events”....
- ▶ Study design: Interventional? Randomized or Quasi-Experimental? Observational? Prospective or Retrospective? Minimum follow-up duration?

3. SEARCHING LITERATURE & SCREENING

For Systematic Review searches we use controlled vocabulary and keywords

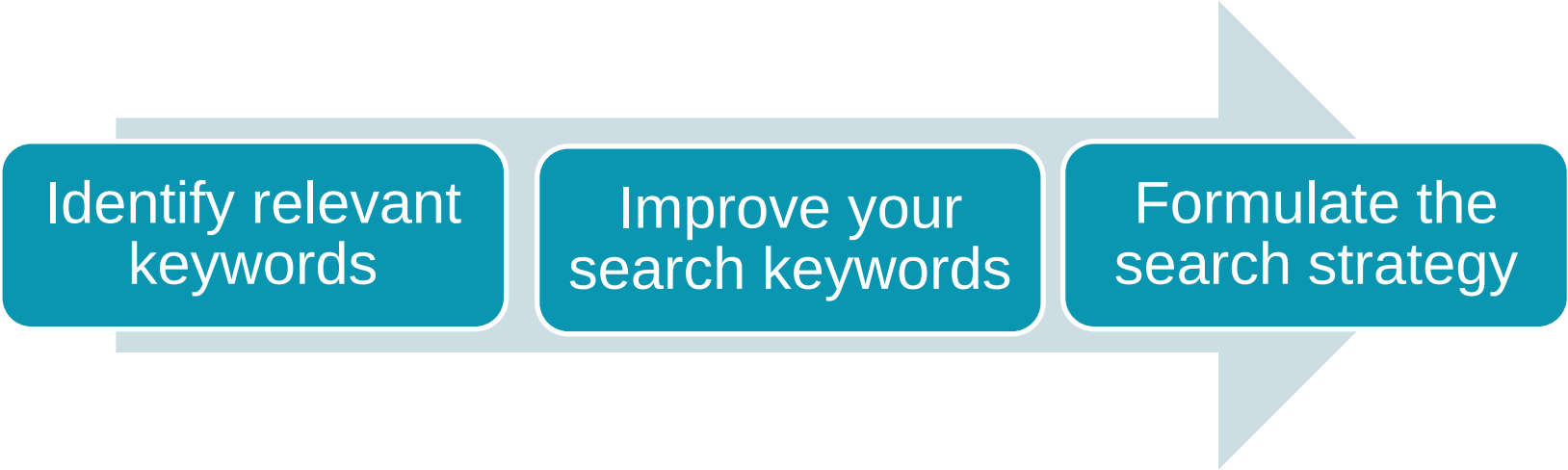


**MEDICAL ELECTRONIC
DATABASES**
Eg:
PubMed, Embase, Scopus

**TRIAL
REGISTERS, GRAY
LITERATURE
SEARCHING**

**PERSONAL
CONTACTS/HAND
SEARCHING &
SNOWBALLING**

- ▶ Try to involve all studies relevant to your research question
- ▶ Search multiple databases
- ▶ Seek help from experts in your speciality



Identify relevant
keywords

Improve your
search keywords

Formulate the
search strategy

4. QUALITY ASSESSMENT

- ▶ One looks to include only “high quality” studies in the Systematic Review and Meta-Analysis
- ▶ **Studies included in Systematic Review and Meta Analysis should be unbiased or minimize the bias in the studies one selects to improve its quality.**
- ▶ **Three main types of biases are:**
 - 1. Selection Bias**
 - 2. Publication Bias**
 - 3. Information Bias**
 - 4. Bias in Analysis**

Studies included in Systematic Review and Meta Analysis should be unbiased or minimize the bias in the studies one selects. Four main types of biases are:

▶ **Selection Bias**

- ▶ It refers to the bias in how treatment was assigned
- ▶ It could mean no randomized sequence was generated or the trial was not randomized
- ▶ It could also mean that even if the trial is randomised, it was not concealed from those who would be doing the assignment i.e. allocation concealment was not done.

INFORMATION BIAS

- ▶ **Information bias** refers to getting misinformation from the participant of the study(patient/clinician)in the data collection form given in the course of the study.
- ▶ Major types of **information bias** are misclassification **bias**, observer **bias**, recall **bias** and reporting **bias**.

REPORTING BIAS

- ▶ Publication Bias: Due to Unpublished/Unauthenticated studies or unrepresentative sampling in the studies.
- ▶ Selective Outcome Reporting or Ascertainment Bias also decreases quality of the analysis.

INCLUSION BIAS AND BIAS IN ANALYSIS

- ▶ Pre-setting of the eligibility criteria for favourable results by the Authors of the Systematic Review or to differentially submit manuscripts for publications to suit the direction/strength of the findings by reviewers lead to **inclusion bias**.
- ▶ **Bias In Analysis** is a result of Losses to follow-up, Non-compliance, withdrawals or Changes in the outcome measure (post-hoc defined outcome i.e. the investigators are changing the outcome of the study either innocently or based on the results they are getting)

QUALITATIVE v/s QUANTITATIVE ASPECTS OF A SYSTEMATIC REVIEW

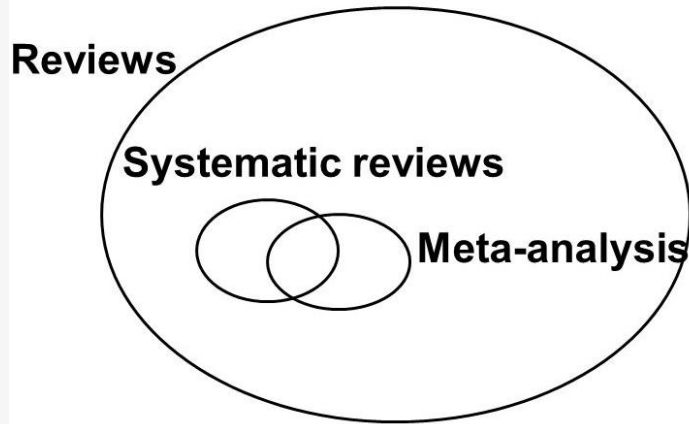
QUALITATIVE ANALYSIS

- ▶ Most important part of a systematic review.
- ▶ Are the studies similar or different?
- ▶ Are the study participants comparable?
- ▶ Are the interventions homogenous across studies included ?
- ▶ Are the studies designed, conducted and reported properly?

QUANTITATIVE ANALYSIS

- ▶ It involves statistical analysis of studies or Meta-Analysis
- ▶ How many studies were assessed?
- ▶ Reasons for excluding studies?
- ▶ Range of study sizes and treatment compared?

META-ANALYSIS



A particular type of systematic review that uses quantitative methods to combine the results from a number of studies.

Note: Not All Systematic Reviews will have the component of Meta-Analysis

- ▶ Meta-Analysis is an optional component of a Systematic Review.
- ▶ It is a statistical analysis which combines the results of several independent studies considered by the analyst to be “combinable”.
- ▶ We can also use Meta-analysis to investigate the heterogeneity in the studies i.e. examine the reasons for different results among mostly similar studies

WHY DO META-ANALYSIS??

- ▶ Studies are estimating-in whole or in part –a common effect.
- ▶ Studies are addressing the same fundamental biological/clinical/mechanistic question

ADVANTAGES OF A META-ANALYSIS

- ▶ Increase Power and Precision of the results from various studies
- ▶ Produce a precise effect estimate
- ▶ Answer questions not posed by individual studies
- ▶ Assess Homogeneity/ Heterogeneity of results
- ▶ Settle controversies arising from conflicting studies

CONCLUSIONS

- ▶ Systematic Reviews uses pre-specified and rigorous methods to identify, appraise and synthesize all evidences on a given topic.
- ▶ Reviewers should minimize bias and errors at each step.
- ▶ The most crucial step is framing an answerable question(PICO).
- ▶ Searching for studies should be comprehensive
- ▶ Risk of Bias assessment helps determine how trustworthy the evidence is.
- ▶ Always conduct qualitative synthesis: when appropriate



THANKS!