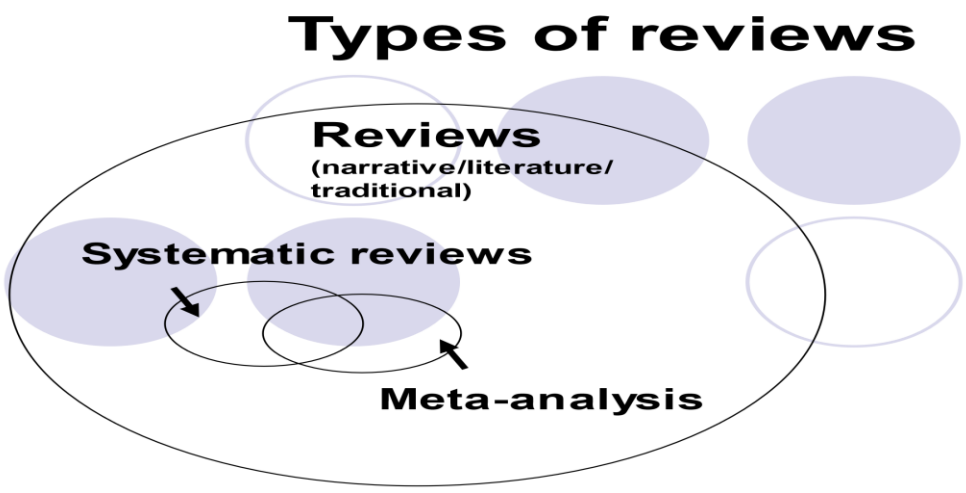
Systematic Reviews and Meta-analysis- lecture 2

Overview-https://training.cochrane.org/interactivelearning/

- Introduction to conducting systematic reviews
- Writing the review protocol
- Searching for studies
- Selecting studies and collecting data
- Introduction to study quality and risk of bias
- Analysing the data
- Interpreting the findings
- Reporting the review

Types of reviews



Narrative reviews

- Usually written by experts in the field
- Use informal and subjective methods to collect and interpret information
- Usually narrative summaries of the evidence

What is a systematic review?

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

Key elements of a systematic review

Structured, systematic process involving several steps :

1. Formulate the question
2. Plan the review
3. Comprehensive search
4. Unbiased selection and abstraction process
5. Critical appraisal of data
6. Synthesis of data (may include meta-analysis)
7. Interpretation of results
8. Reporting the review

All steps described explicitly in the review

Systematic vs. Narrative reviews

- Scientific approach to a review article
- Criteria determined at outset
- Comprehensive search for relevant articles
- Explicit methods of appraisal and synthesis
- Meta-analysis may be used to combine data

- DAuthor gets to pick any criteria
- Search any databases
- Methods not usually specified
- Vote count or narrative summary
- Can't replicate review
- epend on authors' inclination (bias)

Advantages of systematic reviews

- Reduce bias
- Replicability
- Resolve controversy between conflicting studies
- Identify gaps in current research
- Provide reliable basis for decision making

Limitations of systematic reviews

- Results may still be inconclusive
- There may be no trials/evidence
- The trials may be of poor quality
- The intervention may be too complex to be tested by a trial
- Practice does not change just because you have the evidence of effect/effectiveness

Asking an answerable question

Types of review questions

- Intervention review
- Diagnostic test accuracy review
- Prognostic review
- Methodological review
- Qualitative review

Questions of interest

Effectiveness:

- Does the intervention work/not work?
- Who does it work/not work for?

Other important questions:

- How does the intervention work?
- Is the intervention appropriate?
- Is the intervention feasible?
- Is the intervention and comparison relevant?

Answerable questions

EFFECTIVENESS

A description of the populations P

وصف السكان

An identified intervention I

تدخل محدد

An explicit comparison C

مقارنة صريحة

Relevant outcome O

النتائج ذات الصلة

A PICO question

Time-consuming question: What is the best strategy to prevent smoking in young people?

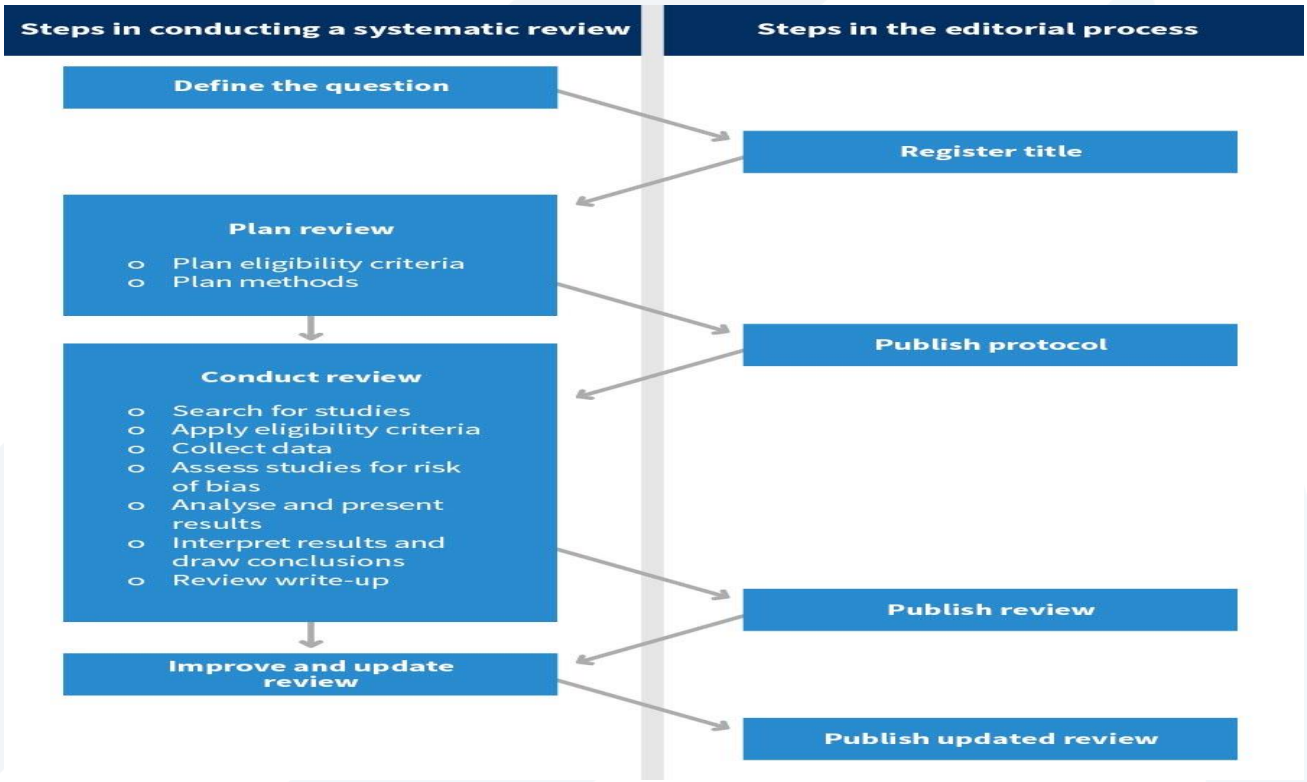
An answerable question: Are mass media *(or school-based or community-based)* interventions effective in preventing smoking in young people?

The PICO(T) chart

Problem, population	**Intervention**	**Comparison**	**Outcome**	**Types of studies**
Young people under 25 years of age	a) Television b) Radio c) Newspapers d) Bill boards e) Posters f) Leaflets g) Booklets	a) School-based interventions b) No intervention	a) objective measures of smoking (saliva thiocyanate levels, alveolar CO) b) self-reported smoking behaviour c) Intermediate measures (intentions, attitude, knowledge, skills) d) Media reach	a) RCT b) Controlled before and after studies c) Time series designs

Finding the evidence

Steps in the process



Writing the review protocol:

- Ensuring transparency ضمان الشفافية
- Ensuring accountability ضمان المساءلة
- Avoiding duplication-PROSPERO تجنب الازدواجية

Writing the Background section of the protocol:

The Background section of the protocol should put your review in the context of what you already know, and the questions you want to answer.

The Objectives section:

- Single sentence

- Derived from the research question
- Should relate to the PICO elements
- In particular the population, intervention and comparison
- **Stay focused on the question**

Planning the review methods:

- Describe planned methods in details but keep it short
- Use the Cochrane Handbook, and it's guidance based on the latest methodological research
- Anticipate finding sufficient studies
- Keep broad inclusion criteria, and be cognizant of rationale for exclusion

Considerations for your protocol

Study selection
- whether two authors will independently assess studies;
- process of assessment (e.g. screening abstracts, then full text);
- how disagreements will be managed;
- any other methods used to select the studies (including the use of software).

Data collection
- data categories to be collected;
- whether two authors will independently collect data;
- piloting and use of instructions for data collection form;
- how disagreements will be managed;
- what attempts will be made to obtain or clarify data from study authors;
- processes for managing missing data.

Systematic review process:

1. Well formulated question

2. Comprehensive data search
3. Unbiased selection and abstraction process
4. Critical appraisal of data
5. Synthesis of data
6. Interpretation of results

A good search:

- ✓ Clear research question
- ✓ Comprehensive search
  - ○ All domains, no language restriction, unpublished and published literature, up-to-date
- ✓ Document the search (replicability)

Components of electronic searching

1. Describe each PICO component
2. Start with primary concept
3. Find synonyms
   a) Identify MeSH / descriptors / subject headings
   b) Add textwords
4. Add other components of PICO question to narrow citations *(may use study filter)*
5. Examine abstracts
6. Use search strategy in other databases (may need adapting)

So you want to do a 'quick & dirty'?

- DARE

- CENTRAL
- PubMed (clinical queries, related records)
- CDC
- NICE
- Organisations who do work in your area
- References
- GOOGLE!!!!

Different bibliographic databases

- Databases use different types of controlled vocabulary
    - Same citations indexed differently on different databases
    - Medline and EMBASE use a different indexing system for study type
    - PsycINFO and ERIC do not have specific terms to identify study types

Need to develop search strategy for each database

Study design filters:

- RCTs
    - See Cochrane Reviewer's Handbook
- Non-RCTs
    - Not yet developed, research in progress
- Qualitative research
    - Specific subject headings used in CINAHL, 'qualitative research' used in Medline
    - CINAHL Filter: Edward Miner Library

http://www.urmc.rochester.edu/hslt/miner/digital_library/tip_sheets/Cinahl_eb_filters.pdf

- Systematic reviews/meta-analyses
  - CINAHL: as above
  - Medline http://www.urmc.rochester.edu/hslt/miner/digital_library/tip_sheets/OVID_eb_filters.pdf
  - Medline and Embase

http://www.sign.ac.uk/methodology/filters.html

  - PubMed

1. **Unpublished literature:**
   - Not all known published trials are identifiable in Medline (depending on topic)
   - Only 25% of all medical journals in Medline
   - Non-English language articles are under-represented in Medline (and developing countries)
   - Publication bias – tendency for investigators to submit manuscripts and of editors to accept them, based on strength and direction of results (Olsen 2001)
2. **Unpublished literature:**
   - Hand searching of key journals and conference proceedings
   - Scanning bibliographies/reference lists of primary studies and reviews
   - Contacting individuals/agencies/ academic institutions
     - Neglecting certain sources may result in reviews being biased

Sources

Type of information/ resource	Completion/publication status			
	Ongoing	Completed	Published	Unpublished (or grey literature only)
Trials registers	✓	✓	✓	✓
Clinical study reports	✓	✓		✓
Studies identified by colleagues	✓	✓	✓	✓
Dissertations/ theses		✓		✓
Conference abstracts/ proceedings	✓	✓		✓

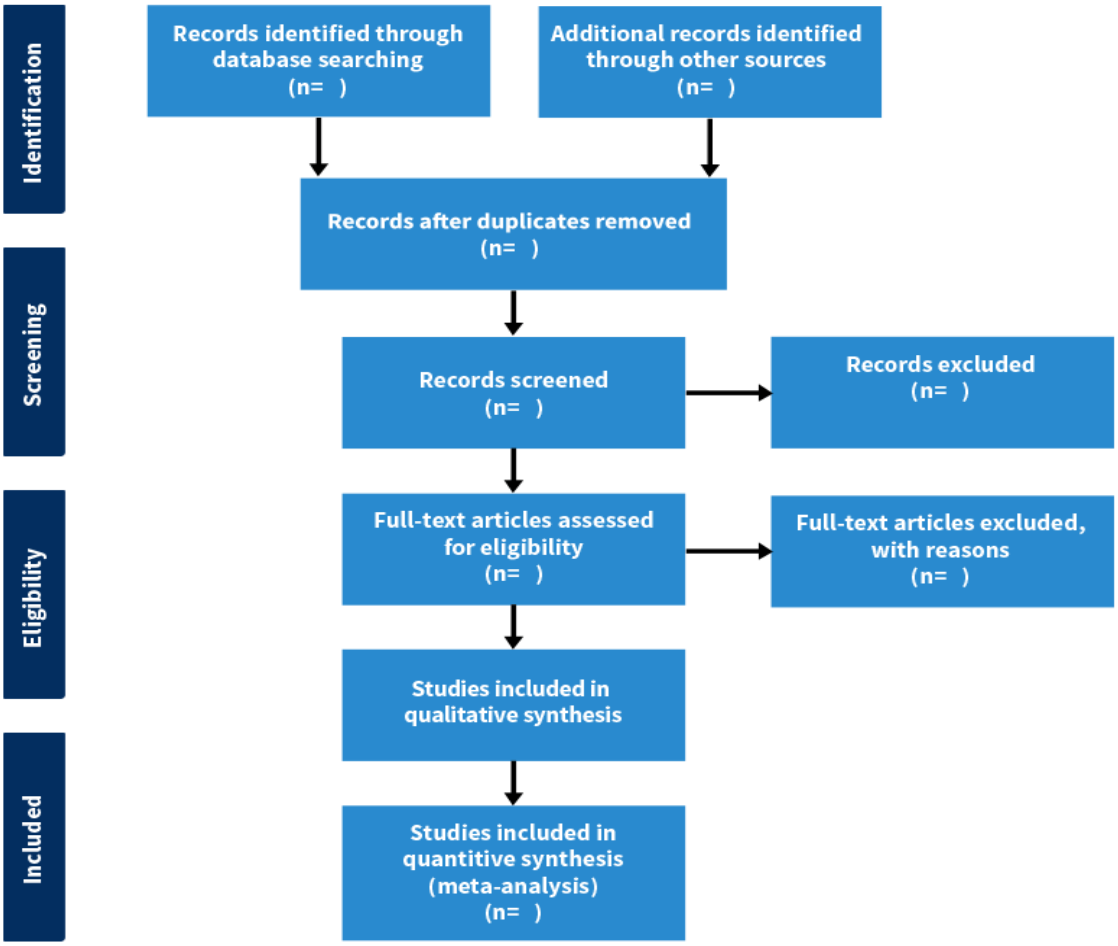
Managing the references:

- Endnote
- Zotero, etc
- Organize your search results, and to identify and remove any duplicate
- Reasons for exclusion
- Importing references to analytic software

Selecting studies

- Keep accurate records and track
- give a summary of the total number of records identified in your search
- identify the number excluded at each stage of the screening process
- provide reasons for any articles excluded when assessed in full text
- present a PRISMA flow diagram.
- Keeping records complete

PRISMA Statement



Minimizing bias in selection

- Pre-specified inclusion criteria
- Considering study design as inclusion criterion
- Independent study selection
- At least two people
- Kappa statistic

Assessing risk of bias in included studies

Type of bias	Description	Relevant domains in the Collaboration's 'Risk of bias' tool
Selection bias.	Systematic differences between baseline characteristics of the groups that are compared.	• Sequence generation. • Allocation concealment.
Performance bias.	Systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.	• Blinding of participants and personnel. • Other potential threats to validity.
Detection bias.	Systematic differences between groups in how outcomes are determined.	• Blinding of outcome assessment. • Other potential threats to validity.
Attrition bias.	Systematic differences between groups in withdrawals from a study.	• Incomplete outcome data
Reporting bias.	Systematic differences between reported and unreported findings.	• Selective outcome reporting

Bias due to missing data

- Type of missing data
- Reason for missing data
- Intention to treat analysis

- Address with-
- Sensitivity analysis
- Leave-one-out analysis
- Imputed data

Analyzing the data:

- 'Doing a meta-analysis is easy, doing one well is hard.'
- Three of the most common effect measures for a dichotomous outcome are:
- risk ratios (also known as relative risk);
- odds ratios;
- risk difference (also known as absolute risk reduction).

Risk ratio

- To calculate the risk ratio (RR), take the risk in the intervention group, and divide it by the risk in the control group.
- Risk is calculated by dividing the number of events by the total number of people in a group.

Odds ratio:

- The odds ratio (OR) takes the odds of an event in the intervention group, and divides them by the odds in the control group.
- Odds are calculated by dividing the number of events by the number of non-events.

Risk difference:

- RD is an absolute measure, giving you the absolute difference between the risks in each group.
- Assess risk (events/total no. of population) in the intervention group, and subtract the risk in the control group.

Combining the data:

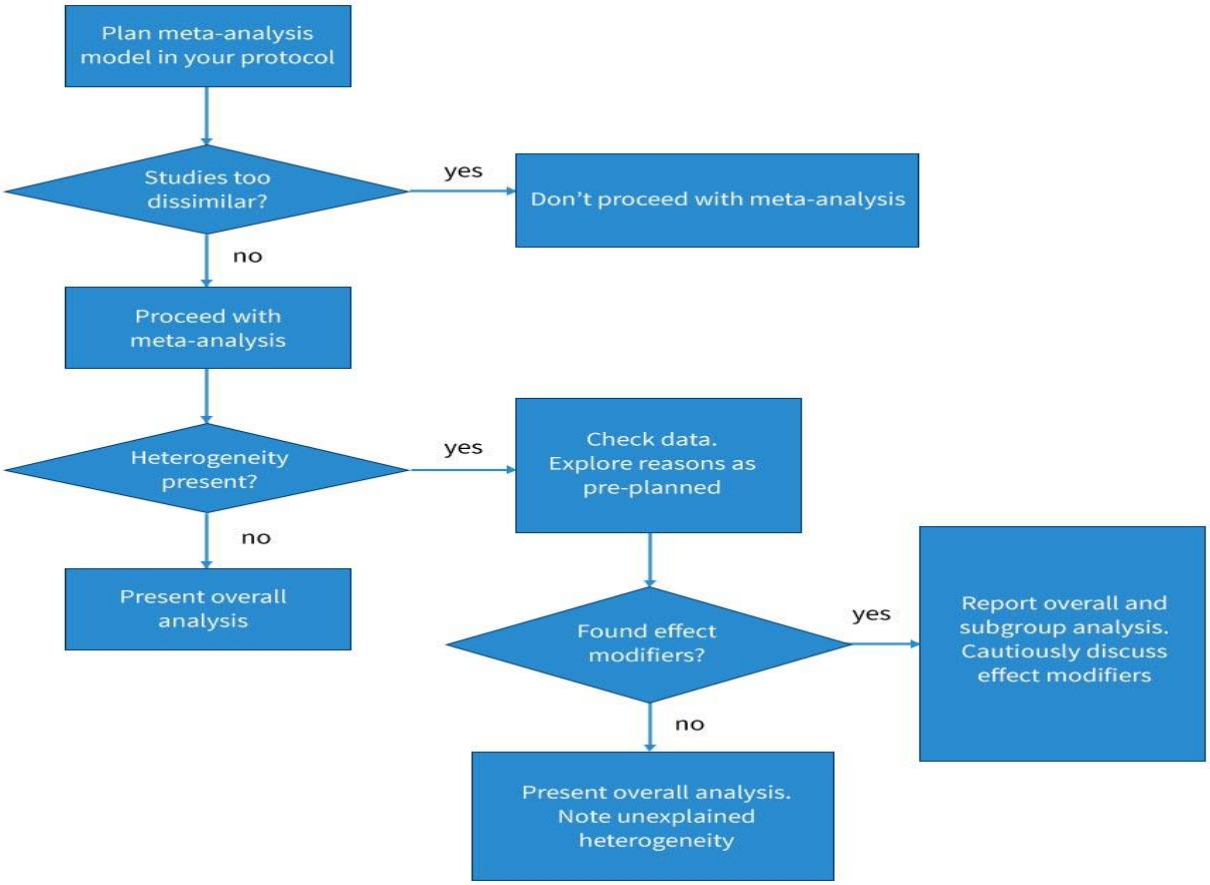
- Step 1: Identify comparisons
- Pairwise comparisons
- Step 2: Identify outcomes and effect measures
- Step 3: Collect data from each relevant study
- Step 4: Combine the results to obtain the summary of effect
- Step 5: Choosing a statistical method

Heterogeneity:

- Heterogeneity means variation or differences across studies.
- clinical; methodological; statistical.
- There are three tools you can use to identify heterogeneity: a visual inspection of the forest plot;
- the Chi-squared (χ^2, or Chi^2) test, otherwise known as the Q test;

  the I^2 statistic.

Dealing with heterogeneity:



Subgroup analysis:

- Sensitivity analysis vs Subgroup analysis
- First, while some sensitivity analyses might analyse a subgroup of studies, they do not attempt to estimate the effect of the intervention in the excluded studies. In subgroup analyses, estimates are produced for each subgroup.
- Second, in sensitivity analyses, informal comparisons are made between different ways of estimating the same thing, whereas in subgroup analyses, formal statistical comparisons are made between the subgroups.

Studies with more than two groups:

- Focus on relevant interventions
- Shared control group
- Combined intervention arms
- Three separate analyses
- Network meta-analysis
- OBTAIN STATISTICAL HELP