

# Systematic Review and Meta-analysis

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# Content

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- General Overview
  - Review Topic Development
  - Protocol Development
  - Search Strategy
  - Critical appraisal
  - Data Extraction
  - Quantitative Data Synthesis
  - Quantitative Data Synthesis
    - Meta analysis
  - Summary
- Activity 1: Review topic development
- Activity 2: Protocol development
- Activity 3: Searching and selecting studies
- Activity 4: Critical appraisal of articles
- Activity 5: Data extraction
- Activity 6: Searching and selecting articles
- Activity 7: Data Synthesis

# Expected Outcomes

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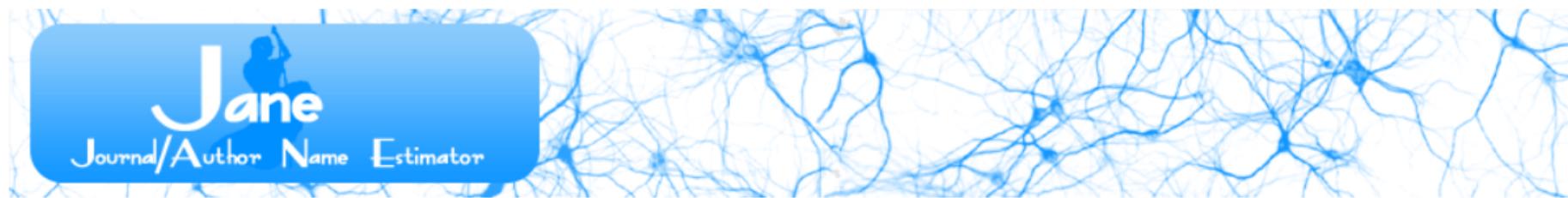
- Basic skill and knowledge on systematic review
  - Qualitative synthesis
- Review question:
  - Draft Protocol will be developed
  - PROSPERO registered protocol
  - Data extraction tool will be developed
  - Data will be extracted from sample articles
- Basic skills and knowledge on meta analysis
  - Quantitative analysis
  - Stata application on Meta analysis
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## Expected Outcomes (Phase II)

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- Draft manuscript
- Journal will be selected
  - <http://jane.biosemantics.org/>
- Manuscript will be submitted for publication
- Policy brief for the institute

# Journal Author Name Estimator (Jane)



Insert your title and/or abstract here: (or, click [here](#) to search using keywords)

Scramble   Clear   Show extra options

[Find journals](#)   [Find authors](#)   [Find articles](#)

## Welcome to Jane

Have you recently written a paper, but you're not sure to which journal you should submit it? Or maybe you want to find relevant articles to cite in your paper? Or are you an editor, and do you need to find reviewers for a particular paper? Jane can help!

Just enter the title and/or abstract of the paper in the box, and click on 'Find journals', 'Find authors' or 'Find Articles'. Jane will then compare your document to millions of documents in *PubMed* to find the best matching journals, authors or articles.

### Keyword search

Instead of using a title or abstract, you can also search using a keyword search, similar to popular web search engines. Click [here](#) to search using keywords.

### Beware of predatory journals

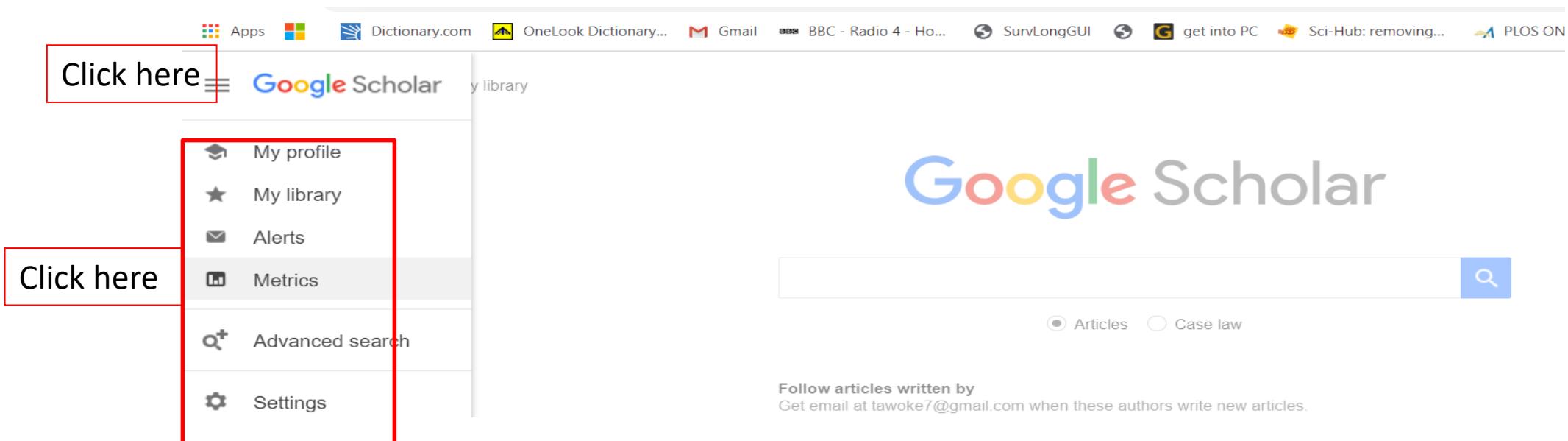
JANE relies on the data in *PubMed*, which can contain papers from predatory journals, and therefore these journals can appear in JANE's results. To help identify high-quality journals, JANE now tags journals that are currently indexed in *MEDLINE*, and open access journals approved by the Directory of Open Access Journals (DOAJ).

[Additional information about Jane](#)

# Option II

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- You can also use “Google scholar” to choose the best journal to submit a manuscript.



# Option II

- Then choose the category of your area of research

Categories	English
Publication	<a href="#">h5-index</a> <a href="#">h5-median</a>
1. Nature	<a href="#">368</a> 546
2. The New England Journal of Medicine	<a href="#">352</a> 603
3. Science	<a href="#">338</a> 511
4. The Lancet	<a href="#">282</a> 464
5. Chemical Reviews	<a href="#">266</a> 443
6. Nature Communications	<a href="#">260</a> 345
7. Advanced Materials	<a href="#">252</a> 342
8. Chemical Society reviews	<a href="#">251</a> 378
9. Cell	<a href="#">250</a> 383
10. IEEE/CVF Conference on Computer Vision and Pattern Recognition	<a href="#">240</a> 383
11. Journal of the American Chemical Society	<a href="#">236</a> 329
12. Proceedings of the National Academy of Sciences	<a href="#">227</a> 303
13. Angewandte Chemie International Edition	<a href="#">221</a> 309
14. Nucleic Acids Research	<a href="#">217</a> 413
15. JAMA	<a href="#">211</a> 330



Categories > Health & Medical Sciences > Subcategories

Subcategories	Health & Medical Sciences (general)	Physical Education & Sports Medicine
Addiction	Heart & Thoracic Surgery	Physiology
AIDS & HIV	Hematology	Plastic & Reconstructive Surgery
Alternative & Traditional Medicine	Hospice & Palliative Care	Pregnancy & Childbirth
Anesthesiology	Immunology	Primary Health Care
Audiology, Speech & Language Pathology	Medical Informatics	Psychiatry
Bioethics	Medicinal Chemistry	Psychology
Biomedical Technology	Molecular Biology	Public Health
Cardiology	Natural Medicines & Medicinal Plants	Pulmonology
Child & Adolescent Psychology	Neurology	Radiology & Medical Imaging
Clinical Laboratory Science	Neurosurgery	Rehabilitation Therapy
Communicable Diseases	Nuclear Medicine, Radiotherapy & Molecular Imaging	Reproductive Health
Critical Care	Nursing	Rheumatology
Dentistry	Nutrition Science	Social Psychology
Dermatology	Obesity	Surgery
Developmental Disabilities	Oncology	Toxicology
Diabetes	Ophthalmology & Optometry	Transplantation
Emergency Medicine	Oral & Maxillofacial Surgery	Tropical Medicine & Parasitology
Endocrinology	Orthopedic Medicine & Surgery	Urology & Nephrology
Epidemiology	Otolaryngology	Vascular Medicine
Gastroenterology & Hepatology	Pain & Pain Management	Veterinary Medicine
Genetics & Genomics	Pathology	Virology
Gerontology & Geriatric Medicine	Pediatric Medicine	
Gynecology & Obstetrics		

# Academics and Research

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- Initiatives for publication

- One of the pillar in academics
- Academic promotion? **Publish or Perish!**
- Collaboration? Scholarships?

- Journals

- Quality of publisher;
  - Impact factor (NEMJ, Nature, Lancet, ...)
  - Indexing
  - Peer reviewed
  - Volume
  - ...

## Publisher

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- New England **Journal** of Medicine (79.258)
- Lancet (London, England) (53.254)
- JAMA (47.661)
- Nature (43)
- .
- .
- Ethiopian journal of health development (AAU)
- Ethiopian journal of health and biomedical sciences (UoG)

# Search Sources

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- **Predatory publishing** is a business model that involves charging publications fees to authors without checking articles for **quality** and **legitimacy** and without providing the other editorial and publishing services associated with legitimate journals
- The University has lists of predatory journals
- Check before submission a manuscript for publication

# Science Scandals

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- Three types of research **misconduct**:
  - Fabrication
  - falsification, and
  - plagiarism
- A Major Publisher scandals and Retracted
  - BMC, the publisher of over 270 peer-reviewed journals, pulled 43 papers earlier this year on account of "fabricated" peer reviews (~16%)
  - Three published papers
    - A young psychologist who studied the effects of motivation and reward on cognitive control is found to have falsified data
  - Altering statistical significance
    - A Case Western Reserve University researcher is found guilty of altering the number of samples and results
  - Clinical trials
    - A researcher working for US pharmaceutical company's Scotland branch is sent to prison for falsifying data on experimental drugs

# Industrial revolutions

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## □ Industrial revolutions:

- The first revolution (1765):
  - ▣ Going from hand to machine production, the increasing use of steam and water power
- Second revolution (1870)
  - ▣ Expansion of electricity, petroleum and steel
- The third Revolution (1920)
  - ▣ Digital technology: Clever software, robots, and a whole range of web-based services
- **The fourth industrial revolution??**
  - ▣ The raw power for the fourth revolution is data
  - ▣ **Data is the new oil!**
  - ▣ Unlike oil, data is created by people, not geology
  - ▣ Can solve so many of the problem:
    - Health
    - Economy
    - Lifestyle, climate, ....

# Data

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- Data are not just numbers, they are numbers with a context
  - In data analysis, context provides meaning
- Context includes who collected the data, how were the data collected, why the data were collected, when and where were the data collected what exactly was collected



# Data

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- We can think of the who, how and why question referring to
  - Pragmatics of data collection
    - is the study of language from the point of view of usage
  - Where and what refer to data semantics
    - study of meaning and is related to both philosophy and logic

# Models

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- Statistics includes the process of finding out about patterns in the real world using data
- When solving statistical problems it is often helpful to make models of real world situations based on;
  - Observed data
  - Assumptions about the context, and
  - Theoretical probability
- The model can then be used to make predictions, test assumptions, and solve problems

# Statistical Modelling

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- "If you torture the data long enough, it will confess." **Ronald H. Coase**
  - We use models to "torture" the data
- Statistical models can be;
  - Deterministic
    - Model parameters are exact
    - $E = mc^2$
    - The output of the model is fully determined by the parameter values and the initial conditions
- Stochastic;
  - Models possess some inherent randomness
  - $$g(y) = \beta_0 + \beta X + \varepsilon_{ij}$$
  - Output has variation
- The natural world is buffeted by stochasticity

# Statistical Modelling

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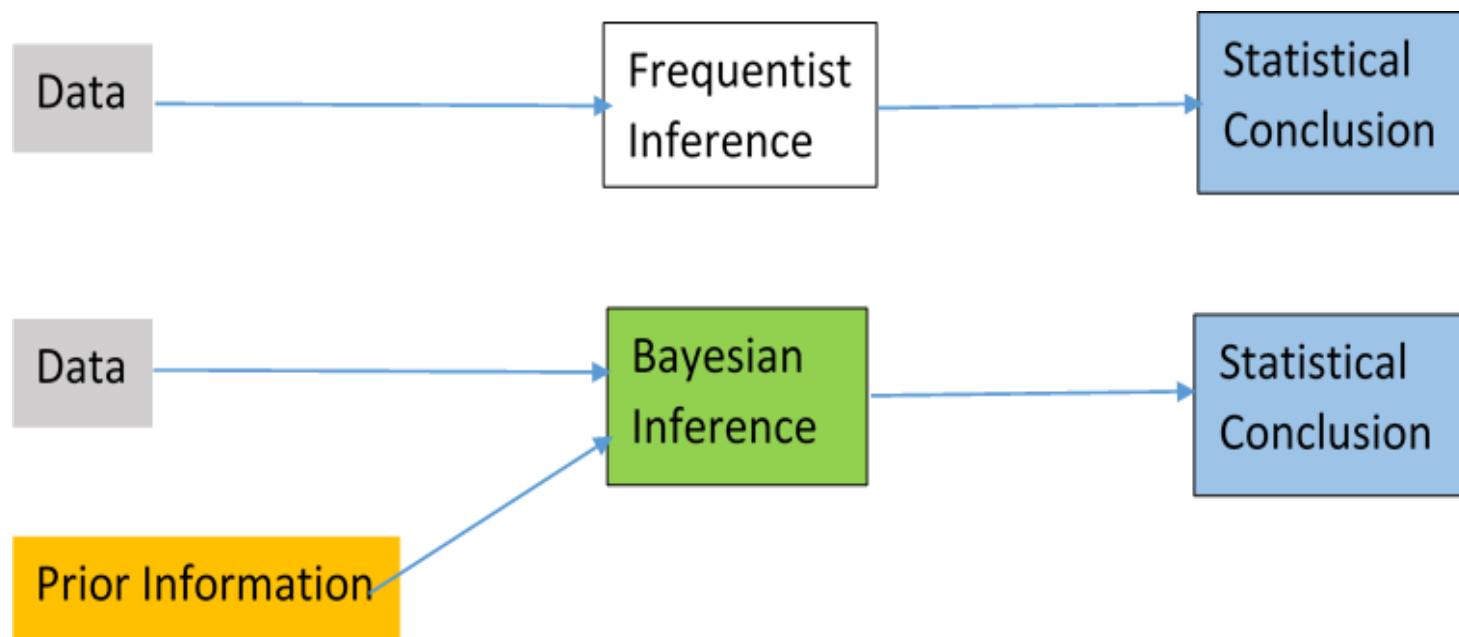
## □ Two Schools of thought in Statistics

### ■ Frequentists

- Parameters are fixed and unknown
- Data is sufficient to estimate

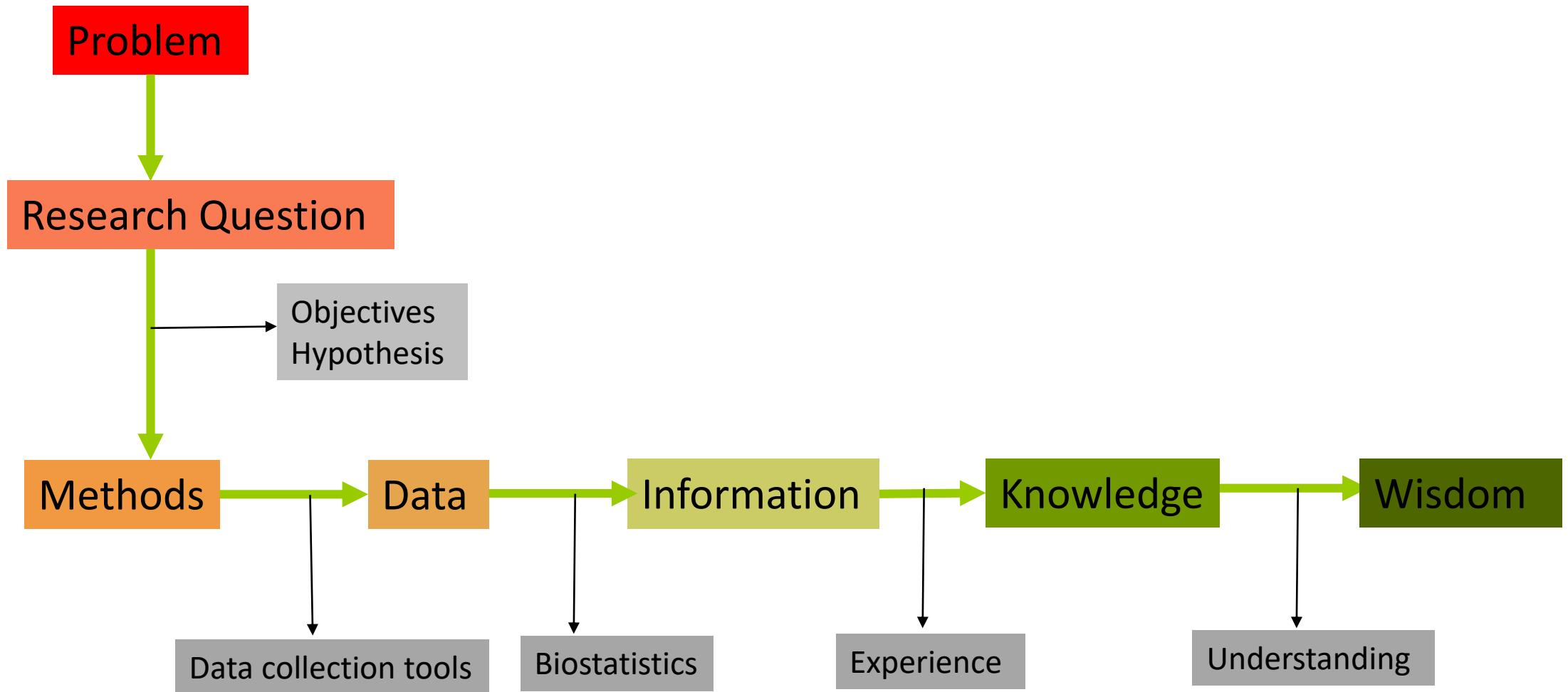
### ■ Bayesian

- Parameters are random and unknown
- Data is not sufficient to estimate
- Require Prior information in addition to data

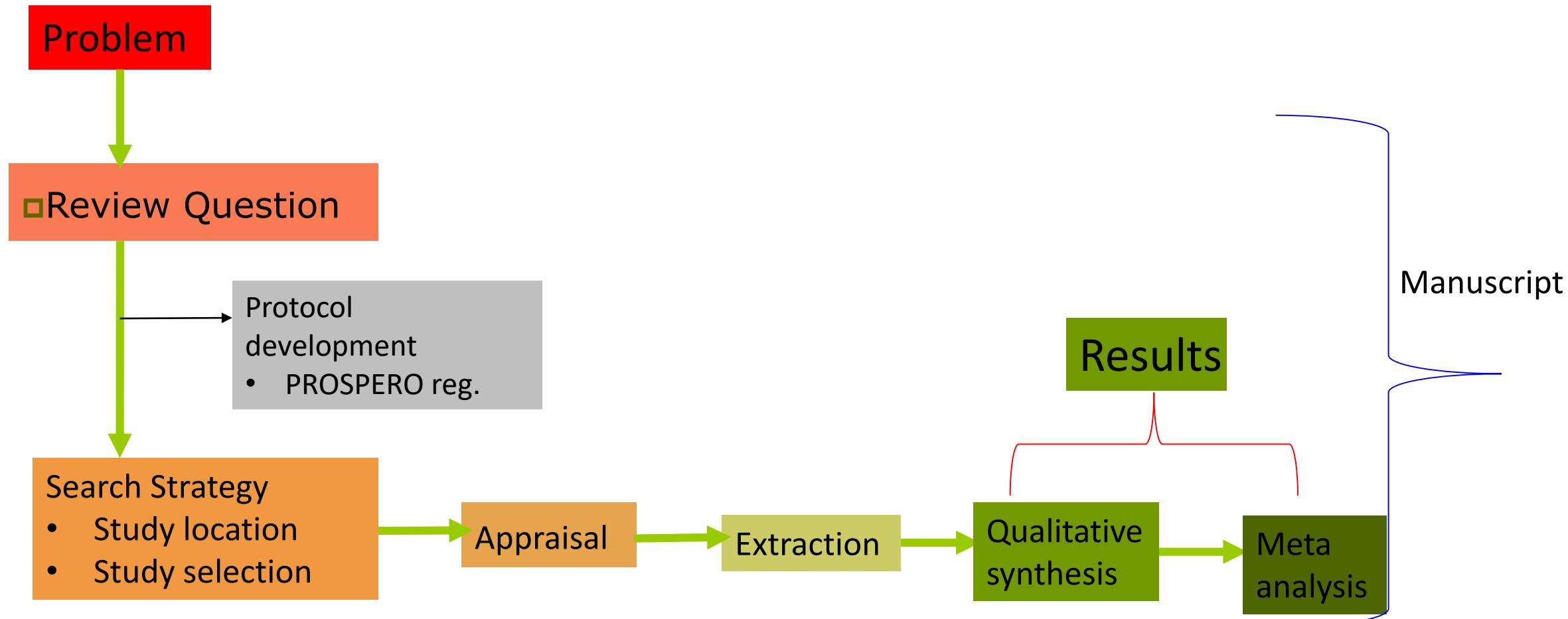


# Steps of generating evidence (Primary Study)

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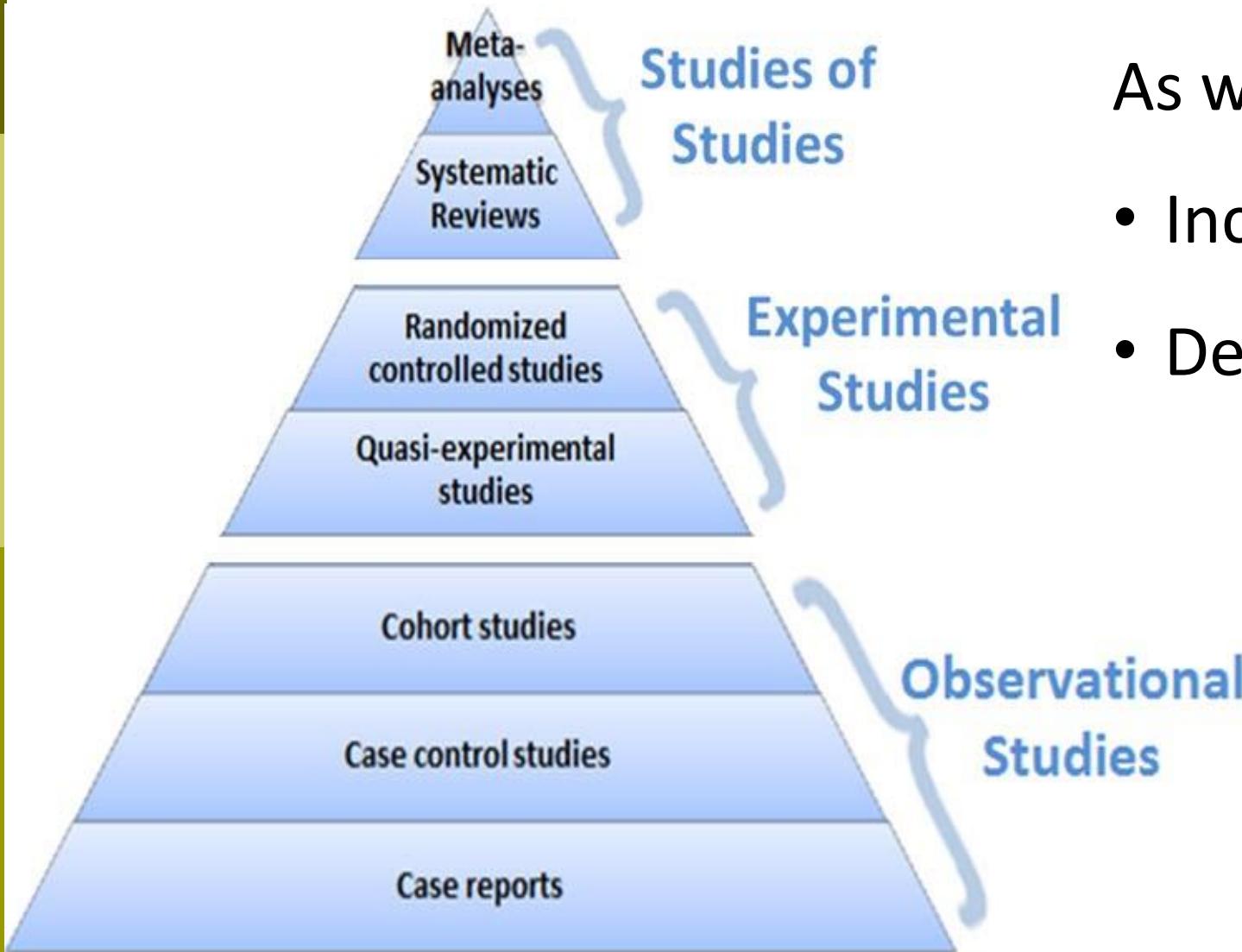


# Steps of generating evidence (Systematic Review)



# Hierarchy of Design

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As we move up:

- Increase strength of the evidence
- Decrease the bias

# Overview of Systematic Review

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- Systematic reviews aim to provide a **comprehensive, unbiased** synthesis of many relevant studies in a single document using rigorous and transparent methods
- A systematic review does not seek to create new knowledge but rather to synthesize and summarize existing knowledge

# Aims of Systematic Review

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□ The aims of a systematic review:

1. uncover the international evidence
2. confirm current practice/ address any variation
3. identify areas for future research
4. investigate conflicting results
5. produce statements to guide decision-making

# Steps in conducting a systematic review

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- Formulate review question
- Define inclusion and exclusion criteria
- Locate studies
- Select studies
- Assess study quality
- Extract data
- Analyse and present results
- Interpret results

# Types of Systematic Reviews

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1. Effectiveness Reviews
2. Qualitative Reviews
3. Costs/Economics Reviews
4. Prevalence or Incidence Reviews
5. Diagnostic Test Accuracy Reviews
6. Etiology and Risk Reviews
9. Umbrella Reviews

# Effectiveness Reviews

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- Reviews synthesise primary studies to establish the effect of treatment
- Aim to establish a causal relationship between two variables
- Question Development: **PICO**
  - **P**opulation
  - **I**ntervention
  - **C**omparator/control
  - **O**utcome

# Effectiveness Reviews

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## Example:

- Are **non-pharmacological interventions** compared with **control interventions (e.g. usual care)** effective in reducing **depressive symptoms** of **older adults with depressive disorders?**

Population

Intervention

Comparison

Outcome

# Qualitative Reviews

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- Focus on analysing human experiences and cultural and social phenomena
- Question Development: **PICo**
  - **P**opulation
  - Phenomena of **I**nterest
  - **C**ontext
- The phenomena of interest relates to a defined event, activity, experience or process
- Context is the setting or distinct characteristics

# Qualitative Reviews

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## Example:

- What is the **experience of recovering from burns injuries** in **adult (over 18 years of age) patients** during their stay in a **hospital burns care unit**?

Population

Phenomena of Interest

Context

# Costs/Economics Reviews

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- Reviews assessing the costs of a certain intervention, process, or procedure
- Question Development: **PICO**
  - **P**opulation
  - **I**ntervention
  - **C**omparator
  - **O**utcome

Context also considered

# Costs/Economics Reviews

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## Example:

- What is the **cost effectiveness** of **Mohs micrographic surgery** compared to **other surgical interventions** for **non-melanoma skin cancer** in **developed countries**?

Population

Intervention

Comparison

Outcome

Context

# Prevalence or Incidence Reviews

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- Measure frequency of disease
- Question Development: **CoCoPop**
  - **Condition**
  - **Context**
  - **Population**
- The variable of interest is the condition and can be a health condition, disease, symptom, event or factor
- Define context or specific setting since prevalence/incidence can be impacted by environmental factors

# Prevalence or Incidence Reviews

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## Example:

- What is the prevalence and incidence of **perinatal depression** among **women** in **Ethiopia**?

Condition

Context

Population

# Diagnostic Test Accuracy Reviews

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- Diagnostic tests are used by clinicians to identify the presence/absence of a condition in a patient
- This review provide a summary of test performance in order to determine the accuracy of the diagnostic tests they use or are considering using
- Question Development: **PIRD**
  - **P**opulation
  - **I**nDEX test
  - **R**eference test
  - **D**iagnosis of interest

# Diagnostic Test Accuracy Reviews

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## Example:

- What is the diagnostic accuracy of currently available **laboratory tests** for **swine flu (H1N1)** compared to **viral culture** as a reference test amongst **people presenting with suspected flu**?



## Etiology and Risk Reviews

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- Assess associations between epidemiological factors and the outcomes
- The exposure of interest refers to a particular risk factor or several factors associated with a disease
- Important in informing health care planning and resource allocation
- Question Development: **PEO**
  - **P**opulation
  - **E**xposure of interest
  - **O**utcome or response

# Etiology and Risk Reviews

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## Example:

- Are **children** exposed to **tobacco smoke (maternal smoking) during pregnancy** at risk for **obesity in childhood**?

Population

Exposure

Outcome

# Umbrella Reviews

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- Compare and contrast published reviews and provide an overall examination of a body of information that is available for a given topic

## Example:

- What are effective non-pharmacological interventions to manage aggressive behavior in elderly patients with dementia?



# Summary of Question Development

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Review Type	Mnemonic
Effectiveness	PICO
Qualitative	PICo
Costs/Economics	PICO
Prevalence or Incidence	CoCoPop
Diagnostic Test Accuracy	PIRD
Etiology and Risk	PEO
Umbrella	PICO or PICo or PIRD or CoCoPop or PEO

# Inclusion Criteria

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- Step 2: define inclusion and exclusion criteria
- Determines which research articles will be selected
- Allows the reader to understand the focus of the review
- Clarity of inclusion criteria ensures replicability of the review
- Consider:
  - Participants/population characteristics
  - Intervention, interest, exposure or phenomenon under investigation
  - Outcomes
  - Context
  - Types of studies to be included
  - Publication language
  - Time period



## Activity 1

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- Develop the Review Question
- Define the question development
- List the inclusion and exclusion criteria
- Register the review topic on PROSPERO

# Protocol Development



# Protocol Development

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- A protocol:
  - Guides the specific direction of the review
  - Describes inclusion criteria
  - Identifies the appropriate search sources and resources
  - Describes methods of study selection, appraisal, extraction and synthesis

# Protocol Structure

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- Title
- Authors
- Review question
- Background
- Keywords
- Methods:
  - Inclusion criteria
  - Search strategy
  - Study selection
- Critical appraisal
- Data extraction
- Data synthesis
- Assessing confidence
- Conflicts of Interest
- Acknowledgements
- References
- Appendices
  - Search strategy example
  - Appraisal instruments
  - Data extraction instruments

## PROSPERO registration

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- The review topic should be registered in PROSPERO
- This will avoid duplication of works
- <https://www.crd.york.ac.uk/prospero/>

## Activity 2

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- Develop the protocol
  
- Finalize PROSPERO registration

# Developing a Searching Strategy



1. Locate studies
2. Select studies

# Searching

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- A key characteristic of systematic reviews is a comprehensive search → based on search methodology
- A key component in any definition of a systematic review is the attempt to locate “**ALL**” published and unpublished evidence relevant to a review question
- General approach to conducting a comprehensive search involves:
  - identifying appropriate resources and sources to search
  - developing search strategies
  - searching bibliographic databases
  - looking for unpublished literature
  - Hand-searching
  - reference list searching

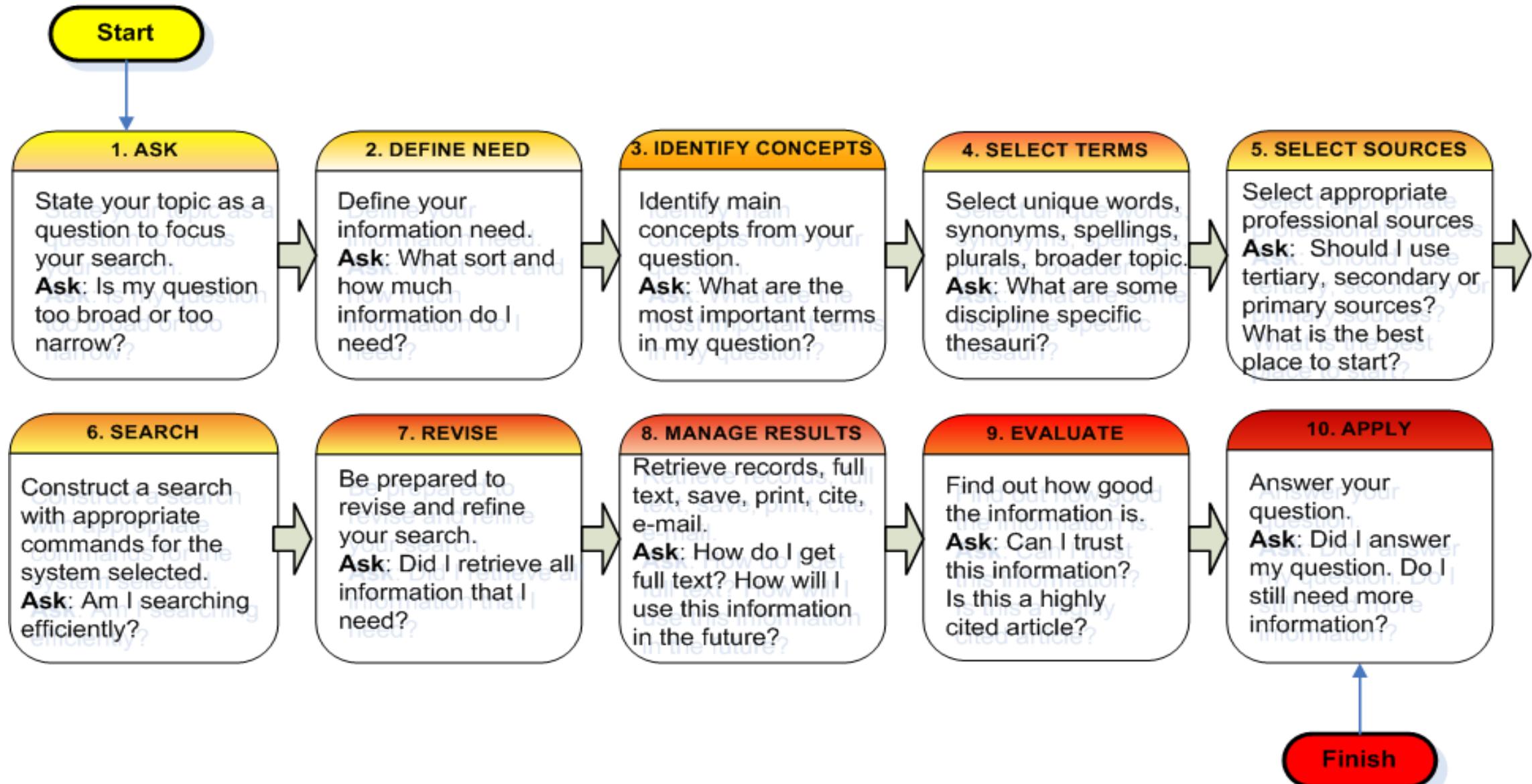


## Search Strategy

### □ Features of an effective search strategy:

- Sensitivity – ability to identify all the relevant studies
  - ▣ Over sensitive search → capture all necessary studies but labor-intensive
- Specificity – ability to exclude irrelevant studies, also known as precision.
  - ▣ Over specific search → yield fewer results but may omit important studies
  - ▣ Inverse relationship between sensitivity and specificity
- Minimize bias – think about finding/including studies that are not in major databases
- Efficient – look in the place you expect to have highest yield

# Developing a Search Strategy: Process Overview



**Remember:** Your question drives the search strategy. There is no one best way to search. Avoid one stop searching to prevent bias.

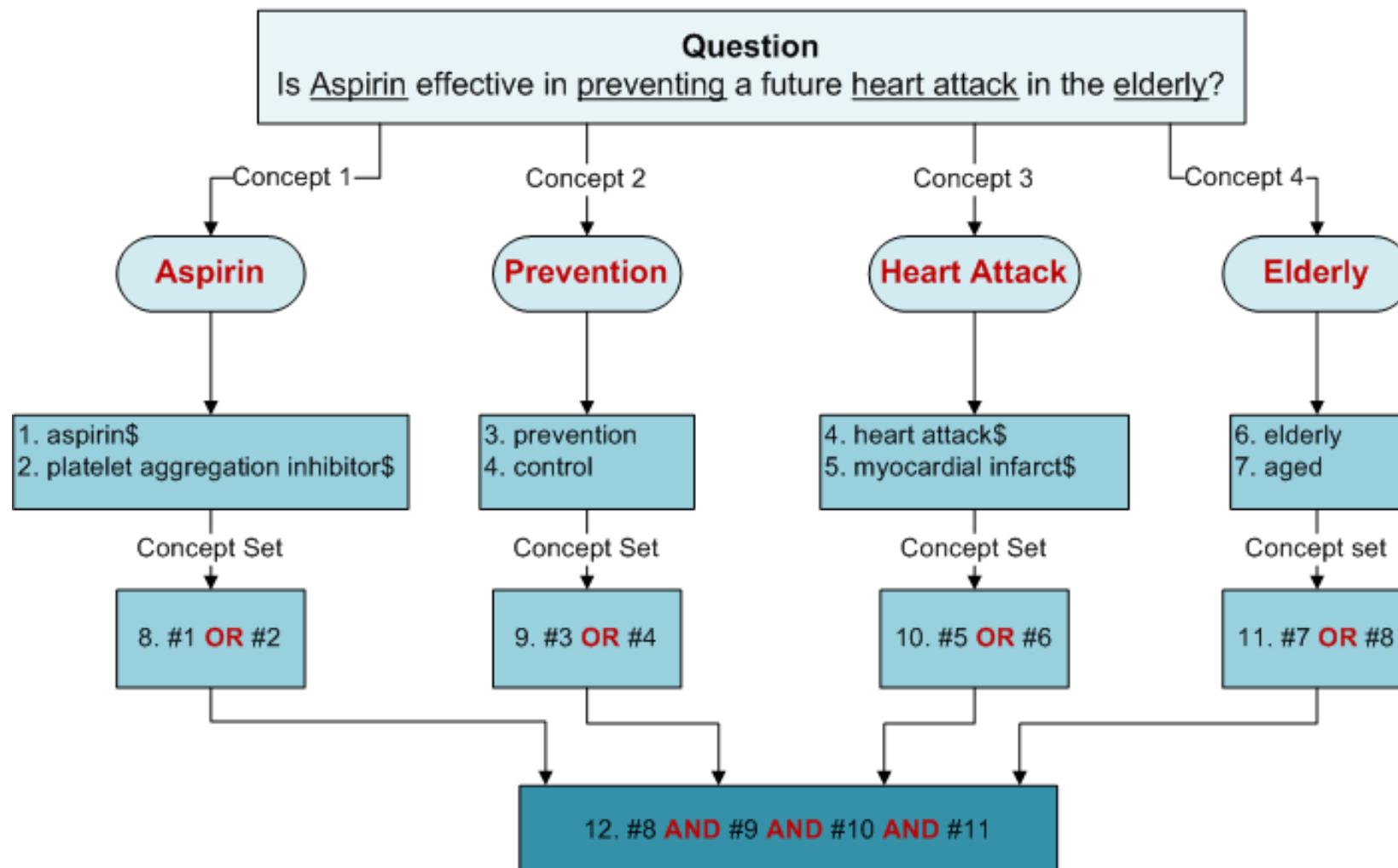
## Example (Steps 1-4)

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1. Ask: What **health** problems are associated with **water pollution**?
2. Need: scholarly primary research
3. Main Concepts: health, water, pollution
4. Select terms:
  - Broader terms: 'health', environmental degradation', 'agricultural management',
  - Synonyms:  
**health**, illness, disease, etc.  
**water**, rivers, lakes, sea, domestic water, etc.  
**pollution**, 'oil spills', chemical, biological, toxicity, etc
  - Alternative spellings: none
  - Plurals: river(s), lake(s), disease(s)
  - Capitals: e.g. name of a specific lake, disease, region

# Example

## Construct a Search using Appropriate Commands and Best Practices



When searching enter one term/phrase at a time; keep terms in separate concept sets; combine search terms with OR first; then with AND.

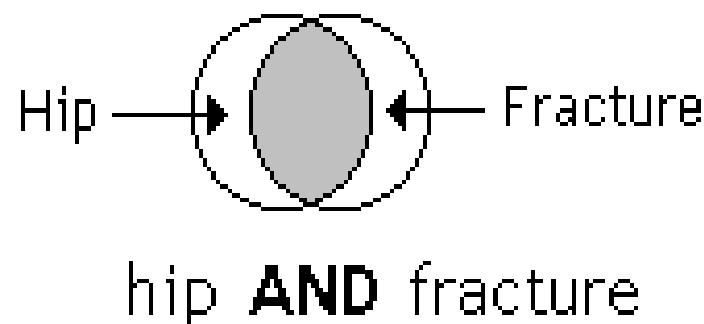
## Boolean (Search) Operators

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- Connect terms and locate records containing matching terms
- Inserted in a search box – **AND, OR, NOT**
- Must be in UPPERCASE when used
- AND, NOT operators are processed in a left- to right sequence. These are processed first before the OR operators
- OR operators are also processed from left-to-right

## AND Operator

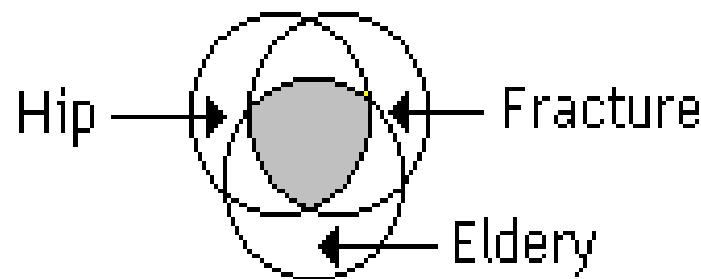
(to combine two concepts and narrow a search)



the **AND** operator is used to combine two concepts e.g. hip **AND** fracture – in the shaded area; retrieves items containing all the search terms

## AND Operator

(to combine three concepts)

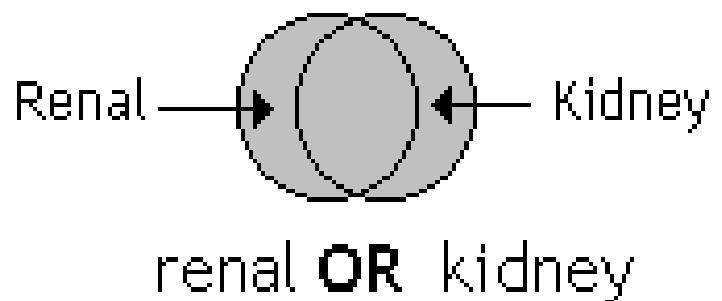


hip **AND** fracture **AND** elderly

the **AND** operator is used to combine three concepts e.g. hip **AND** fracture **AND** elderly – in the shaded area.

## OR Operator

(info containing one or other term; will broaden a search)



renal **OR** kidney – in the shaded area with the overlap in the middle having both search terms; retrieves items containing either search term or both search terms

## NOT Operator

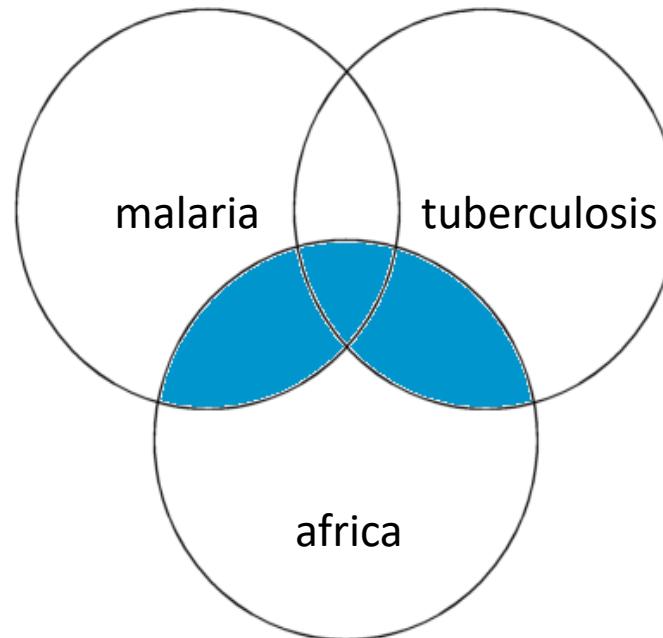
(in one term or the other - will narrow a search)



pig **NOT** guinea – in the shaded area; eliminates  
items in 2<sup>nd</sup> term (guinea) or both terms

## Africa AND (malaria OR tuberculosis)

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Africa AND (malaria or tuberculosis) – in the shaded area  
The **(OR)** operator retains items in each term and the **AND** operator is used to combine two concepts

# Other search engine functions

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- Phrase or proximity searching: “...” or (...)
  - allows you to search for an exact phrase
  - E.g. “information literacy”
  - E.g. prevention and (malaria parasite)
- Truncation/wildcards: \*
  - allow you to search alternative spellings
  - E.g. child\* for child OR childs OR children
  - E.g. parasite\* for parasite OR parasites
- Alternate spellings: ?
  - can be used to substitute for characters anywhere in a word
  - E.g. wom?n would search for “woman” and “women”

# More Search Techniques

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- Field Specific Searching
  - author, title, journal, date, url, etc.
- Language Restrictions, Humans or Animals, Gender and other limits
- Relevancy Ranking
  - a grading that gives extra weight to a document when the search terms appear in the headline or are capitalized
  - every found document is calculated as 100% multiply by the angle formed by weights vector for request and weights vector for document found

# Review Question

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- Soda drinks leads to obesity and overweight in children
- Question development
- Mnemonics
  - PEO
- Soda drinks leads to obesity and overweight in children

Population

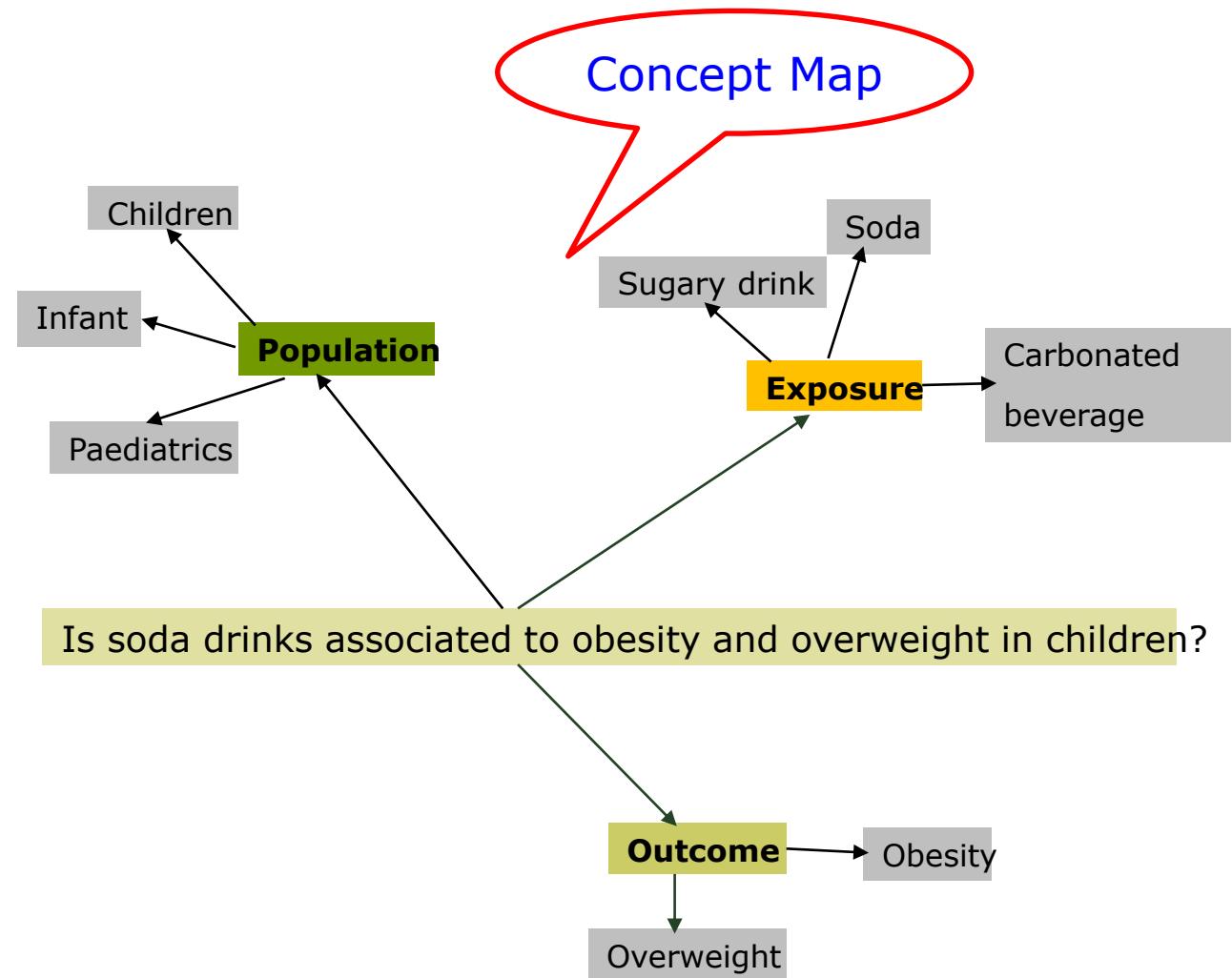
Exposure

Outcome

# Logic Grid and Concept Map

Logic Grid

Population	Exposure	Outcome
Children	Soda	Obesity
Infant	Sugary drink	Overweigh
	Carbonated beverage	



## Documenting your Search

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- Important to keep an accurate record of the search and how it was performed
  - Numbers of titles identified by search are reported in review report
  - Avoids having to repeat searches
  - Use reference management software to document
  - Consider both published and unpublished studies/papers
  - Specify the timeframe chosen for the search and any language restrictions
  - Specify the databases to be searched and including the platform used to search a particular database
  - List the initial keywords to be used

## Activity 3

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- ❑ For your topic of review develop search strategy

# Searching for Studies



Types of Resources

# Types of resources

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- **Research4Life** is the collective name for five programmes
  - Hinari
  - AGORA
  - OARE
  - ARDI and
  - GOALI
- that provide developing countries with free or low-cost access to academic and professional peer-reviewed content online.
- It is a public-private partnership of WHO, FAO, UNEP, WIPO, ILO, Cornell and Yale Universities, the International Association of Scientific, Technical & Medical Publishers and up to 155 international publishers



# Research 4life

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- The goal of Research4Life is to reduce the knowledge gap between high-income countries and low- and middle-income countries by providing affordable access to scholarly, professional and research information.
- Since 2002, the five programmes
  - Research in Health (Hinari),
  - Research in Agriculture (AGORA),
  - Research in the Environment (OARE),
  - Research for Development and Innovation (ARDI)
  - Research for Global Justice (GOALI)
- have provided researchers at more than 9,000 institutions in more than 120 low- and middle-income countries with free or low-cost online access to up 100,000 leading journals and books

# Research 4life

The screenshot shows the homepage of the research4life.org website. At the top, there is a browser header with a red box highlighting the URL bar containing "research4life.org". Below the header, the website's logo "research4life" is displayed with three stylized circular icons (orange, green, blue) integrated into the letter "l". To the right of the logo, language links are provided for English, Français, Español, and Português. Social media icons for search, Twitter, Facebook, LinkedIn, YouTube, and email are also present. A banner at the bottom of the page features a photograph of a person working at a computer and text about research partners committing to free and low-cost access and training through 2025.

research4life.org

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English Français Español Português

SEARCH

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THROUGH 2025

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# Registration

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- It requires user name and password to get access
- Usually registration is simple by the institute
  - Individual will take long time
- Once you have username and password, then signin



# Registration

← → C ⓘ Not secure | login.research4life.org/tacgw/AppPortal/ ⋮

Apps Dictionary.com OneLook Dictionary... Gmail BBC - Radio 4 - Ho... Google Translate Google Scholar get into PC Electronic library. D... Sci-Hub: removing... Journals » Other bookmarks

 [Sign Out](#)

Search...

	AGORA - Agriculture, Forestry, Fisheries, Climate & Food Security →
	ARDI - Innovation & Technology →
	GOALI - Law →
	Hinari - Health →
	OARE - Environment →

# Medline versus Embase

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- Elsevier opens up Embase to Research4Life

<u>MEDLINE</u>	<u>EMBASE</u>
Over 23 million references to journal articles	Over 31 million indexed records
More than 5600 journals	More than 8500 indexed peer-reviewed journals
1946 to present with some older material	Biomedical literature from 1947 to present
Indexed with NLM Medical Subject Headings (MeSH)	Elsevier Life Science thesaurus Emtree
MeSH is updated once a year	Emtree is updated every three months

# HINARI

in.research4life.org/tacsgr0extranet\_who\_int/hinari/en/journals.php

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## Journals collection

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# Other Resources

---

- Peer reviewed journal articles (via scientific databases, libraries, the journals themselves)

## Databases

- The JBI Database
- The Cochrane Database
- **MEDLINE**
- EMBASE
- CINAHL
- ScienceDirect
- Web of Science

- 
- ```
graph LR; A[Databases] --> B[Grey Literature]; B --> C[Other Resources]
```
- PsycInfo
  - Scopus
  - OTseeker
  - PEDro
  - POPLINE
  - Proquest
  - + many more...!

## Grey Literature

- Research and Trials Registers
- Theses/Dissertations
- Organizations/websites
- Data – Statistics
- Circulars
- Reports

  [Advanced Scholar Search](#)

Articles ( include patents)  Legal opinions and journals

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Google Scholar provides a simple way to broadly search for scholarly literature. You can search across many disciplines and sources: peer-reviewed papers, theses, books, abstracts and articles, from academic publishers, professional societies, preprint repositories, universities and other scholarly organizations.

## Find articles

with **all** of the words

Results per page:

10   
10  
20  
30  
50  
100

with the **exact phrase**with **at least one** of the words

without the words

where my words occur

 anywhere in the article 

## Author

Return articles written by

e.g., "PJ Hayes" or McCarthy

## Publication

Return articles published in

e.g., J Biol Chem or Nature

## Date

Return articles published between

 — 

e.g., 1996

## Collections

## Articles and patents

 Search articles in all subject areas ( include patent) Search only articles in the following subject areas: Biology, Life Sciences, and Environmental Sciences Business, Administration, Finance, and Economics Chemistry and Materials Science Engineering, Computer Science, and Mathematics

We have displayed the Advanced Scholar Search option of Google Scholar. Note the various options for refining a search and also that you can change the number of results per page.

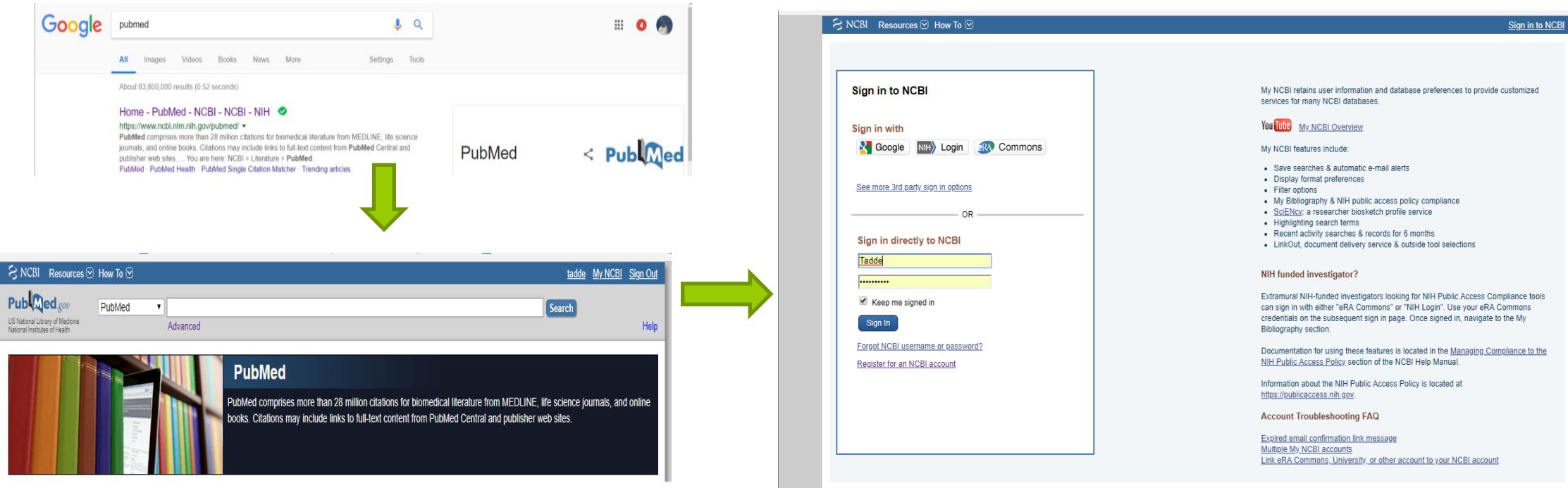
 Social Sciences, Arts, and Humanities

## Legal opinions and journals

 Search all legal opinions and journals. Search only US federal court opinions. Search only court opinions from the following states:

# PubMed Search

- Write “PubMed” on google and click Ok



# Medical Subject Headings (MeSH)

- It is a controlled vocabulary produced by the National Library of Medicine
  - used for indexing
  - Cataloging
  - searching for biomedical and health-related information and documents
  - searching with the MeSH controlled vocabulary give you more precise search results

The image consists of three side-by-side screenshots of web pages related to MeSH:

- Left Screenshot:** A Google search results page for "MeSH". The first result is a link to the NCBI MeSH homepage, which is highlighted with a red circle. Below the search bar, there are links for "All", "Images", "News", "Videos", and "More".
- Middle Screenshot:** The NCBI MeSH homepage. At the top, there's a search bar with "MeSH" typed into it. Below the search bar, there are "Limits" and "Advanced" buttons. In the footer, there's a link "MeSH Home" which is also circled in red.
- Right Screenshot:** The official U.S. National Library of Medicine MeSH homepage. At the top, there's a navigation bar with links for "Products and Services", "Resources for You", "Explore NLM", and "Grants and Funding". Below the navigation bar, there's a section titled "Welcome to Medical Subject Headings!" with a sub-section "What's New". In the top right corner of this section, there's a link "MeSH Browser" which is circled in red.

# Search Terms

- To find the meaning and possible terms for search term (i.e Khat)
- It gives the meaning
- It also gives possible names

The screenshot shows the MeSH Descriptor Data 2017 page for Catha. The URL is https://meshb.nlm.nih.gov/record/ui?ui=D029754. The page includes the NIH logo and the U.S. National Library of Medicine header. Below the header are links for Search, Tree View, MeSH on Demand (NEW), MeSH 2016, MeSH Suggestions, About MeSH Browser, and Contact Us. The main content area displays the following information:

| MeSH Heading     | Catha                                                                                                                                                                    |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tree Number(s)   | B01.650.940.800.575.100.197.155                                                                                                                                          |
| Unique ID        | D029754                                                                                                                                                                  |
| Scope Note       | A plant genus of the family CELASTRACEAE. The leafy stems of khat are chewed by some individuals for: norpseudoephedrine), cathinone, cathedulin, cathinine & cathidine. |
| Entry Term(s)    | Catha edulis<br>Khat<br>Mairungi<br>Miraa<br>Qat Plant                                                                                                                   |
| Public MeSH Note | 2002; MIRAA was indexed under PLANT EXTRACTS 1981-2002                                                                                                                   |
| History Note     | 2002; for MIRAA use MIRAA (NM) 1981-2002                                                                                                                                 |
| Date Established | 2002/01/01                                                                                                                                                               |
| Date of Entry    | 2001/07/25                                                                                                                                                               |
| Revision Date    | 2016/06/28                                                                                                                                                               |

These terms will be combined with “OR”

The screenshot shows the NCBI MeSH search results for the term "Catha". The search interface includes a dropdown menu set to "MeSH" and a search bar containing "Catha". Below the search bar are links for Create alert, Limits, and Advanced. The results summary indicates 2 items found. The results list includes:

- [Catha](#)  
1. A plant genus of the family CELASTRACEAE. The leafy stems of **khat** are chewed by some individuals for stimulating effect. Members contain ((+)-norpseudoephedrine), cathionine, cathedulin, cathinine and cathidine.  
Year introduced: 2002
- [cathinone \[Supplementary Concept\]](#)  
2. alkaloid from **khat** shrub, Catha edulis; RN given refers to parent cpd without isomeric designation  
Date introduced: April 22, 1980

hinarilogin.research4life.org/uniquesigwww.ncbi.nlm.nih.gov/uniquesig0/pubmed?myncbshare=hinari

Apps The New York Times GatorLink Webmail

NCBI Resources How To

PubMed.gov US National Library of Medicine National Institutes of Health

MeSH

- Genome
- GEO DataSets
- GEO Profiles
- GSS
- HomoloGene
- MedGen
- MeSH**
- NCBI Web Site
- NLM Catalog
- Nucleotide
- OMIM
- PMC
- PopSet
- Probe
- Protein
- Protein Clusters
- PubChem BioAssay
- PubChem Compound
- PubChem Substance
- PubMed

To access the MeSH Database from the PubMed homepage, click on the link from the right column of the PubMed home page. A second way to access MeSH is to open the Databases drop down menu and then to click on MeSH.

Help



## Using PubMed

[PubMed Quick Start Guide](#)

[Full Text Articles](#)

[PubMed FAQs](#)

[PubMed Tutorials](#)

[New and Noteworthy](#)

## PubMed Tools

[PubMed Mobile](#)

[Single Citation Matcher](#)

[Batch Citation Matcher](#)

[Clinical Queries](#)

[Topic-Specific Queries](#)

## More Resources

[\*\*MeSH Database\*\*](#)

[Journals in NCBI Databases](#)

[Clinical Trials](#)

[E-Utilities](#)

[LinkOut](#)

MeSH

MeSH

Infant



Search

Create alert Limits Advanced

Help

Summary ▾ 20 per page ▾

## Search results

Items: 1 to 20 of 40

From these results, note that the MeSH has listed 40 terms for *infant*.

 [Infant](#)

1. A child between 1 and 23 months of age.

 [Infant Death](#)

2. The death of a live-born INFANT within its first year of life.  
Year introduced: 2015

 [Infant, Extremely Premature](#)

3. A human infant born before 28 weeks of GESTATION.  
Year introduced: 2013

 [Infant, Extremely Low Birth Weight](#)

4. An infant whose weight at birth is less than 1000 grams (2.2 lbs), regardless of GESTATIONAL AGE.  
Year introduced: 2007

MeSH (Medical Subject Headings) is the controlled vocabulary for indexing articles in Medline – National Institute of Health's bibliographic database of life sciences and biomedical information.

MeSH Terms are assigned as Keywords to each record that is “Indexed for MEDLINE”. In MeSH, complete search for the term *infant*

Find related data

Database: Select

Find items

Search details

"infant"[MeSH Terms] OR Infant[Text Word]

MeSH

Mesh

Limits Advanced

Search

Help

Full ▾

**Infant**

A child between 1 and 23 months of age.

PubMed search builder options

Subheadings:

- abnormalities
- adverse effects
- analysis
- anatomy and histology
- blood
- blood supply
- cerebrospinal fluid
- chemistry
- classification
- complications
- diagnosis
- diagnostic imaging
- drug effects

To complete a PubMed search with the *Infant MeSH* term, click on **Add to search builder** and then click on **Search PubMed**.

Note how "*Infant[Mesh]*" is displayed in the **PubMed search builder** box.

- abnormalities*
- adverse effects*
- analysis*
- anatomy and histology*
- blood*
- blood supply*
- cerebrospinal fluid*
- chemistry*
- classification*
- complications*
- diagnosis*
- diagnostic imaging*
- drug effects*
- genetics*
- growth and development*
- history*
- immunology*
- injuries*
- instrumentation*
- metabolism*
- microbiology*
- mortality*
- nursing*
- parasitology*
- physiopathology*
- poisoning*
- prevention and control*
- psychology*
- radiation effects*
- statistics and numerical data*
- surgery*
- therapeutic use*
- therapy*
- toxicity*
- urine*

Send to: ▾

PubMed Search Builder

"*Infant*" [Mesh]

Add to search builder AND ▾

Search PubMed

YouTube Tutorial

**Related information**

- PubMed
- PubMed - Major Topic
- Clinical Queries
- NLM MeSH Browser
- dbGaP Links

citations.nbib



01-intro.R



00-install-packages.R



Show all

MeSH

MeSH

 Limits Advanced

Search

Help

Full ▾

**Child**

A person 6 to 12 years of age. An individual 2 to 5 years old is C

PubMed search builder options

Subheadings:

- adverse effects
- analysis
- anatomy and histology
- blood
- cerebrospinal fluid
- classification
- complications
- diagnosis
- drug therapy
- education
- epidemiology
- etiology

- genetics
- growth and development
- history
- immunology
- injuries
- metabolism
- microbiology
- mortality
- pathogenicity
- pathology
- pharmacology

- physiology
- physiopathology
- prevention and control
- psychology
- rehabilitation
- statistics and numerical data
- surgery
- therapeutic use
- therapy
- toxicity
- urine

The term “children” was checked for MeSH term. Infant and child were combined with OR as they are in the same mnemonics

Send to: ▾

PubMed Search Builder

("Infant"[Mesh]) OR "Child"[Mesh]

Add to search builder OR ▾

Search PubMed

YouTube Tutorial

Then click “search pubmed”

PubMed - Major Topic

Clinical Queries

NLM MeSH Browser

Recent Activity

Turn Off Clear

Show all

 Restrict to MeSH Major Topic

citations.nbib



01-intro.R



00-install-packages.R



US National Library of Medicine  
National Institutes of Health

PubMed

("Infant"[Mesh]) OR "Child"[Mesh]

Population

Search

Create RSS Create alert Advanced

Help

## Article types

Clinical Trial

Review

Customize ...

## Text availability

Abstract

Free full text

Full text

## Publication dates

5 years

10 years

Custom range...

## Species

Humans

Other Animals

[Clear all](#)[Show additional filters](#)

Format: Summary ▾ Sort by: Most Recent ▾ Per page: 20 ▾

Send to ▾

Filters: [Manage Filters](#)

## Sort by:

[Best match](#)

Most recent

## Search results

Items: 1 to 20 of 2411373

&lt;&lt; First &lt; Prev Page 1 of 120569 Next &gt; Last &gt;&gt;

 [Antimicrobial central venous catheters do not reduce infections in pre-term babies.](#)

1. Cook R, Fortescue-Webb D, Martin R; NIHR Dissemination Centre.

BMJ. 2019 Nov 4;367:l4993. doi: 10.1136/bmj.l4993.

PMID: 31685481

[Similar articles](#) [\[Changes of lactate levels in diabetic ketoacidosis and in newly diagnosed type 1 diabetes mellitus\].](#)

2. Jenei K, Szatmári I, Szabó E, Mariam A, Luczay A, Zsidegh P, Tóth-Heyn P.

Orv Hetil. 2019 Nov;160(45):1784-1790. doi: 10.1556/650.2019.31533. Hungarian.

PMID: 31680540

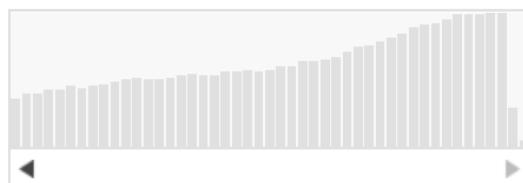
[Similar articles](#) [\[Hereditary spherocytosis in the experience of two pediatric clinics from Targu Mures\].](#)

3. Papp ZE, Chincesan M, Horváth AM, Kelemen I.

Orv Hetil. 2019 Nov;160(45):1798-1803. doi: 10.1556/650.2019.31345. Hungarian.

PMID: 31680538

## Results by year

[Download CSV](#)

## Titles with your search terms

Mother to child transmission of hepatitis B: What more needs to be done to eli [J Viral Hepat. 2019]

Maternal and infant Health Care Costs Related to Preeclampsia. [Obstet Gynecol. 2019]

Opioid prescription rates and risk for



## Article types

Clinical Trial

Review

Customize ...

## Text availability

Abstract

Free full text

Full text

## Publication dates

5 years

10 years

Custom range...

## Species

Humans

Other Animals

[Clear all](#)[Show additional filters](#)

Format: Summary ▾ Sort by: Most Recent ▾ Per page: 20 ▾

Send to ▾

Filters: [Manage Filters](#)

## Sort by:

[Best match](#)[Most recent](#)

Items: 1 to 20 of 3463

&lt;&lt; First &lt; Prev Page 1 of 174 Next &gt; Last &gt;&gt;

[Dental erosion. Etiologic factors in a sample of Valencian children and adolescents. Cross-sectional study.](#)

1. [Marqués Martínez L, Leyda Menéndez AM, Ribelles Llop M, Segarra Ortells C, Aiuto R, Garcovich D. Eur J Paediatr Dent. 2019 Sep;20\(3\):189-193. doi: 10.23804/ejpd.2019.20.03.04.](#)  
PMID: 31489816 [Free Article](#)  
[Similar articles](#)

[Color stability, roughness, and water sorption/solubility of glass ionomer-Based restorative materials.](#)

2. [Savas S, Colgecen O, Yasa B, Kucukyilmaz E. Niger J Clin Pract. 2019 Jun;22\(6\):824-832. doi: 10.4103/njcp.njcp\\_592\\_18.](#)  
PMID: 31187769  
[Similar articles](#)

[The frequency and magnitude of price-promoted beverages available for sale in Australian supermarkets.](#)

## Results by year

[Download CSV](#)

## Titles with your search terms

Beware **Energy Drinks**: A Case of a Toxic Triad Syndrome in a Diabetic Pat [Am J Med Sci. 2019]

Effects of Acute Consumption of Noni and Chokeberry . [Evid Based Complement Alternat...]

Anxiety-like behavior and whole-body cortisol



## Article types

Clinical Trial

Review

Customize ...

## Text availability

Abstract

Free full text

Full text

## Publication dates

5 years

10 years

Custom range...

## Species

Humans

Other Animals

[Clear all](#)[Show additional filters](#)

Format: Summary ▾ Sort by: Most Recent ▾ Per page: 20 ▾

Send to ▾ Filters: [Manage Filters](#)

Sort by:

[Best match](#)

Most recent

## Search results

Items: 1 to 20 of 21

Once you finished all the mnemonics,  
then click “advanced to go to history”

&lt;&lt; FIRST &lt; Prev Page 1 or 1000 | Next &gt; Last &gt;&gt;

 [Calorie labelling to reduce obesity.](#)

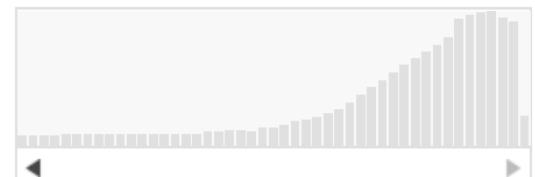
1. Kaur A; researcher, Briggs ADM; academic visitor.  
BMJ. 2019 Oct 30;367:l6119. doi: 10.1136/bmj.l6119. No abstract available.  
PMID: 31666229  
[Similar articles](#)

 [Estimating the effect of calorie menu labeling on calories purchased in a large restaurant franchise in the southern United States: quasi-experimental study.](#)

2. Petimar J, Zhang F, Cleveland LP, Simon D, Gortmaker SL, Polacsek M, Bleich SN, Rimm EB, Roberto CA, Block JP.  
BMJ. 2019 Oct 30;367:l5837. doi: 10.1136/bmj.l5837.  
PMID: 31666218 **Free Article**  
[Similar articles](#)

 [Obesity ipopulation!Inducing acute respiratory distress syndrome: we should choose the right](#)

3. Honore PM, Gutierrez LB, Redant S, Kaefer K, Gallerani A, De Bels D.

**Results by year**[Download CSV](#)**Titles with your search terms**

Hepatocellular adenoma in Taiwan: Distinct ensemble of male [J Gastroenterol Hepatol. 2019]

Gold nanoparticles synthesized with Smilax glabra rhizome i [J Photochem Photobiol B. 2019]

Maternal employment and childcare during

[Show all](#)

Use the builder below to create your search

[Edit](#)

[Clear](#)

### Builder

All Fields ▼  [Show index list](#)

AND ▼ All Fields ▼  [Show index list](#)

[Search](#) or [Add to history](#)

### History

| Search | Add to builder      | Query                                                                                        | Items found | Time     |
|--------|---------------------|----------------------------------------------------------------------------------------------|-------------|----------|
| #58    | <a href="#">Add</a> | Search ("Infant"[Mesh]) OR "Child"[Mesh]                                                     | 2411373     | 07:57:25 |
| #56    | <a href="#">Add</a> | Search ("Overweight"[Mesh]) OR "Pediatric Obesity"[Mesh] OR "Obesity"[Mesh]                  | 212002      | 07:56:31 |
| #52    | <a href="#">Add</a> | Search (("Carbonated Water"[Mesh]) OR "Carbonated Beverages"[Mesh]) OR "Energy Drinks"[Mesh] | 3463        | 07:54:47 |

Population

Outcomes

Exposure

((("Carbonated Water"[Mesh]) OR "Carbonated Beverages"[Mesh]) OR "Energy Drinks"[Mesh])) AND ((("Infant"[Mesh]) OR "Child"[Mesh])) AND ((("Overweight"[Mesh]) OR "Pediatric Obesity"[Mesh]) OR "Obesity"[Mesh])

Edit

## Search Terms

Clear

### Builder

All Fields

((("Carbonated Water"[Mesh]) OR "Carbonated Beverages"[Mesh]) OR "Energy Drinks"[Mes

Show index list

AND ▾ All Fields

("Infant"[Mesh]) OR "Child"[Mesh]

Show index list

AND ▾ All Fields

((("Overweight"[Mesh]) OR "Pediatric Obesity"[Mesh]) OR "Obesity"[Mesh])

Show index list

AND ▾ All Fields

Show index list

**Search** or Add to history

Click here

Click add to include in the builder

### History

Download history Clear history

| Search | Add to builder | Query                                                                                                                                                                                                                 | Items found | Time     |
|--------|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|----------|
| #58    | Add            | Search ("Infant"[Mesh]) OR "Child"[Mesh]                                                                                                                                                                              | 2411373     | 07:57:25 |
| #56    | Add            | Search (("Overweight"[Mesh]) OR "Pediatric Obesity"[Mesh]) OR "Obesity"[Mesh]                                                                                                                                         | 212002      | 07:56:31 |
| #52    | Add            | Search ((("Carbonated Water"[Mesh]) OR "Carbonated Beverages"[Mesh]) OR "Energy Drinks"[Mesh]) AND ((("Infant"[Mesh]) OR "Child"[Mesh])) AND ((("Overweight"[Mesh]) OR "Pediatric Obesity"[Mesh]) OR "Obesity"[Mesh]) | 3463        | 07:54:47 |

**Article types**

Clinical Trial

Review

Customize ...

**Text availability**

Abstract

Free full text

Full text

**Publication dates**

5 years

10 years

Custom range...

**Filters****Species**

Humans

Other Animals

[Clear all](#)[Show additional filters](#)

Format: Summary ▾ Sort by: Most Recent ▾ Per page: 20 ▾

Send to ▾ Filters: [Manage Filters](#)**Sort by:**[Best match](#)[Most recent](#)**Search results**

Items: 1 to 20 of 213

**Results from the search**

&lt; Prev Page 1 of 11 Next &gt; Last &gt;&gt;

 [Overweight Risk and Food Habits in Portuguese Pre-school Children.](#)

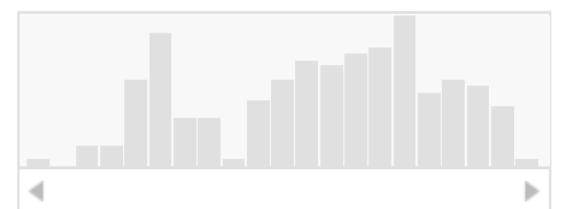
1. Machado-Rodrigues AM, Fernandes RA, Silva MR, Gama A, Mourão I, Nogueira H, Rosado-Marques V, Padez C.  
*J Epidemiol Glob Health.* 2018 Dec;8(3-4):106-109. doi: 10.2991/j.jegh.2017.10.006.  
PMID: 30864750  
[Similar articles](#)

 [Soda industry influence on obesity science and policy in China.](#)

2. Greenhalgh S.  
*J Public Health Policy.* 2019 Mar;40(1):5-16. doi: 10.1057/s41271-018-00158-x.  
PMID: 30626895  
[Similar articles](#)

 [The food environment of Brazilian public and private schools.](#)

3. Carmo ASD, Assis MM, Cunha CF, Oliveira TRPR, Mendes LL.  
*Cad Saude Publica.* 2018 Nov 29;34(12):e00014918. doi: 10.1590/0102-311X00014918.

**Results by year**[Download CSV](#)**Find related data**Database: [Select](#)[Find items](#)**Search details**[Show all](#)

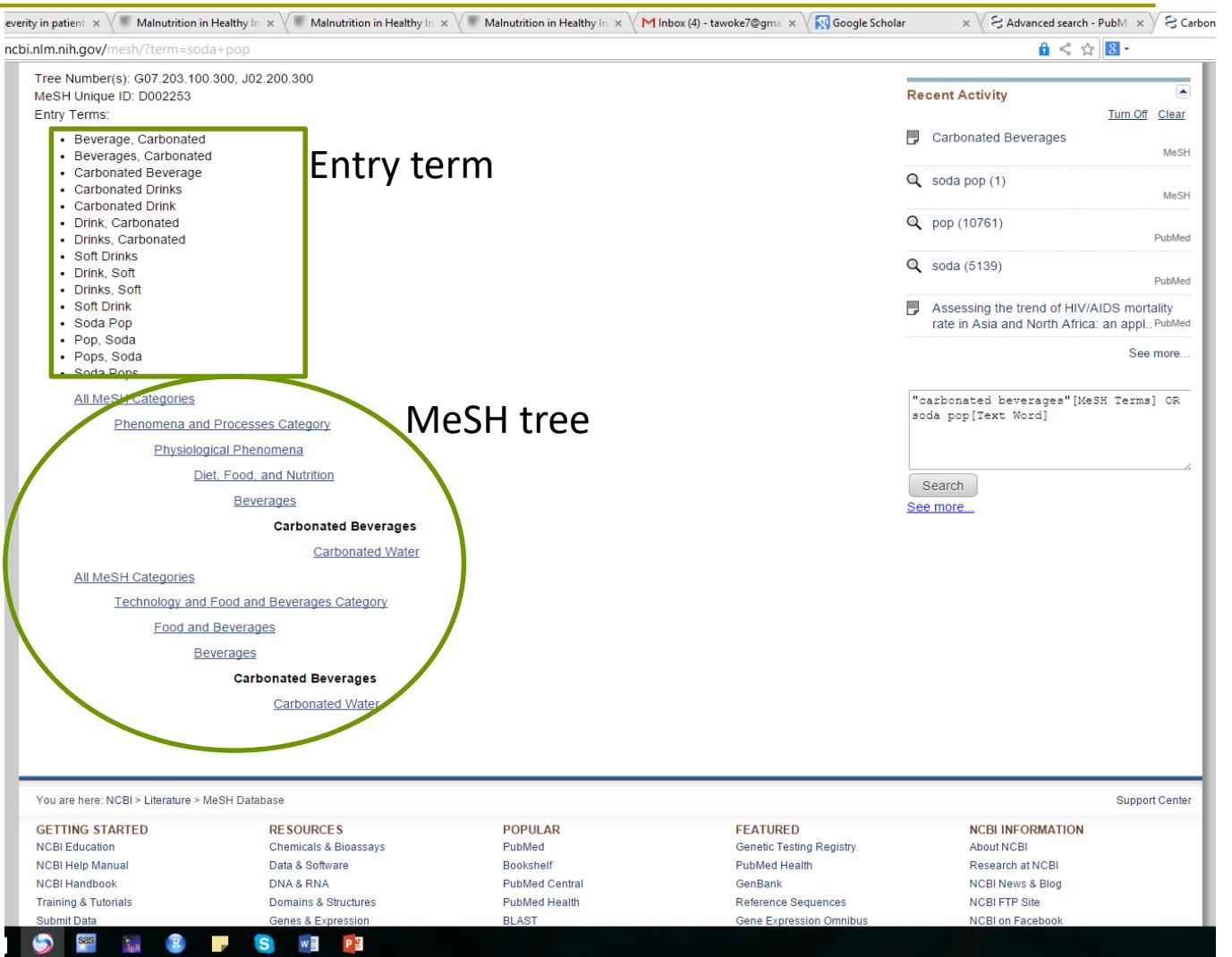
## Subheading

---

- ❑ Sub-headings are used with other subject headings to limit the type of articles retrieved
- ❑ The **sub-heading/*diagnostic use*** can be added to names of agents, investigations, etc. to restrict the findings to those mentioning using the agent or investigation for diagnostic purposes

# Entry Term

- We need the entry term to find newly published papers
- MeSH only searches those which are assigned to MeSH
- Then we have to use the entry term to find newly published papers



# Refining the search

- To refine your search, you can use different options
  - Article type
  - Text availability
  - PubMed
  - Publication date
  - Species
  - Age
- Customize and Show additional filter will also give you other options to filter

The screenshot shows a PubMed search results page with a red box highlighting the 'Filters' sidebar on the right. A green arrow points from the 'Show additional filters' link in the sidebar back towards the main search results area.

**Article types**  
Clinical Trial  
Systematic Reviews  
Customize ...

**Text availability**  
Abstract  
Free full text  
Full text

**PubMed**  
Commons  
Reader comments  
Trending articles

**Publication dates**  
5 years  
10 years  
Custom range...

**Species**  
Humans  
Other Animals

**Ages**  
Child: birth-18 years  
Infant: birth-23 months  
Infant: 1-23 months  
Adult: 19+ years  
Adult: 19-44 years  
Aged: 65+ years  
Customize ...

**Show additional filters**

**Search results**  
Items: 1 to 20 of 155

Format: Summary Sort by: Most Recent Per page: 20

Send to Filters: Manage Filters

Results by year

Download CSV

Titles with your search terms

Meta-analysis of the effects of Bifidobacterium preparations for it [Complement Ther Med. 2017]

[A prospective control study of <>Saccharomyces [Zhonghua Nei Ke Za Zhi. 2017]

Probiotics for prevention of radiation-induced diarrhea: A meta-analysis of r [PLOS One. 2017]

See more...

Find related data

Database: Select

Find items

Search details

((((prevent>Title/Abstract) OR prevent>Title/Abstract) OR prevent>Title/Abstract) OR prevent>Title/Abstract) OR prevent>Title/Abstract)

Search See more...

Recent Activity

Turn Off Clear

Q (((((prevent>Title/Abstract) AND diar\*

# Download history

---

- This is the search history

The screenshot shows a Microsoft Excel spreadsheet titled "history.csv - Excel". The spreadsheet contains a table with columns labeled "Recent queries in pubmed", "Query", "Items found", and "Time". The data consists of approximately 37 rows of search history entries. The first few rows are:

| Recent queries in pubmed | Query                                                 | Items found | Time     |
|--------------------------|-------------------------------------------------------|-------------|----------|
| 2                        | Search ((((( "Carbonated Beverages/adverse effect     | 89          | 03:19:35 |
| 4                        | #24 Search (((("Carbonated Beverages/adverse effects  | 89          | 03:13:10 |
| 5                        | #23 Search ((( "Carbonated Beverages/adverse effects" | 89          | 03:05:45 |
| 6                        | #22 Search ((Adolescent) OR infant) OR child          | 3405762     | 03:04:44 |
| 7                        | #17 Search ("Obesity/blood"[Mesh] OR "Obesity/compl   | 120577      | 02:58:31 |
| 8                        | #9 Search obesity                                     | 266141      | 02:54:23 |
| 9                        | #14 Search ("Carbonated Beverages/adverse effects"[M  | 913         | 02:50:22 |
| 10                       | #12 Search (((soda) OR pop)) AND obesity)) AND pedia  | 33          | 02:37:07 |
| 11                       | #11 Search (((soda) OR pop)) AND obesity              | 466         | 02:36:36 |
| 12                       | #10 Search pediatrics                                 | 400972      | 02:35:42 |
| 13                       | #8 Search (soda) NOT pop                              | 5071        | 02:34:06 |
| 14                       | #7 Search (soda) OR pop                               | 15832       | 02:32:09 |
| 15                       | #6 Search (soda) AND pop                              | 68          | 02:31:38 |
| 16                       | #5 Search soda*                                       | 6590        | 02:26:06 |
| 17                       | #4 Search "soda pop"                                  | 60          | 02:24:29 |
| 18                       | #3 Search soda pop                                    | 2802        | 02:22:54 |
| 19                       | #2 Search pop                                         | 10761       | 02:21:21 |
| 20                       | #1 Search soda                                        | 5139        | 02:18:18 |
| 21                       |                                                       |             |          |
| 22                       |                                                       |             |          |
| 23                       |                                                       |             |          |
| 24                       |                                                       |             |          |
| 25                       |                                                       |             |          |
| 26                       |                                                       |             |          |
| 27                       |                                                       |             |          |
| 28                       |                                                       |             |          |
| 29                       |                                                       |             |          |
| 30                       |                                                       |             |          |
| 31                       |                                                       |             |          |
| 32                       |                                                       |             |          |
| 33                       |                                                       |             |          |
| 34                       |                                                       |             |          |
| 35                       |                                                       |             |          |
| 36                       |                                                       |             |          |
| 37                       |                                                       |             |          |

# Exporting articles to EndNote

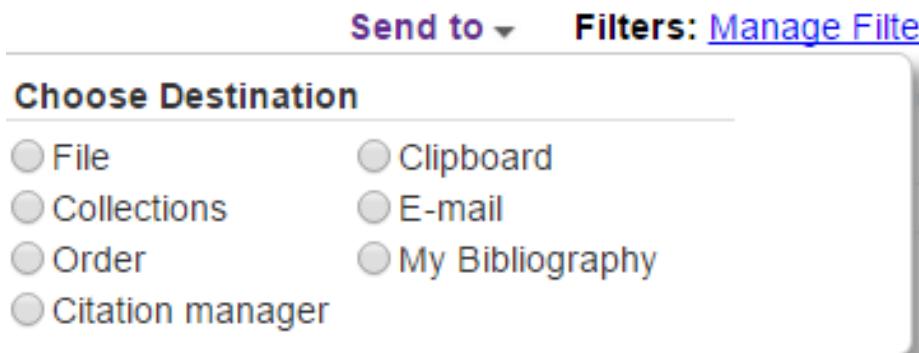
---

- Click review → select the articles you want to export
  - Click “send to”
  - Choose file
  - Under format, select Medline
  - Click “create file”
  - Open endnote
  - Go to file and click “import” → select “file”
  - Choose the file you created
  - in the import option, choose PubMed

# Send to EndNote first

---

- There are different ways to send to endnote

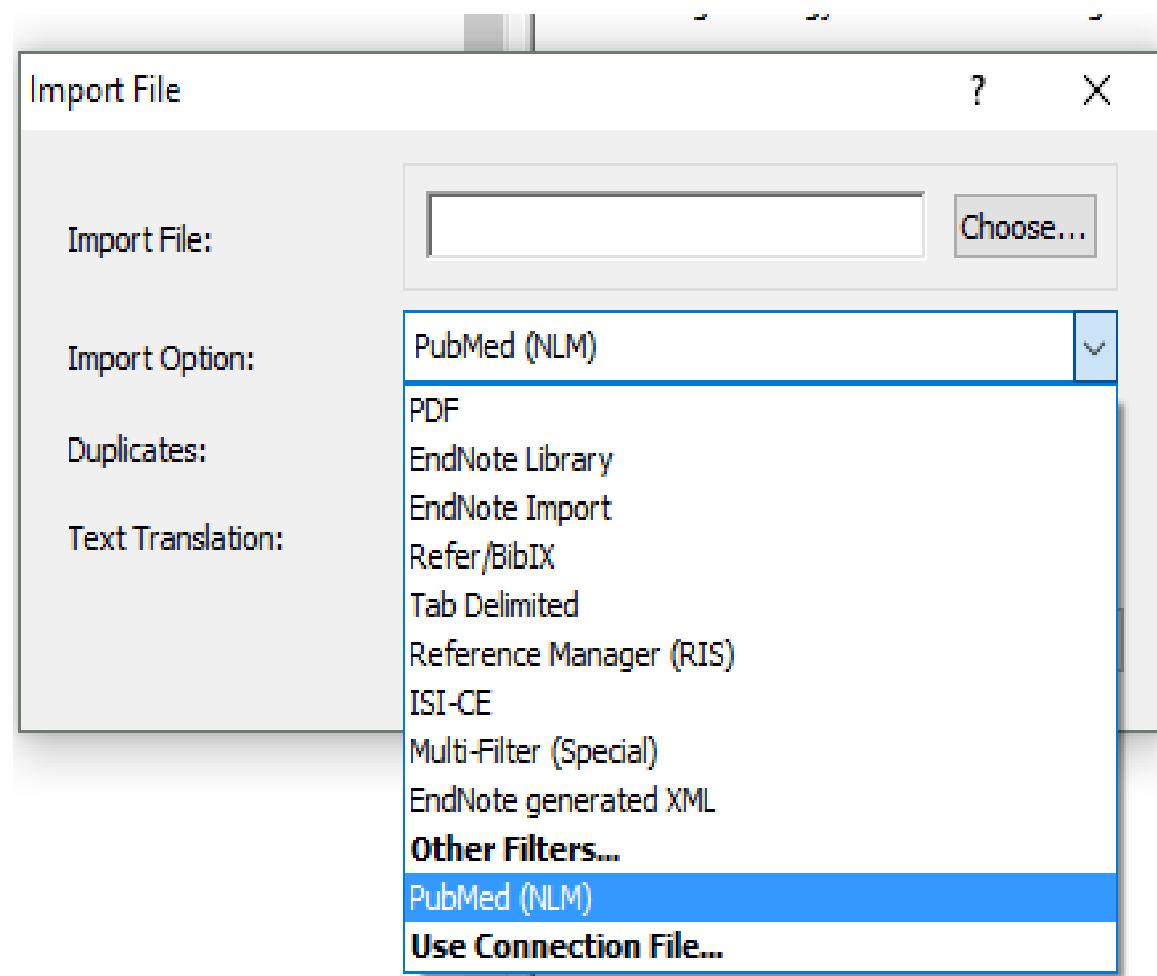


- If “citation manager” then only 200 papers will be exported
- If you want to take all the articles in PubMed, use “file”
- Then all available articles will be saved in .txt format.
- To take this to EndNote, you can use “import”. Then choose PubMed

# Import

---

- If PubMed is not available in the list, click “other files” and look for PubMed(NLM)
  
- Then open



# Removing duplicates

- Refining paper
  - Duplicate removal
  - Removal by title
  - Title and abstract
  - Full paper review
  - Approval

The screenshot shows the EndNote desktop application interface. The menu bar includes File, Edit, References, Groups, Tools, Window, and Help. The 'References' menu is open, showing options like New Reference, Edit References, Move References to Trash, Go To..., Copy References To, E-mail Reference, and Find Full Text. Below this is a search panel with three dropdown menus: 'Contains' (selected), 'Contains', and 'Contains'. A search bar at the top right says 'Search Whole Group' with checkboxes for 'Match Case' and 'Match Words'. The main window displays a grid of 89 references. The columns are: Title, Rating, Journal, Ref Type, URL, and Last Updated. The 'Find Duplicates' option in the References menu is highlighted with a blue selection bar.

| Title                                                | Rating | Journal            | Ref Type        | URL                            | Last Updated |
|------------------------------------------------------|--------|--------------------|-----------------|--------------------------------|--------------|
| Soft drinks in schools                               |        | Pediatrics         | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Randomised trials link sugary drinks to weight ...   |        | Bmj                | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Babies from Pakistani communities eat high su...     |        | Nurs Child You...  | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Drink to your health?                                |        | CDS Rev            | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Soft drinks and obesity                              |        | J Pediatr          | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| The problems of pouring-rights contracts             |        | Duke Law J         | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Bubbling over: soda consumption and its link t...    |        | Policy Brief U...  | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| The effect of school district nutrition policies ... |        | Econ Hum Biol      | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| How sugar-containing drinks might increase ad...     |        | Lancet             | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| A culturally appropriate intervention to impro...    |        | Child Obes         | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Associations of sugar-containing beverages wit...    |        | Eur J Clin Nutr    | Journal Article | http://www.nature.com...       | 08/08/2017   |
| Concerns about the discretion of sweetened b...      |        | J Am Diet Assoc    | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Effects of sugar-sweetened beverages on chil...      |        | Pediatr Ann        | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Fast food and obesity in children                    |        | Pediatrics         | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Television in the bedroom and increased body ...     |        | Pediatr Obes       | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| School soft drinks not the problem                   |        | Tex Med            | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Sugar-sweetened carbonated beverage consu...         |        | BMC Public He...   | Journal Article | https://bmcpublichealth...     | 08/08/2017   |
| How discretionary can we be with sweetened ...       |        | J Am Diet Assoc    | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Decreasing sugar-sweetened beverage consu...         |        | J Pediatr Healt... | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| The effect of soft drink availability in element...  |        | J Am Diet Assoc    | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Beverage intake of girls at age 5 y predicts adi...  |        | Am J Clin Nutr     | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| A risk analysis model of the relationship betwe...   |        | Risk Anal          | Journal Article | http://onlinelibrary.wiley...  | 08/08/2017   |
| Availability and consumption of competitive fo...    |        | J Am Diet Assoc    | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Fried, E. J.; Nestl...                               | 2002   | Jama               | Journal Article | http://jama.jamanetwork...     | 08/08/2017   |
| Gibson, S.                                           | 2008   | Hypertension       | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Ginevan, M. E.                                       | 2004   | J Pediatr          | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Gollust, S. E.; Bar...                               | 2014   | Prev Med           | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Gracey, M.                                           | 2005   | Nestle Nutr W...   | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Harrington, S.                                       | 2008   | J Sch Nurs         | Journal Article | http://journals.sagepub...     | 08/08/2017   |
| Hawkes, C.                                           | 2010   | Am J Prev Med      | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| He, F. J.; Marrero...                                | 2008   | Hypertension       | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Henry, J.; Warre...                                  | 2001   | Lancet             | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Hoare, A.; Virgo...                                  | 2014   | BMC Res Notes      | Journal Article | https://bmcresearchnotes.bi... | 08/08/2017   |
| James, J.; Thoma...                                  | 2004   | Bmj                | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Juul, F.; Hemmin...                                  | 2015   | Public Health N... | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Katelaris, A.                                        | 2012   | Med J Aust         | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Katzmarzyk, P. T...                                  | 2016   | Nutrients          | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Kavey, R. E.                                         | 2010   | J Am Diet Assoc    | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |
| Keast, R. S.; Swi...                                 | 2015   | Br J Nutr          | Journal Article | https://www.cambridge...       | 08/08/2017   |
| Kerr, D.; James, J.                                  | 2002   | Lancet             | Journal Article | http://www.bmjjournals.org...  | 08/08/2017   |

# CABI Database

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- ❑ CAB Abstracts is the leading English-language bibliographic information service providing access to the world's applied **life sciences** literature
- ❑ It incorporates two bibliographic databases: CAB Abstracts and Global Health
- ❑ CAB Direct is an access point for multiple bibliographic databases produced by CABI

# MeSH demand

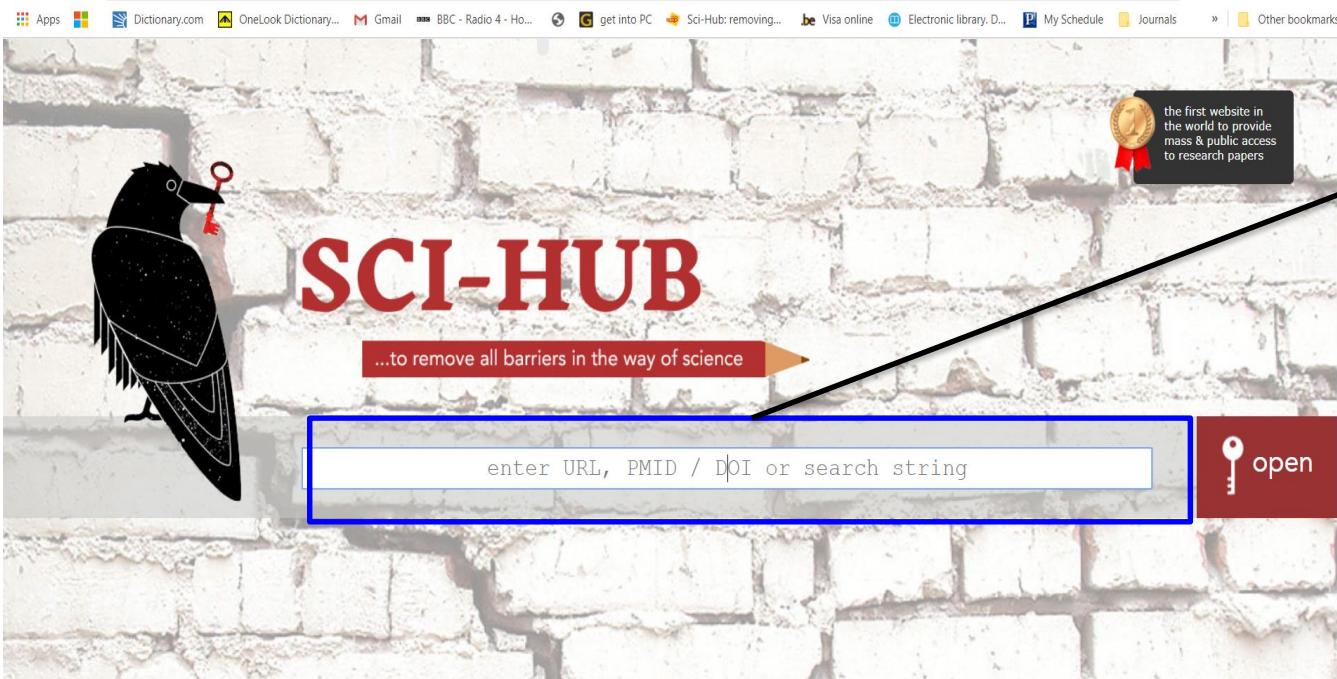
The screenshot shows a web browser window with the following details:

- Address Bar:** https://meshb.nlm.nih.gov/MeSHonDemand
- Header:** NIH U.S. National Library of Medicine
- Navigation:** Search, Tree View, MeSH on Demand, MeSH 2020, MeSH Suggestions, About MeSH Browser, Contact Us
- Content Area:**
  - Section Title:** MeSH Demand
  - Text:** MeSH on Demand identifies MeSH® terms in your submitted text (abstract or manuscript). MeSH on Demand also lists PubMed similar articles relevant to your submitted text.
  - Buttons:** Search, Reset, Help/FAQ, Features
  - Input Field:** Enter text to be processed here - then click Search
  - Text Box:** Copy and paste the
    - Title or abstract here
    - Click search to get the MeSH terms
- Bottom Navigation:** Sci-Hub.zip, ansteywatkins2018.pdf, Show all, X

# When the article is not free, where can we find it?

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- There are ways to locate the articles
  - Science hub: <https://sci-hub.tw/>



- Copy and paste the URL to the box and search

- Bookzz: <https://b-ok.org/>

## Study Selection Process

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- Aims to select only those studies that address the review question and that match the inclusion criteria documented in your protocol
- Selection should be transparent and reproducible
- Consider resource implications
- Issues may arise during study selection that require discussion/clarification between assessors
- Discuss how disagreements will be resolved
  - E.g. will a third reviewer be used?
- Assessors may want to pilot some papers before undertaking full study selection

# Study Selection Process

---

- Scan titles and abstracts
- Some common problems with identifying studies/papers:
  - Duplication of studies
  - Unclear titles
  - Lack of abstract
- If uncertain? Retrieve - scan full text
- Is the article published in the stated years?
- Does the population studied meet the criteria?
  - E.g. adults or children or both?
- Is it the correct study design?
  - E.g. RCT or meta-analysis

## Study Selection process

---

- Study selection is an initial assessment that occurs following the review search
- It addresses the question “should the full text of the paper be retrieved?”
- It is essential to use two assessors in the selection process to limit the risk of error and bias.
- This should be done independently

# Study Selection Process

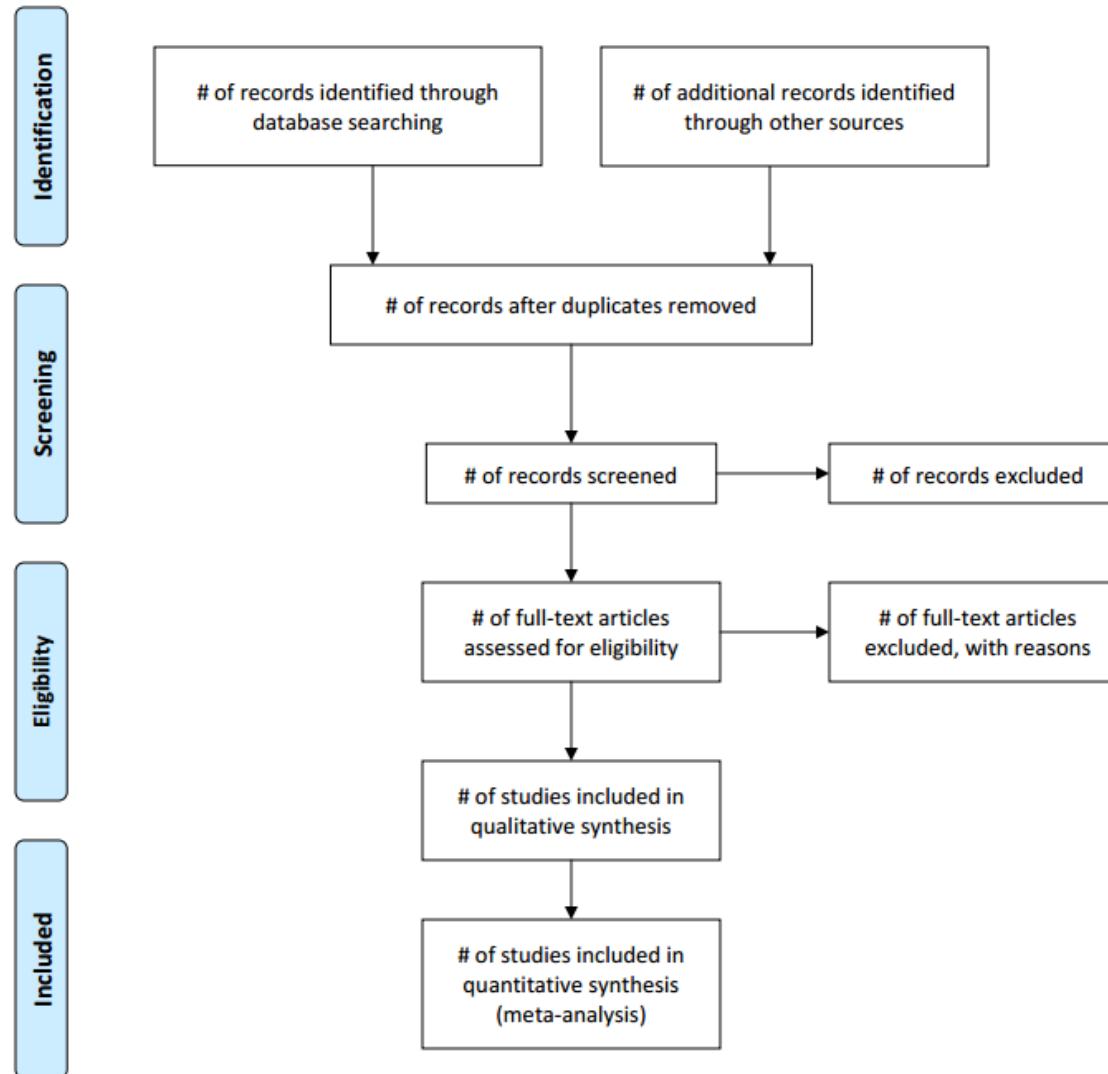
---

## Stages of Study Selection:

1. Collect all results
  2. Remove duplicates
  3. Screen title and abstract for potential retrieval of full text
  4. Screen full text for inclusion / exclusion in the review
  5. Screen reference lists of included studies
- Studies excluded at the full text phase require a reason for exclusion

# PRISMA Searching Process

PRISMA 2009 Flow Diagram



## Activity 4

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- Search articles from PubMed
- Use the MeSH term and Boolean operators
- Filter your search
- Export the search result to Endnote

# Critical Appraisal



# Critical Appraisal

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- A process that assesses the methodological quality of a study and determines the extent to which the study has addressed the risk of bias in its design, conduct and analysis
- Required in all systematic reviews
- Also referred to as:
  - Assessment of risk of bias
  - Assessment of methodological quality

## Why is it Important?

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- Combining results of poor quality research may lead to biased or misleading results
- Aim is to establish *validity* (Internal and External)
- Ensures that the review is credible and useful for informing health care policy, clinical practice and future research
- Facilitates deeper knowledge of the included studies

# Bias

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- ❑ A bias is a systematic error, or deviation from the truth, in results or inferences
- ❑ Studies may be at risk of bias due to issues with the conceptualization, design, conduct or interpretation of the study
- ❑ There are many different types of bias that can arise in research
- ❑ Major sources of bias which may affect internal validity:
  - Selection bias
  - Performance bias
  - Detection bias
  - Attrition bias

# Appraisal Tools

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- Differs based on the study design
  - Experimental studies
  - Quasi-experimental studies
  - Observational studies
    - Cohort
    - Case control
    - Analytic cross-sectional
    - ...

# JBI Critical Appraisal Tool

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[JBI Critical Appraisal-Checklist for Analytical Cross Sectional Studies](#)

[JBI Critical Appraisal-Checklist for Case Control Studies](#)

[JBI Critical Appraisal-Checklist for Cohort Studies](#)

[JBI Critical Appraisal-Checklist for Diagnostic Test Accuracy Studies](#)

[JBI Critical Appraisal-Checklist for Economic Evaluations](#)

[JBI Critical Appraisal-Checklist for Prevalence Studies](#)

[JBI Critical Appraisal-Checklist for Qualitative Research](#)

[JBI Critical Appraisal-Checklist for Systematic Reviews](#)

[JBI Critical Appraisal-Checklist for Text and Opinion](#)

[JBI Quasi-Experimental Appraisal Tool](#)

[JBI RCTs Appraisal Tool](#)

# JBI Cohort Study Critical Appraisal Tool

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1. Were the groups similar and recruited from the same population?
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
3. Was the exposure measured in valid and reliable way?
4. Were confounding factors identified?
5. Were strategies to deal with confounding factors stated?
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
7. Were the outcomes measured in a valid and reliable way?
8. Was the follow up time reported and sufficient to belong enough for outcomes to occur?
9. Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?
10. Were strategies to address incomplete follow-up utilized?
11. Was appropriate statistical analysis used?

# JBI Case-Control Study Critical Appraisal Tool

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1. Were the groups comparable other than presence of disease in cases or absence of disease in controls?
2. Were cases and controls matched appropriately?
3. Were the same criteria used for identification of cases and controls?
4. Was exposure measured in a standard, valid and reliable way?
5. Was exposure measured in the same way for cases and controls?
6. Were confounding factors identified?
7. Were strategies to deal with confounding factors stated?
8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?
9. Was the exposure period of interest long enough to be meaningful?
10. Was appropriate statistical analysis used?

## Activity 5

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- Critically apprise the articles you select using your search
- Compare your result with your colleague
- Compute the measure of agreement

# Data extraction tools



## Data extraction tools

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- Data extraction is the process by which researchers obtain the necessary information about study characteristics and findings from the included studies
  - requirements vary from review to review,
  - extraction forms should be tailored to the review question
- The first stage of any data extraction is
  - plan the type of analyses
  - list the tables that will be included in the report
- This will help to identify which data should be extracted
- A sample data extraction form and details of the data extraction process should be included in the review protocol

# Data extraction tools

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- General guidance on the process is given here
- However, the specific details will clearly depend on the individual review topic
  
- The extraction of data is linked to assessment of study quality in that both processes are often undertaken at the same time
- Standardised data extraction forms can provide consistency in a systematic review, whilst reducing bias and improving validity and reliability

# Data extraction tools

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- Participant characteristics
  - Characteristics of participants at the beginning of the study (Age, Gender, Socioeconomic status, Disease characteristics, Comorbidities ...)
- Number of participants in intervention and control group(s) or mean/median characteristic values (record whether it is the number eligible, enrolled, or randomised that is reported in the study)
- Description of the intervention(s) and control(s)
  - e.g. dose, route of administration
  - number of cycles, duration of cycle, care provider,
  - how the intervention was developed, theoretical basis (where relevant))
- Description of co-interventions

# Data extraction tools

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- Outcome data/results
  - Unit of assessment/analysis
  - Statistical techniques used
- For each prespecified outcome:
  - Definition used in study
  - Measurement tool or method used
  - Unit of measurement (if appropriate)
  - Length of followup,
  - number and/or times of followup
  - Measurements
- For all intervention and control group(s):
  - Number of participants enrolled
  - Number of participants included in analysis
  - Number of withdrawals, exclusions, lost to followup

# Data extraction tools

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- Type of analysis used in study (e.g. intention to treat, per protocol)
- Results of study analysis e.g.
  - Dichotomous: odds ratio, risk ratio and confidence intervals, pvalue
  - Continuous: mean difference, confidence intervals
- If subgroup analysis is planned the above information on outcome data or results will need to be extracted for each patient subgroup
- Additional outcomes
- Record details of any additional relevant outcomes reported
- [Data extraction tool\\_Cochrane.pdf](#)

# Data Extraction

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- Two phases:
  1. Extraction of study characteristics
    - Citation details
    - Study design and method
    - Setting/Context
    - Population characteristics
    - Intervention/Comparator/Condition/Exposure/Tests
  2. Extraction of results data
    - Outcome data and effect sizes
- Difficulties related to the extraction of data include:
  - poor reporting or missing data
    - Contact the authors
  - reliability of data extraction (i.e. between reviewers)

# Minimizing errors in Data Extraction

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- When extracting data, it is critical to be precise
- Strategies to minimize the chance of error in data extraction include:
  - Using a pre-determined and standardized data extraction form
  - Piloting the data extraction form with all review team members prior to use
  - Training and assessing data extractors
  - Having two independent data extractors

# Phase 1

---

## Extraction of study characteristics

- ❑ Citation
- ❑ Study design and method
- ❑ Setting/Context
- ❑ Population characteristics
- ❑ Intervention/Comparator/Condition/Exposure /Tests

## Phase 2

---

- > Extraction of results data
- Type of outcome data varies depending on the type of review you are undertaking and the specific review question
- Extract data only relevant to your review question
- Data may be dichotomous or continuous
  - Dichotomous = yes/no
  - Continuous = scales, interval or ratio data

# Dichotomous outcomes

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- Only two possibilities or events
  - Dead or alive
  - Lung cancer or no cancer
- Most commonly reported in terms of risk or odds

# Risk

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- ❑ Risk is defined as the probability that an event will occur

# times something happens

---

# opportunities for it to happen

- ❑ 100 patients have chronic disease ill and are treated with a new treatment. 80 of the 100 patients are cured of their illness
- ❑ Risk (probability) of being cured:
  - 80/100
  - .8
  - 80%

# Odds

---

- The odds refers to the probability an event will occur against the probability that it will not occur

$$\frac{\text{\# times something happens}}{\text{\# times it does not happen}}$$

- 100 patients have a disease and are treated with a new treatment. 80 of the 100 patients are cured of their illness
- Odds of being cured:
  - 80/20
  - 4

# Risk and Odds

---

- Interpreting risk and odds should be done carefully – the two are not interchangeable
- When an event is rare, the difference between odds and risk is small
  - Example:
    - In a group of 100 patients given a drug, 10 had an adverse reaction
    - Risk is  $10/100$ , or 0.1
    - Odds is  $10/90$ , or 0.11
  - When events are common, the difference between odds and risk is large
  - Example:
    - In a group of 100 patients given a drug, 80 had an adverse reaction
    - Risk is  $80/100$ , or 0.8
    - Odds is  $80/20$ , or 4

# 2x2 Table

---

- A two by two table is a useful tool for viewing study results and calculating effect measures for comparing groups
- This can be done with relative or absolute effect measures

|                    | Outcome<br>YES | Outcome<br>NO | Total           |
|--------------------|----------------|---------------|-----------------|
| Intervention Group | a              | b             | $a + b$         |
| Control Group      | c              | d             | $c + d$         |
| Total              | $a + c$        | $b + d$       | $a + b + c + d$ |

# Risk

---

- Risk is a proportion of events that occurred out of a total number of opportunities for the event to occur
- Risk of outcome in the experimental group is often referred to as the experimental event rate (EER)
- $EER = a / a + b$
- Risk of outcome in the control group is often referred to as the control event rate (CER)
- $CER = c / c + d$

|                    | Outcome YES | Outcome NO | Total         |
|--------------------|-------------|------------|---------------|
| Experimental Group | a           | b          | a + b         |
| Control Group      | c           | d          | c + d         |
| Total              | a + c       | b + d      | a + b + c + d |

# Risk

- Example: What is the effectiveness of Drug A compared with Drug B on myocardial infarction (MI) in at-risk patients?
- $EER = a / a + b$ 
  - In a group of 100 patients given Drug A, 10 patients had a MI
  - The risk/EER is 0.1 (10/100 patients)
  - This can be expressed as a percentage – there is a 10% risk of MI in patients given the drug
- $CER = c / c + d$ 
  - In the control group of 100 patients given Drug B, 22 people had a MI
  - The risk/CER is 0.22 (22/100 patients)
  - There is a 22% risk of MI in patients given Drug B

|                    | Outcome YES | Outcome NO | Total           |
|--------------------|-------------|------------|-----------------|
| Experimental Group | a           | b          | $a + b$         |
| Control Group      | c           | d          | $c + d$         |
| Total              | $a + c$     | $b + d$    | $a + b + c + d$ |

|        | Outcome MI | Outcome NO MI | Total |
|--------|------------|---------------|-------|
| Drug A | 10         | 90            | 100   |
| Drug B | 22         | 78            | 100   |
| Total  | 32         | 168           | 200   |

# Odds

- Odds are the probability that an event will occur against the probability that it will not occur
- Regarding health-related outcomes, this is the number of people who achieved an outcome against the number of people who did not achieve an outcome
- Odds =  $a / b$
- Example:
  - In a group of 100 patients given Drug A, 10 patients had a myocardial infarction
  - Odds are  $10/90$ , or 0.11

|                    | Outcome YES | Outcome NO | Total           |
|--------------------|-------------|------------|-----------------|
| Intervention Group | a           | b          | $a + b$         |
| Control Group      | c           | d          | $c + d$         |
| Total              | $a + c$     | $b + d$    | $a + b + c + d$ |

|        | Outcome MI | Outcome NO MI | Total |
|--------|------------|---------------|-------|
| Drug A | 10         | 90            | 100   |
| Drug B | 22         | 78            | 100   |
| Total  | 32         | 168           | 200   |

# Relative Risk (RR)

---

- Relative risk (RR, also known as the risk ratio) is the ratio of risk in one group (for example, intervention group) divided by the risk in another group (for example, control group)
- RR is a relative type of effect size
- Minimum possible value for RR is zero
- Maximum possible value for RR is plus infinity
- A value of 1 for RR indicates no difference between compared groups

# Relative Risk

---

- The relative risk (RR) is the ratio of risk of an event happening in one group and the risk of an event happening in another group
- It is an estimate of the relative effect size of an intervention or treatment
- $RR = (a / a + b) / (c / c + d)$
- $RR = EER/CER$
  
- Example:
  - $RR = (10/100) / (22/100)$
  - $RR = 0.45$
  - Patients who take Drug A are 55% less likely to have a MI than patients who take Drug B

|                    | Outcome YES | Outcome NO | Total         |
|--------------------|-------------|------------|---------------|
| Intervention Group | a           | b          | a + b         |
| Control Group      | c           | d          | c + d         |
| Total              | a + c       | b + d      | a + b + c + d |

|        | Outcome MI | Outcome NO MI | Total |
|--------|------------|---------------|-------|
| Drug A | 10         | 90            | 100   |
| Drug B | 22         | 78            | 100   |
| Total  | 32         | 168           | 200   |

# Risk Difference (RD)

---

- Risk difference (RD) is defined as the difference between the risk in one group and the risk in the other group
- RD is an 'absolute' type of effect size
- Minimum possible value for RD is -1
- Maximum possible value for RD is +1
- A value of zero for RD indicates no difference between compared groups
- From the previous example comparing Drug A and Drug B:
  - Risk of MI in patients treated with Drug A =  $10/100 = 0.10$
  - Risk of MI in patients treated with Drug B =  $22/100 = 0.22$
  - Risk difference =  $-0.12$

|        | Outcome<br>MI | Outcome<br>NO MI | Total |
|--------|---------------|------------------|-------|
| Drug A | 10            | 90               | 100   |
| Drug B | 22            | 78               | 100   |
| Total  | 32            | 168              | 200   |

# Odds Ratio (OR)

---

- Odds ratio (OR) is the ratio of the odds in two groups of subjects
- The OR is a 'relative' type of effect size
- The OR of the outcome being present is the ratio of the odds of the outcome being present in the intervention group and the odds of the outcome being present in the control group
- Minimum possible value for OR is zero
- Maximum possible value for OR is plus infinity
- A value of 1 for OR indicates no difference between compared groups

# Odds Ratio

---

- The odds ratio (OR) is the ratio of odds of an event in one group and the odds of an event in another group
- It is an estimate of the relative effect size of an intervention or treatment
- $OR = (a/b)/(c/d)$
- Example:
  - $OR = (10/90)/(22/78)$
  - $OR = 0.39$
  - Patients who take Drug A are 61% less likely to have a MI than patients who take Drug B

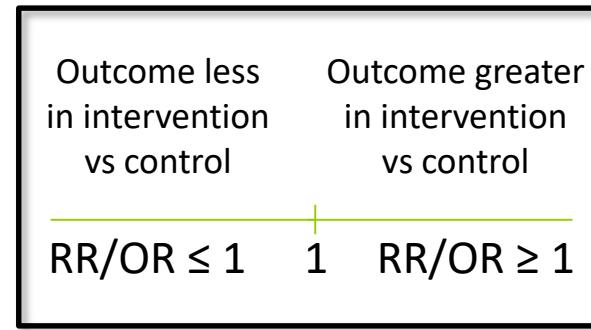
|                    | Outcome YES | Outcome NO | Total           |
|--------------------|-------------|------------|-----------------|
| Intervention Group | a           | b          | a + b           |
| Control Group      | c           | d          | c + d           |
| Total              | a + c       | b + d      | $a + b + c + d$ |

|        | Outcome MI | Outcome NO MI | Total |
|--------|------------|---------------|-------|
| Drug A | 10         | 90            | 100   |
| Drug B | 22         | 78            | 100   |
| Total  | 32         | 168           | 200   |

# Interpreting RR and OR

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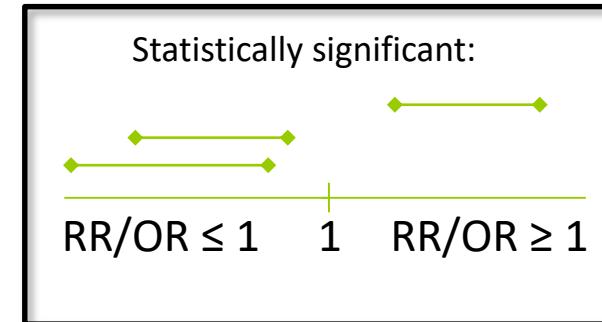
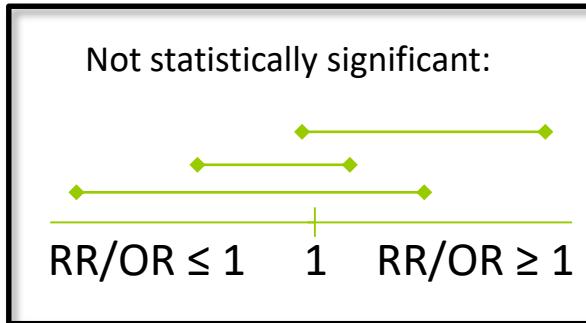
- When the RR or OR is 1 (the null value), there is no difference between two groups – the risk of the outcome is the same in both groups
- When the RR or OR is less than 1, the outcome occurs less in the intervention group than the control group
- When the RR or OR is greater than 1, the outcome occurs more in the intervention group than the control group



# Interpreting RR and OR

---

- RR and OR are usually presented with 95% Confidence Intervals (CIs) and a p value.
- When the 95%CIs cross the null value, the result is not statistically significant. When the 95%CI do not cross the null value and  $p \leq 0.05$ , the difference is statistically significant.
- From our example:
- RR 0.45 (95%CI 0.23 - 0.91;  $p \leq 0.05$ )
- OR 0.39 (95%CI 0.18 - 0.88;  $p \leq 0.05$ )



# Choosing an effect size

---

- Relative or absolute?
- Relative risk or odds ratio?
  1. The relative risk is easy to interpret
  2. Relative risk can be misleading
  3. Odds ratio has superior statistical properties
- Reviewer decision
- We recommend either of the below approaches:
  - Odds ratio
  - Relative risk **and** risk difference

# Continuous data

---

- Continuous data are where an outcome is a value in a range
  - For example: weight, length of stay, blood pressure etc.
  - Typically measured as a mean  $\pm$  standard deviation
- 
- The mean difference (or the difference in means) measures the absolute difference between the mean value of an outcome in two groups

## Weighted mean difference (MD)

---

- Weighted mean difference (MD) or difference of means is used for continuous outcomes if all studies included in meta-analysis measure the same outcome on the same measurement instrument
- The results are expressed in the natural (clinical) units used for the measurement instrument

# Standardized mean difference (SMD)

---

- The standardized mean difference (SMD) is used for continuous outcomes if studies included in meta-analysis measured the same outcome but on different measurement instruments
- The results are expressed in units of standard deviation

# WMD and SMD

---

- Both WMD and SMD are absolute types of effect sizes
- Minimum possible value for both WMD and SMD is minus infinity
- Maximum possible value for both WMD and SMD is plus infinity
- A value of zero for both WMD and SMD indicates no difference between compared groups

# Limitation and Mitigation Strategy

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- ❑ Strength
- ❑ Limitation
- ❑ Strategies to overcome the limitation
- ❑ Conclusion and other information
- ❑ Key conclusions of study authors

# Challenges in Data Extraction

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- Problems in data reporting
- Inconsistencies in published papers
- Data reported in graphs

## Activity 7

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- Develop data extraction tool
- Extract data from critical appraised articles
- Enter the data using Excel spreadsheet
- Compare your result with your colleague

# Data synthesis



1. Qualitative Synthesis
  - Systematic review
  
2. Quantitative synthesis
  - Meta analysis

# Data Synthesis

---

- Approaches to synthesis
  - Narrative
  - Meta-analysis
  - Graphical
  - Tabular
- All systematic reviews must include a narrative synthesis
- Essential Requirements:
  - Description of the search and study inclusion process
  - Descriptive summary of the included studies
  - Indication of study quality
  - Findings of the review

## The synthesis

---

- The key element of a systematic review is the synthesis:
  - Brings together the findings from the set of included studies in order to draw conclusions based on the body of evidence
  - Two main approaches are
    - **Quantitative (statistical pooling)** and **narrative**
    - Sometimes **both approaches** are used to synthesise the same set of data
    - All systematic reviews must include a narrative synthesis

# Presenting Systematic Review Results

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- The systematic review results should be organized into the **following headings:**
  - a. Description of studies
  - b. Assessment of methodological quality
  - c. Review results
  - d. Meta-analysis of quantitative research findings (where performed)

# Synthesis of Review Results: Description of studies

---

- **Description of studies includes:**
  - The **type and number of papers identified** by the search and the numbers of studies that were included and excluded from the review
  - **A PRISMA flowchart** outlining the stages
  - Details of **all full text articles** that were retrieved for critical appraisal
  - Separate appendices for details of **included and excluded** studies (incl reasons for exclusion)
  - Details of included studies

# Synthesis of Review Results: Description of studies

was necessary. When statistical pooling was not appropriate or possible, findings were presented in narrative form.

## Review results

### Description of studies

The database search yielded a total of 3244 papers. After removal of duplicates within each database, 868 potentially relevant papers were identified. One additional article was identified through cross-referencing. After removal of duplicates across databases, titles were reviewed and a total of 68 papers were included for the evaluation of abstracts. Following evaluation of abstracts, 35 articles were set for full-text assessment. Of these, 25 full-text papers were excluded, as they did not meet the inclusion criteria and another five were excluded due to missing full text publications and no provision from the authors. A total of five publications were retained for methodological quality assessment and were critically appraised by the two independent reviewers (Appendix IV). Subsequently, two papers were excluded after the critical appraisal. One, a pre/post-test study, was excluded because the statistical analysis employed was not possible to obtain. The second, a non-RCT, was excluded because the baseline characteristics of the participants in the control and treatment groups were not comparable at study entry (Appendix V). In the end, three publications were retained for final analysis. The search results are described in Figure 1. The findings from the data extraction are summarized in Appendix VI for the included studies and in Appendix VII for the excluded studies.

### Characteristics of included studies

With critical appraisal using the JBI MASTARI assessment, two quasi-experimental studies were excluded for unsatisfactory methodological quality<sup>35,36</sup> and three randomized controlled trials were retained for the purpose of the current review.<sup>37-39</sup>

Characteristics of the included and excluded studies are described in Appendix VII for the included study and Appendix VIII for the excluded studies. As only three studies were finally included in our systematic review, we decided to present the results of the two excluded studies to provide a better understanding of our discussion arguments.

### Participants

The included studies were conducted in the United Kingdom,<sup>37</sup> New Zealand<sup>38</sup> and China.<sup>39</sup> All investigated different multidisciplinary care approaches in adults (aged 18 years and older) with a diagnosis of type 2 diabetes and an evidence of nephropathy. The diagnostic criteria for type 2 diabetes was not explicitly stated for two studies<sup>37,38</sup> while the third referenced WHO criteria (without additional detail).<sup>39</sup> The diagnostic measure and cutoff point used to define nephropathy differed between the studies. Steed *et al.*<sup>37</sup> relied on the presence of microalbuminuria as indicated by two or more albumin creatinine ratios >3.0 mg/mmol or a 24-h urinary albumin excretion rate >30 mg/24 h. Chan *et al.*<sup>39</sup> included participants with plasma creatinine levels range of 150-350 µmol/L. Hotu *et al.*<sup>38</sup> included participants based on a serum creatinine measurement range of 130-300 µmol/l or proteinuria >0.5 g/day.

The RCTs recruited participants from outpatient settings such as hospital clinics and primary care practices.

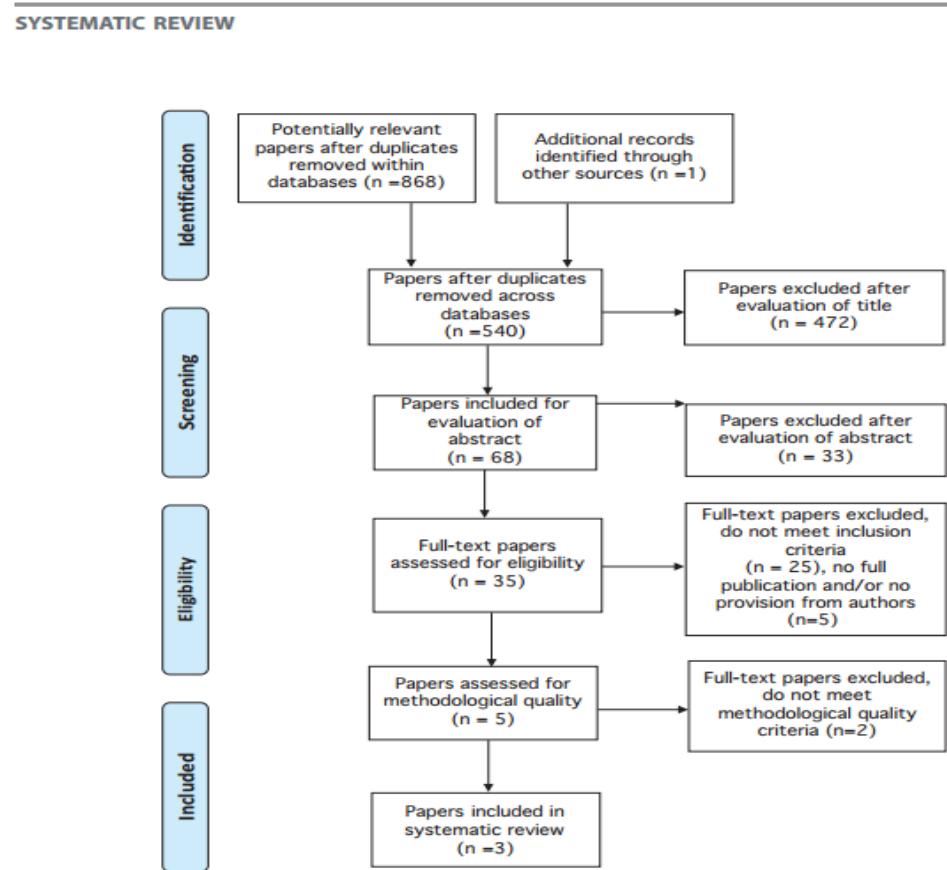
Baseline characteristics of participants in the three studies did not differ between the intervention and the control groups including, but not limited to, the duration of diabetes and the glycated hemoglobin (HbA1c). Similarly, no differences were observed at baseline for eGFR or BP for the studies of Chan *et al.*<sup>39</sup> and Hotu *et al.*<sup>38</sup> Data on baseline eGFR and BP were not available for the other study.<sup>37</sup>

### Intervention

Steed *et al.*<sup>37</sup> investigated the effect of a multidisciplinary group education program provided by a nurse and a dietician. The intervention was provided in addition to usual standard care and focused on diabetes self-management and developing problem-solving techniques. The usual standard care was provided by the diabetes clinic or general medical clinic according to physician practice. Patients in the intervention group received five weekly group education sessions, each lasting 2.5 h. This was followed, 3 months later, by a sixth "booster session" (also 2.5 h in duration). Patients received in total 15 contact hours of education.<sup>37</sup>

Chan *et al.*<sup>39</sup> examined the impact of a multidisciplinary follow-up, at a diabetes clinic, by a specialized team including diabetologists, diabetes

N. Helou *et al.*



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed.1000097

Figure 1: Flowchart of the review search results

From Helou et al 2016

# Synthesis of Review Results: Description of studies

*Appendix Table 1. Benchmark Leaders in Health Information Technology Research\**

| Study, Year (Reference),<br>Type of Study<br>(n = 54) | Institution           | Data Collection | Primary HIT Intervention | Setting    | Purpose (To Determine the Effect of . . .)                                                                                  | Dimensions of Care End Points | Effect Evaluated       | Key Finding                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------|-----------------------|-----------------|--------------------------|------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Quality adherence<br/>(n = 20)</b>                 |                       |                 |                          |            |                                                                                                                             |                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Dexter et al., 2004 (18), RCT                         |                       |                 |                          |            |                                                                                                                             |                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Dexter et al., 2004 (18), RCT                         | Regenstrief Institute | 1998–1999       | DS/EHR                   | Inpatient  | Computer-based standing orders vs. computerized physician reminders                                                         | Effectiveness                 | Adherence/surveillance | 12-percentage point absolute increase (from 30% to 42%) in influenza vaccinations and 20-percentage point absolute increase (from 31% to 51%) in pneumococcal vaccinations in the standing-orders group; computer identified 50% and 22% of hospitalized patients as eligible for influenza and pneumococcal vaccinations, respectively; 19% and 7% of patients screened by computer as eligible for influenza and pneumococcal vaccines stated that they had previously been vaccinated and did not require another vaccination (data from outside facilities not present in evaluated system) |
| Dexter et al., 1998 (19), RCT                         | Regenstrief Institute | NS              | DS/EHR                   | Outpatient | Computer-generated, paper-based reminders on planning for end-of-life care vs. usual care (no reminder)                     | Effectiveness                 | Adherence              | 20-percentage point absolute increase (from 4% to 24%) in physicians who discussed advance directives; 11-percentage point absolute increase (from 4% to 15%) in physicians caring for patients who completed advanced care plans                                                                                                                                                                                                                                                                                                                                                               |
| Overhage et al., 1997 (20), RCT                       | Regenstrief Institute | 1992–1993       | DS/CPOE                  | Inpatient  | Point-of-care computerized reminders on adherence to guideline-based care vs. usual care (CPOE without evaluated reminders) | Effectiveness/efficiency      | Adherence              | 24-percentage point absolute increase (from 22% to 46%) in adherence to guidelines; adherence increased for immediate, 24-h, and total hospital stays; little increase between immediate and 24-h adherence; 33% relative decrease (from 156 to 105) in number of pharmacist interventions; no statistically significant difference in costs or length of stay                                                                                                                                                                                                                                  |

*Continued on following page*

# Results..Systematic review incidence preeclampsia in SSAs

| Study ID | Author, year     | Countries                                                                                  | Total pregnant women | Incidence of preeclamptic women | Proportion incidence preeclampsia [%] | Incidence preeclampsia |                    | GA at inclusion |
|----------|------------------|--------------------------------------------------------------------------------------------|----------------------|---------------------------------|---------------------------------------|------------------------|--------------------|-----------------|
|          |                  |                                                                                            |                      |                                 |                                       | With severe-fet        | Without severe fet |                 |
| 1        | Francois F, 2014 | Cameroon                                                                                   | 569                  | 117                             | 20.56                                 | 102[87%]               | 15[13%]            | 20wks           |
| 2        | Megumi I,2017    | Kenya                                                                                      | 1226                 | 4                               | 0.33                                  |                        |                    | 20wks           |
| 3        | Solwayo N,2017   | Zimbabwe                                                                                   | 9,086                | 121                             | 1.33                                  | 95[79%]                | 26[21%]            | 20wks           |
| 4        | L. Browne,2015   | Ghana                                                                                      | 789                  | 14                              | 1.77                                  |                        |                    | <17wks          |
| 5        | Adeosun O,2015   | Nigeria                                                                                    | 159                  | 79                              | 48.68                                 |                        |                    | 34-38wk         |
| 6        | Pierre-M,2017    | Cameroon                                                                                   | 152                  | 96                              | 63.15%                                |                        |                    | 20wks           |
| 7        | Jonah M,2018     | Nigeria                                                                                    | 307                  | 27                              | 8.79                                  |                        |                    | <=20wks         |
| 8        | Annettee ,2014   | Uganda                                                                                     | 118, 849             | 9130                            | 7.68                                  |                        |                    | <28wks          |
| 9        | Olympe C,2013    | Uganda                                                                                     | 2413                 | 317                             | 13.14                                 |                        |                    | <28wks          |
| 10       | Josaphat B,2014  | Uganda                                                                                     | 2506                 | 90                              | 3.59                                  |                        |                    | <34wks          |
| 11       | Alison M,2013    | Cape Verde                                                                                 | 6215                 | 331                             | 5.33                                  |                        |                    | <34wks          |
| 12       | Pontiano K,2014  | Somalia                                                                                    | 165001               | 986                             | 0.6                                   |                        |                    | <28wks          |
| 13       | Florence,2014    | Uganda                                                                                     | 15639                | 356                             | 2.28                                  |                        |                    | 24wks           |
| 14       | Morrison S,2015  | Botswar  | 9539                 | 95                              | 0.99                                  |                        |                    | 20wks           |
| 15       | Emmanuel,2010    | Uganda                                                                                     | 25000                | 200                             | 0.8                                   | 160[80%]               | 25[16%]            | 20wks           |
| 16       | Francois F,2014  | Cameroon                                                                                   | 5610                 | 117                             | 2.08                                  | 37[32%]                | 15[13%]            | >=20wks         |
| 17       | Paul K,2014      | Uganda                                                                                     | 932                  | 13                              | 1.39                                  | 5[39%]                 |                    | 12-22wk         |
| 18       | Michael J,2013   | Tanzania                                                                                   | 19,811               | 137                             | 0.69                                  |                        |                    | 20wks           |
| 19       | U. Vivian,2017   | Mozambique                                                                                 | 696                  | 55                              | 7.90                                  |                        |                    | 20-27 wk        |
| 20       | David R,2009     | South Africa                                                                               | 4735                 | 169                             | 3.57                                  |                        |                    | 20-34wk         |
| 21       | Igbaruma,2016    | Nigeria                                                                                    | 11 308               | 10                              | 0.08                                  |                        |                    | >=24wks         |
| 22       | Beatriz M,2018   | Mozambique                                                                                 | 472                  | 135                             | 29                                    |                        |                    | 24wks           |
| 23       | Fadalallah,2014  | Sudan                                                                                      | 188                  | 165                             | 88                                    | 29[18%]                | 136[82%]           | 20wks           |

# Synthesis of Review Results : Methodological quality

| Table 3. Details of the Papers Included in the Systematic Review |         |                        |                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |                                                                                                                                                                                                                                                                                                                                                              |          |
|------------------------------------------------------------------|---------|------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| Author                                                           | Country | Target of Intervention | Goal                                             | Intervention                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Design                                 | Key Findings                                                                                                                                                                                                                                                                                                                                                 | Quality  |
| Ngabo et al <sup>20</sup>                                        | Rwanda  | CHWs                   | Communication between CHWs and health facilities | <ul style="list-style-type: none"> <li>Rapid SMS system: facilitates communication between CHWs and the rest of the health system (health providers, ambulance, etc.)</li> <li>CHWs trained using cascade approach</li> <li>432 CHWs trained; 500 cell phones distributed among them</li> </ul>                                                                                                                                                                                                         | Before and after with no control group | <ul style="list-style-type: none"> <li>11,502 pregnancies (81% of estimated total in district) registered over 1 y</li> <li>163 SMS alerts associated with danger signs</li> <li>3 maternal deaths and 137 child deaths registered in system</li> <li>100% of CHWs complied with reporting</li> <li>27% increase in facility-based deliveries</li> </ul>     | Low      |
| Cole-Ceesay et al <sup>28</sup>                                  | Gambia  | TBAs and CHWs          | Communication between CHWs and health facilities | <ul style="list-style-type: none"> <li>Complex intervention package</li> <li>Mobile phone component: phones linked community with emergency ambulance service and hospitals</li> </ul>                                                                                                                                                                                                                                                                                                                  | Endline assessment                     | <ul style="list-style-type: none"> <li>Mobile phone component outcomes not independently addressed</li> <li>109 patients transferred from communities to local hospitals over 3 y</li> <li>Main limitations: lack of call credit and short battery life</li> </ul>                                                                                           | Low      |
| Lori et al <sup>22</sup> ; Munro et al <sup>21</sup>             | Liberia | TBAs                   | Data collection                                  | <ul style="list-style-type: none"> <li>Part of I-ROPE project: mobile phone data collection and training non- or low-literate TBAs (<math>n = 99</math>)</li> <li>TBAs trained to send real-time SMS for data collection on the total number of pregnant women in the community; asked to send an SMS to local server with personal information and information of identified pregnant woman using a 10-digit code</li> <li>TBAs provided with mobile phones, call credit, and solar charger</li> </ul> | Before and after with no control group | <ul style="list-style-type: none"> <li>Mean increase in cell phone knowledge score was 3.67 between pre- and post-test</li> </ul>                                                                                                                                                                                                                            | Moderate |
|                                                                  |         |                        |                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        | <ul style="list-style-type: none"> <li>Significant improvement in following abilities on 1-y post-test assessment: turn on the mobile without help, make calls without help, identify mobile coverage, identify if mobile is charged, create messages without help, send SMS without help; continued to have difficulty adding minutes to a phone</li> </ul> | Moderate |

# Synthesis of Review Results : Methodological quality

| Table 3. continued        |         |                        |                      |                                                                                                                                                                                                                                                                                                     |                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
|---------------------------|---------|------------------------|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Author                    | Country | Target of Intervention | Goal                 | Intervention                                                                                                                                                                                                                                                                                        | Design                                                                | Key Findings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Quality |
|                           |         |                        |                      | <ul style="list-style-type: none"> <li>Frequencies of the messages: 2/mo before 36 wk gestation and 2/wk from week 36 until delivery</li> <li>Women in the control group received standard care (ANC, skilled attendance at delivery, postnatal visit)</li> </ul>                                   | <p>health facilities,<br/>1239 women</p>                              | <ul style="list-style-type: none"> <li>59% of the women in the intervention group said text message influenced their decision to attend the antenatal visit</li> <li>71% felt that the educational messages helped them learn about danger signs in pregnancy and to feel that the health system cared for them</li> </ul> <p><i>Skilled birth attendance outcomes</i></p> <ul style="list-style-type: none"> <li>Increased skilled birth attendance in the intervention group (60%) compared with the control group (47%)</li> <li>Significant increase in skilled delivery attendance in urban areas (OR, 5.73; 95% CI, 1.51-21.81); did not affect women from rural areas</li> <li>Higher levels of skilled delivery attendance among women who attended secondary school vs. those who had not (OR, 1.33; 95% CI, 1.01-1.77) and who were primigravida vs. those who had multiple pregnancies (OR, 1.86; 95% CI, 1.41-2.46)</li> </ul> <p><i>Perinatal outcomes</i></p> <ul style="list-style-type: none"> <li>2482 children were born alive, 54 were stillborn, and 36 died within first 42 d of life</li> <li>Overall perinatal mortality rate was 27/1000 total births; 19/1000 births in intervention clusters vs. 36/1000 births in control clusters</li> <li>Intervention associated with a reduction in perinatal mortality (OR, 0.50; 95% CI, 0.27-0.93)</li> <li>Insignificant changes in stillbirths and deaths within the first 42 d of life</li> </ul> | High    |
| Odeny et al <sup>32</sup> | Kenya   | Clients                | Appointment reminder | <ul style="list-style-type: none"> <li>Up to 14 SMS sent to HIV-positive pregnant women; SMS sent every 2 wk starting on week 28 of pregnancy (max 8 depending on gestation); additional messages sent weekly during first 6 wk postpartum</li> <li>Control group received standard care</li> </ul> | <p>RCT<br/>Intervention group, n = 195<br/>Control group, n = 193</p> | <ul style="list-style-type: none"> <li>19.6% of intervention women attended a maternal postpartum clinic vs. 11.8% women in control group (RR, 1.66; 95% CI, 1.02-2.70)</li> <li>92% of intervention group infants received HIV testing compared with 85% of control group (RR, 1.0.8; 95% CI, 1.00-1.16)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | High    |

# Synthesis of Review Results: Review results

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- **Review results:**
  - Include a detailed **description of the results of the review**
  - No standardized approach so consider whether the specific review question can be used to structure the results section
    - If findings can be reported under the outcomes or if findings can be reported by study design (**e.g. RCT-based data, non-RCT data**)
  - Generally findings are discussed textually and supported with **forest plots, tables and figures as appropriate**

# Meta-Analysis



Quantitative Synthesis

# Dataset

---

## Extraction tool (Questionnaire)

| S.N | Question                             | Answer                                                          |
|-----|--------------------------------------|-----------------------------------------------------------------|
| 1   | General information                  |                                                                 |
|     | Study ID                             |                                                                 |
|     | First Author and year                |                                                                 |
|     | Study site (setting)                 |                                                                 |
|     | Enrolment and follow up period       |                                                                 |
| 2   | Study Characteristics                |                                                                 |
|     | Study design                         |                                                                 |
|     | Inclusion criteria of the study      |                                                                 |
|     | Exclusion criteria of the study      |                                                                 |
| 3   | Sample size                          | n=_____,<br>n <sub>EFV</sub> =_____,<br>n <sub>NVP</sub> =_____ |
|     | Sampling methods                     |                                                                 |
|     | Intervention/exposed group           |                                                                 |
|     | Control/unexposed group              |                                                                 |
| 4   | Statistical analysis                 |                                                                 |
| 5   | Result                               |                                                                 |
|     | Length of follow up                  |                                                                 |
|     | Participants include in the analysis |                                                                 |
|     | Lost to follow up/drop               |                                                                 |
|     | Number of total person-years         |                                                                 |
| 6   | Participants characteristics         |                                                                 |
|     | Categorical variables n(%)           | Efavirenz<br>(EFV),n(%)                                         |
|     |                                      | Nevirapine<br>(NVP) n(%)                                        |
|     | Gender: Male =<br>Female=            | Male =<br>Female=                                               |
|     |                                      | Male =<br>Female=                                               |

## Dataset in Excel

| study | Author                      | Year | design                      | country      | Event              | N     | EFVcases | EFV    | NVPcases | NVP  | Nfemale |
|-------|-----------------------------|------|-----------------------------|--------------|--------------------|-------|----------|--------|----------|------|---------|
|       | Stringer<br>6JS, et al      | 2010 | Prospective Cohort          | Multicenter  | Treatment Failure  | 878   | 15       | 58     | 231      | 820  | 878     |
|       | Kwobah<br>CM, et<br>7al     | 2012 | case-control                | Kenya        | Treatment Failure  | 3233  | 155      | 427    | 894      | 2633 | 1992    |
|       | Nachega<br>8JB, et al       | 2008 | Cohort                      | South Africa | Treatment Failure  | 2817  | 251      | 1822   | 203      | 995  | 1771    |
|       | Boulle<br>A, et al<br>92007 | 2007 | Cohort                      | South Africa | NNRTI substitution | 2679  | 25       | 1612   | 63       | 1067 | 1896    |
|       | Shearer<br>10K, et al       | 2014 | Cohort                      | South Africa | Treatment Failure  | 8854  | 307      | 8211   | 43       | 643  | 5668    |
|       | Shearer<br>10K, et al       | 2014 | Cohort                      | South Africa | Death              | 12840 | 1006     | 11,962 | 55       | 878  | 7962    |
|       | Sarfo<br>11FS, et al        | 2014 | Retrospective Observational | Ghana        | Treatment Failure  | 3990  | 633      | 2369   | 495      | 1621 | 2717    |
|       | Sarfo<br>11FS, et al        | 2014 | Retrospective Observational | Ghana        | Death              | 3990  | 208      | 2369   | 110      | 1621 | 2717    |
|       | Sarfo<br>11FS, et al        | 2014 | Retrospective Observational | Ghana        | NNRTI Substitution | 3990  | 219      | 2369   | 254      | 1621 | 2717    |



# Software for Meta-Analysis

---

- Softwares which can be used for Meta-analysis are:
  - RevMan
  - CMA
  - Stata
  - R
  - SAS
  - Open Meta analysis Software
  - ...

# Meta-Analysis using Stata



# Introduction to STATA

---

- ❑ Basics of Stata
- ❑ Data Entry
- ❑ Data management
  - Editing
  - Coding
  - Renaming
  - Generating
  - Outlier observations
  - Missing Observations
- ❑ Data analysis
  - Descriptive statistics
  - Inferential Statistics
    - ❑ Estimation
    - ❑ Hypothesis testing

## Meta analysis using stata

---

- Stata using **metan** command
- Considering STATA, either we must have STATA version 11 or install STATA packages that analyze meta data
- Steps to install the package will be given

# Installing meta-analysis in STATA

---

- Normally, there is no menu in stata which can perform meta analysis
- We have to use “metan” command without installing the menu or we can also bring the menu under “user” main menu
- There are different options to install “packages” for meta analysis

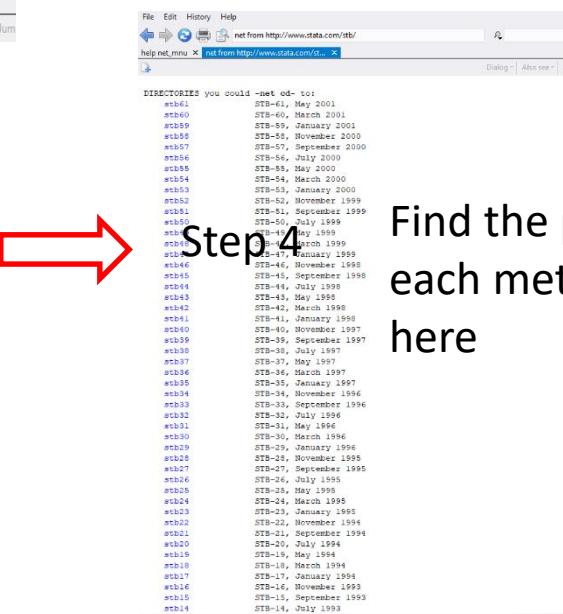
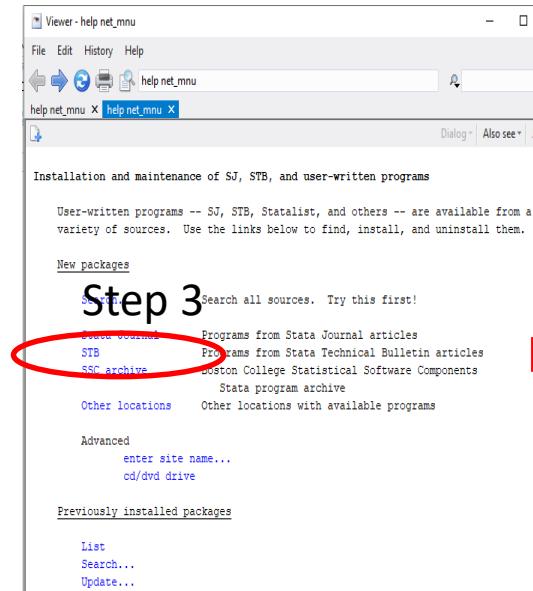
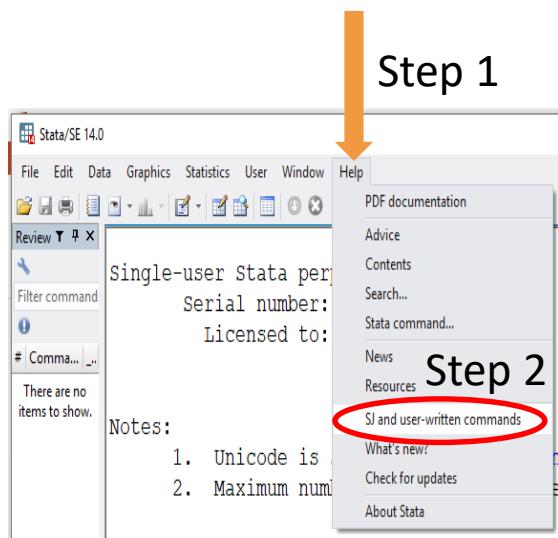
# Option I

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- As a first step make sure that your installation is up-to-date by typing **update all** in the command window
  - Stata will automatically connect to [www.stata.com](http://www.stata.com) and update the core package.
  - It will also download brief descriptions of all user-written commands published in the Stata Technical Bulletin
  - Those relating to meta-analysis can be displayed by typing **search meta**.
  - The most convenient way to install user-written commands is from within Stata.
    - Go into the “Help” menu and
    - Click on “SJ and User-Written Programs” option
    - click “STB” option.
    - Now click on <http://www.stata.com> and then on stb (for Stata Technical Bulletins).
    - The meta-analysis routines described in this chapter can then be downloaded as follows:

# Option I

- Downloading and installing user-written meta-analysis commands
- Click help
  - Click SJ and user written commands
    - Click STB



Find the package of each meta function here

| STB   | Date                   |
|-------|------------------------|
| stb61 | STB-61, May 2001       |
| stb60 | STB-60, March 2001     |
| stb59 | STB-59, February 2001  |
| stb58 | STB-58, November 2000  |
| stb57 | STB-57, September 2000 |
| stb56 | STB-56, July 2000      |
| stb55 | STB-55, June 2000      |
| stb54 | STB-54, March 2000     |
| stb53 | STB-53, January 2000   |
| stb52 | STB-52, November 1999  |
| stb51 | STB-51, October 1999   |
| stb50 | STB-50, July 1999      |
| stb49 | STB-49, April 1999     |
| stb48 | STB-48, March 1999     |
| stb47 | STB-47, February 1999  |
| stb46 | STB-46, November 1998  |
| stb45 | STB-45, September 1998 |
| stb44 | STB-44, July 1998      |
| stb43 | STB-43, May 1998       |
| stb42 | STB-42, April 1998     |
| stb41 | STB-41, January 1998   |
| stb40 | STB-40, November 1997  |
| stb39 | STB-39, September 1997 |
| stb38 | STB-38, August 1997    |
| stb37 | STB-37, May 1997       |
| stb36 | STB-36, March 1997     |
| stb35 | STB-35, January 1997   |
| stb34 | STB-34, December 1996  |
| stb33 | STB-33, September 1996 |
| stb32 | STB-32, July 1996      |
| stb31 | STB-31, May 1996       |
| stb30 | STB-30, April 1996     |
| stb29 | STB-29, January 1996   |
| stb28 | STB-28, November 1995  |
| stb27 | STB-27, September 1995 |
| stb26 | STB-26, July 1995      |
| stb25 | STB-25, May 1995       |
| stb24 | STB-24, March 1995     |
| stb23 | STB-23, January 1995   |
| stb22 | STB-22, November 1994  |
| stb21 | STB-21, September 1994 |
| stb20 | STB-20, July 1994      |
| stb19 | STB-19, May 1994       |
| stb18 | STB-18, April 1994     |
| stb17 | STB-17, January 1994   |
| stb16 | STB-16, November 1993  |
| stb15 | STB-15, September 1993 |
| stb14 | STB-14, July 1993      |

## Main functions to install

---

- On the DIRECTORIES list, find the following and follow the row

| <i>Click on...</i> | <i>... then click on</i> | <i>to install commands</i>                                    |
|--------------------|--------------------------|---------------------------------------------------------------|
| stb45              | sbe24.1                  | <code>metan</code> , <code>funnel</code> , <code>labbe</code> |
| stb43              | sbe16.2                  | <code>meta</code>                                             |
| stb42              | sbe22                    | <code>metacum</code>                                          |
| stb56              | sbe26.1                  | <code>metainf</code>                                          |
| stb58              | sbe19.3                  | <code>metabias</code>                                         |
| stb42              | sbe23                    | <code>metareg</code>                                          |

- You should check whether updated versions or new commands have become available (**update all, search meta**).

# Installing Missing functions

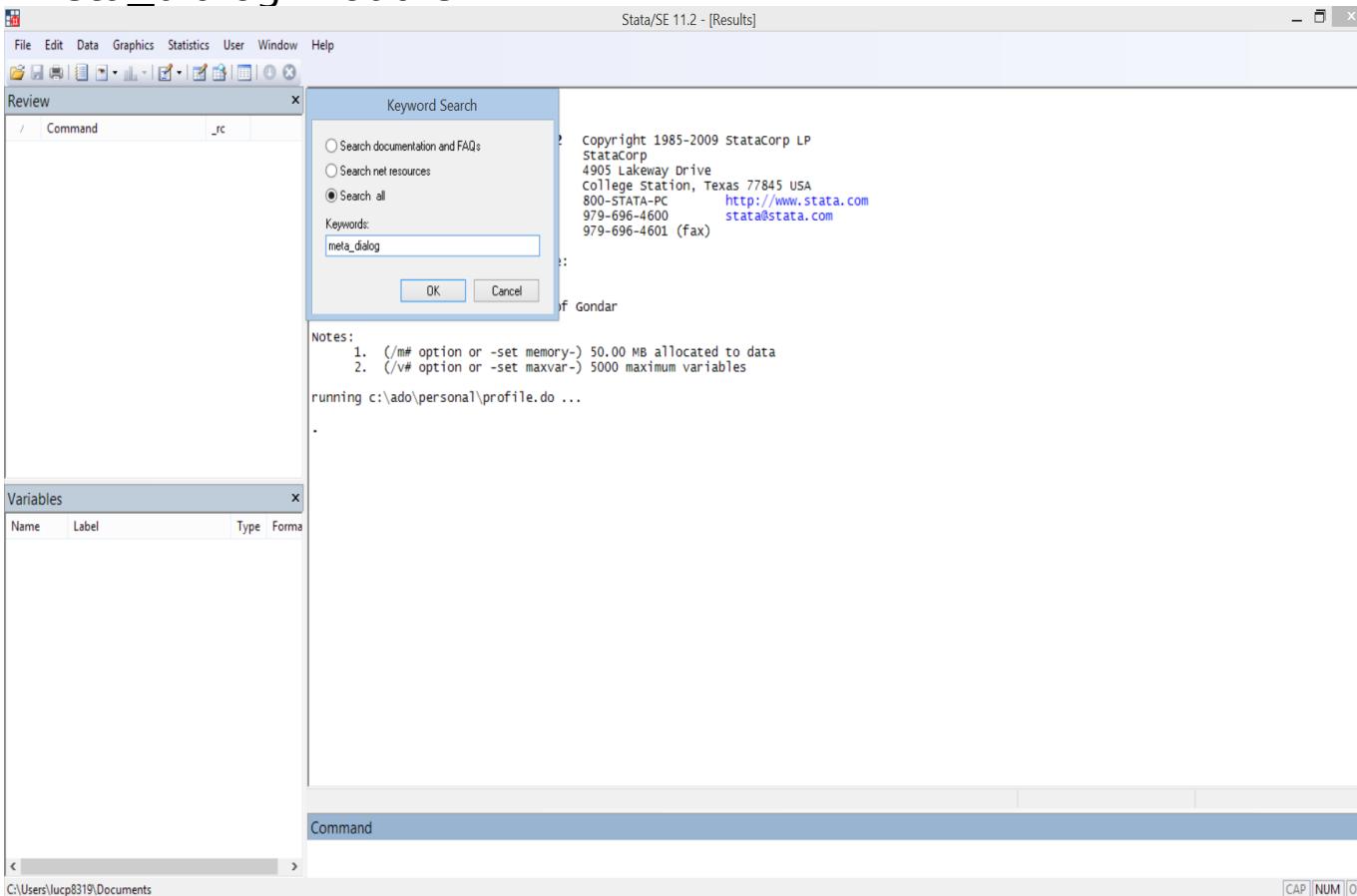
---

- When there is error “no function”
  - Then we can install the required function using
    - `ssc install function (the required function)`
      - `ssc install metatrim`
      - `ssc isntall metafunnel`
- Option I is better and simple to install the packages

# Option II

---

1. Pull down the help menu in STATA;
  1. select “search”; and search for “meta\_dialog” with the “search all” option checked.
  2. Install the meta\_dialog module



# Installing the package



# Installing the package

The screenshot shows a web browser window titled "Viewer (#1) [net describe metadialog, from(http://fmwww.bc.edu/RePEc/bocode/m)]". The page content is as follows:

package **metadialog** from <http://fmwww.bc.edu/RePEc/bocode/m>

**TITLE** 'METADIALOG': module to provide sub-menu and dialogs for meta-analysis commands

**DESCRIPTION/AUTHOR(S)**

This module provides Stata Version 8 dialog boxes (.dlg files) and the commands needed to create a Meta-Analysis sub-menu that contains the publicly available meta-analysis commands. The 14 dialogs, included in this package, that may be placed on the menu are: meta, metan, metap, metareg, metacum, funnel, metafunnel, tabbe, metannt, metaninf, metainf, galbr, metabias, and metatrim. The actual programs (.ado files) must be installed separately. Please read the instructions in the included help file, `meta_dialog.hlp`, to install the menu and use the dialogs.

KW: meta-analysis

Requires: Stata version 8.0

Author: Thomas Steichen  
Support: email [steichen@triad.rr.com](mailto:steichen@triad.rr.com)

Distribution-Date: 20051205

**INSTALLATION FILES**

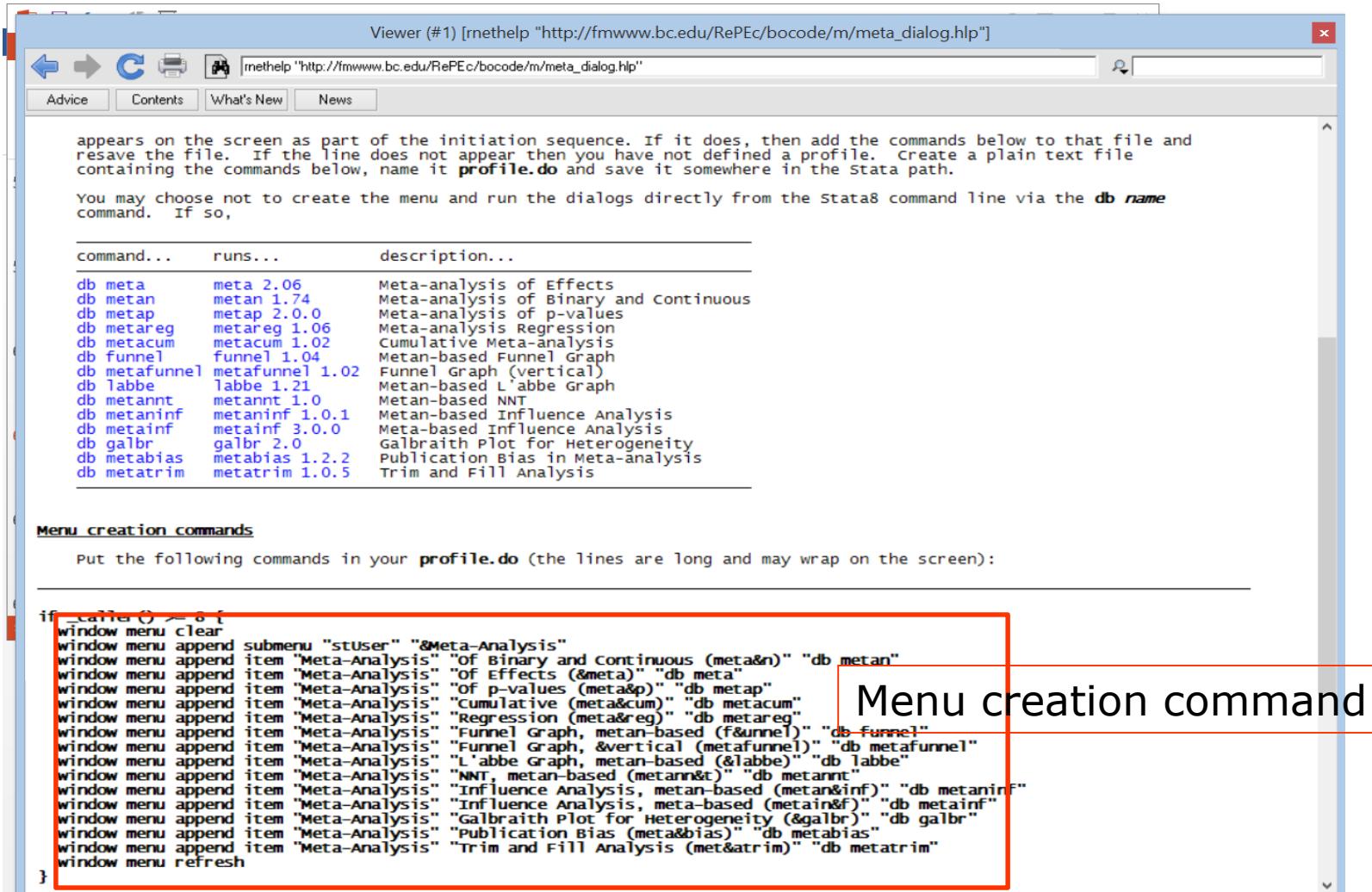
.../f/funnel.dlg  
.../g/galbr.dlg  
.../l/labebe.dlg  
**meta\_dialog.hlp**  
meta.dlg  
metabias.dlg  
metacum.dlg  
metafunnel.dlg  
metainf.dlg  
metan.dlg  
metaninf.dlg  
metannt.dlg

[\(click here to install\)](#)

**Step 1: Click here to install**

**Step 2: `meta_dialog.hlp` to find “menu creation commands”**

# Finding the menu creation command



Viewer (#1) [rnethelp "http://fmwww.bc.edu/RePEc/bocode/m/meta\_dialog.hlp"]  
metahelp "http://fmwww.bc.edu/RePEc/bocode/m/meta\_dialog.hlp"

Advice | Contents | What's New | News

appears on the screen as part of the initiation sequence. If it does, then add the commands below to that file and resave the file. If the line does not appear then you have not defined a profile. Create a plain text file containing the commands below, name it **profile.do** and save it somewhere in the Stata path.

You may choose not to create the menu and run the dialogs directly from the Stata8 command line via the **db name** command. If so,

| command...    | runs...         | description...                         |
|---------------|-----------------|----------------------------------------|
| db meta       | meta 2.06       | Meta-analysis of Effects               |
| db metan      | metan 1.74      | Meta-analysis of Binary and Continuous |
| db metap      | metap 2.0.0     | Meta-analysis of p-values              |
| db metareg    | metareg 1.06    | Meta-analysis Regression               |
| db metacum    | metacum 1.02    | Cumulative Meta-analysis               |
| db funnel     | funnel 1.04     | Metan-based Funnel Graph               |
| db metafunnel | metafunnel 1.02 | Funnel Graph (vertical)                |
| db labbe      | labbe 1.21      | Metan-based L'abbe Graph               |
| db metannt    | metannt 1.0     | Metan-based NNT                        |
| db metainf    | metainf 1.0.1   | Metan-based Influence Analysis         |
| db metainf    | metainf 3.0.0   | Meta-based Influence Analysis          |
| db galbr      | galbr 2.0       | Galbraith Plot for Heterogeneity       |
| db metabias   | metabias 1.2.2  | Publication Bias in Meta-analysis      |
| db metatrim   | metatrim 1.0.5  | Trim and Fill Analysis                 |

**Menu creation commands**

Put the following commands in your **profile.do** (the lines are long and may wrap on the screen):

```
if $caller == "stata"  
window menu clear  
window menu append submenu "stUser" "&Meta-Analysis"  
window menu append item "Meta-Analysis" "of Binary and continuous (meta&n)" "db metan"  
window menu append item "Meta-Analysis" "of Effects (&meta)" "db meta"  
window menu append item "Meta-Analysis" "of p-values (meta&p)" "db metap"  
window menu append item "Meta-Analysis" "Cumulative (meta&cum)" "db metacum"  
window menu append item "Meta-Analysis" "Regression (meta&eg)" "db metareg"  
window menu append item "Meta-Analysis" "Funnel Graph, metan-based (f&funnel)" "db funnel"  
window menu append item "Meta-Analysis" "Funnel Graph, &vertical (metafunnel)" "db metafunnel"  
window menu append item "Meta-Analysis" "L'abbe Graph, metan-based (&labbe)" "db labbe"  
window menu append item "Meta-Analysis" "NNT, metan-based (metannt)" "db metannt"  
window menu append item "Meta-Analysis" "Influence Analysis, metan-based (metainf)" "db metainf"  
window menu append item "Meta-Analysis" "Influence Analysis, meta-based (metainf&F)" "db metainf"  
window menu append item "Meta-Analysis" "Galbraith Plot for Heterogeneity (&galbr)" "db galbr"  
window menu append item "Meta-Analysis" "Publication Bias (meta&bias)" "db metabias"  
window menu append item "Meta-Analysis" "Trim and Fill Analysis (metatrim)" "db metatrim"  
window menu refresh
```

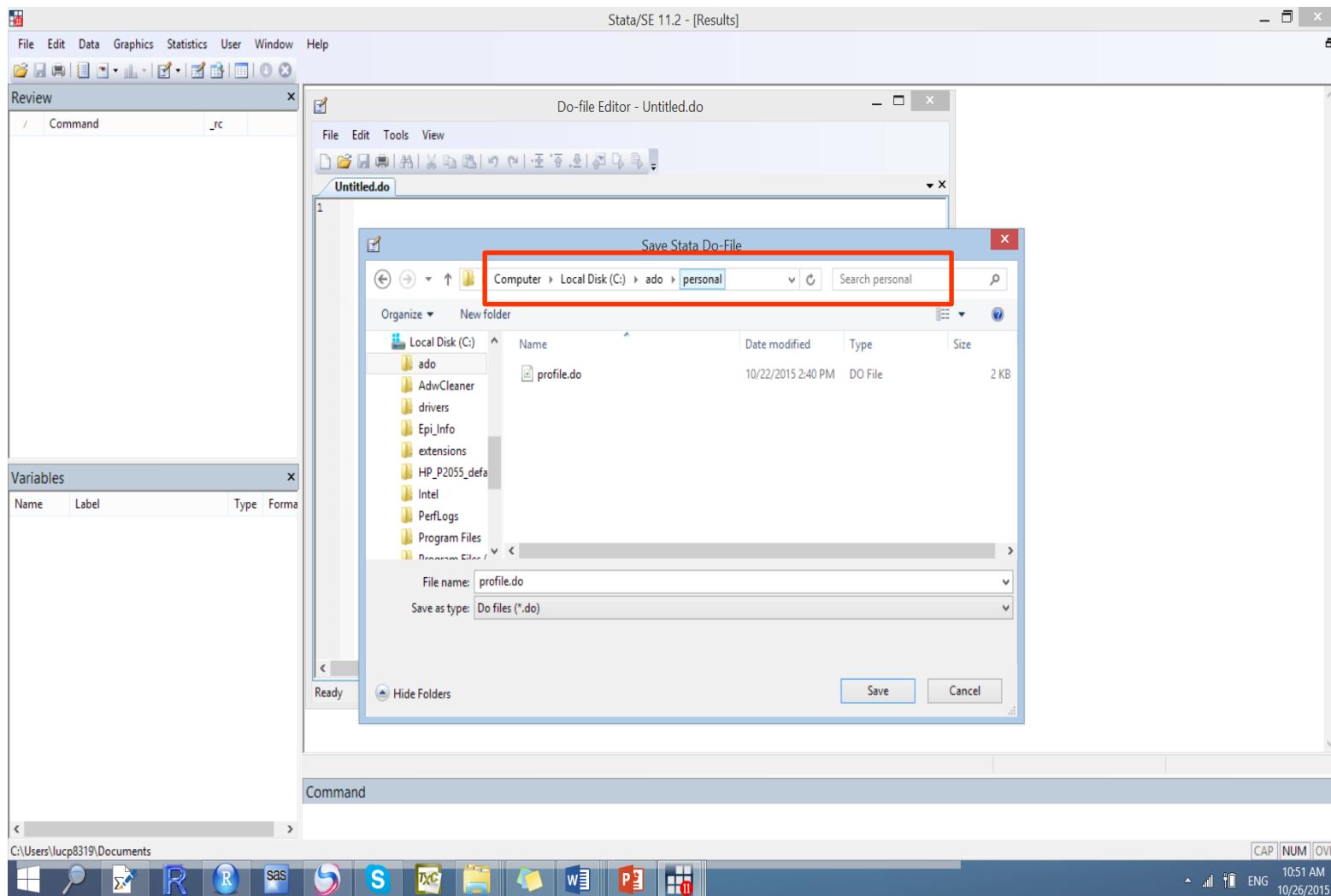
Menu creation command

## Steps of including meta analysis...

---

- Create a profile.do file and add it to your STATA do file list.
- To create open empty do file, and save the file in some path that STATA will recognize at the time of initialization:
  - C:\data\STATA\profile.do OR
  - C:\ado\personal\profile.do by the file name of “profile.do” (This can be found in C:\ where you install stata).

# Creating the profile.do file



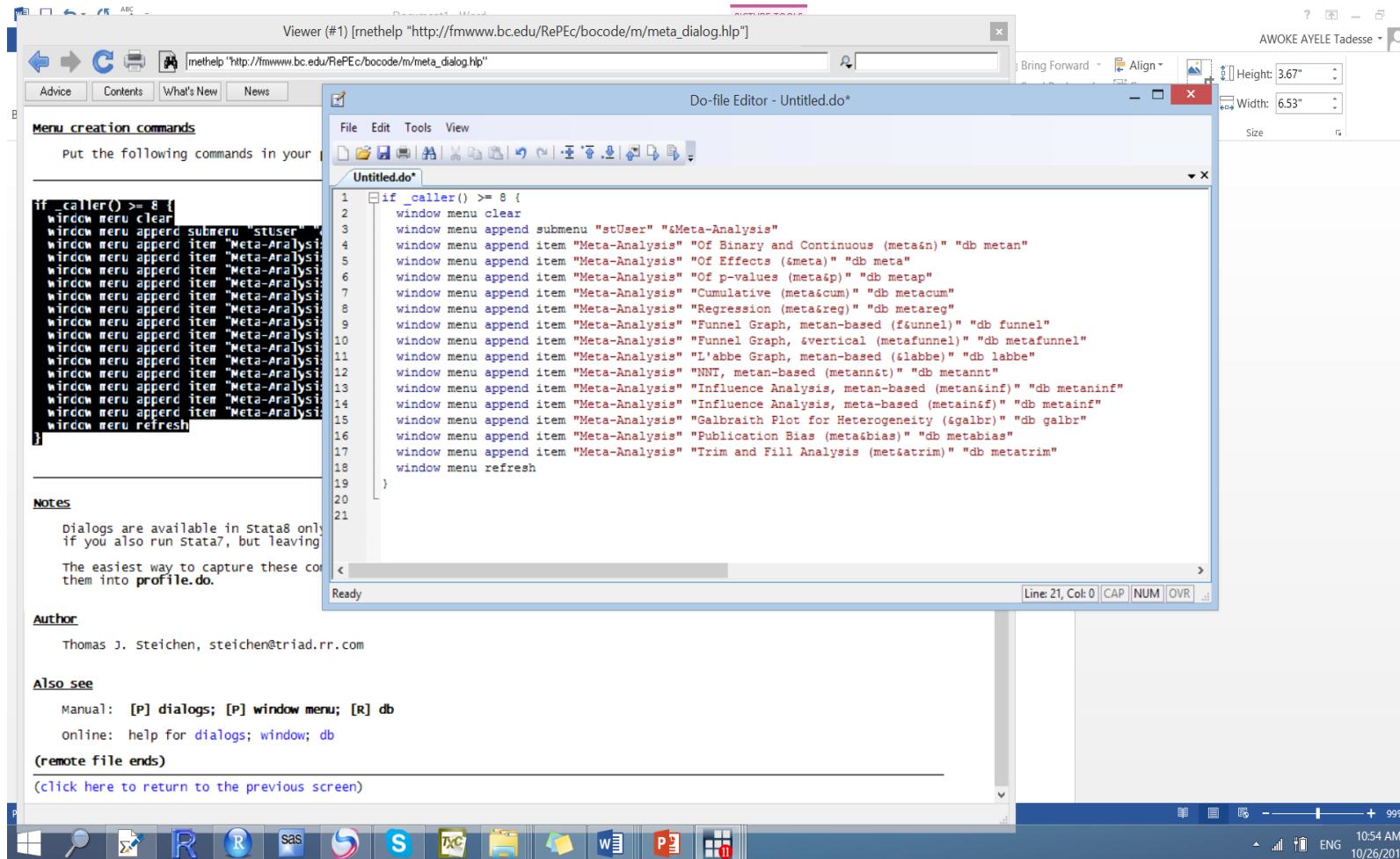
## Steps of including meta analysis ...

---

1. Copy and pest the program below “Menu Creation Commands” in to the profile.do file created above and save it there.
2. Run the command and then “Meta analysis” will appear in the menu.
3. The menu creation command can be obtained in the file we opened during the search

# Pasting menu creating commands

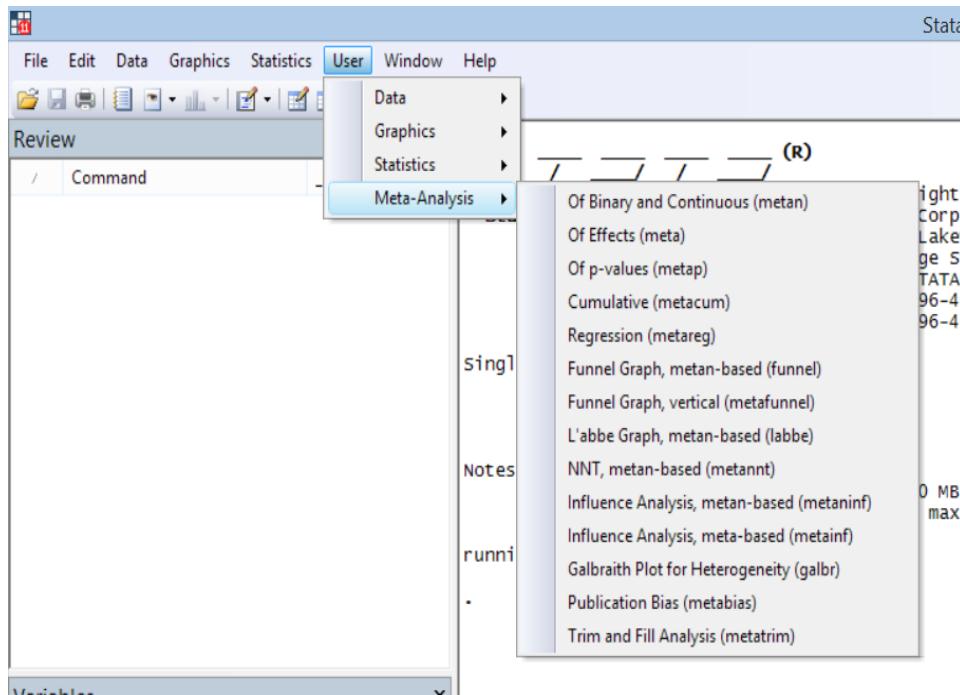
## □ Copy and past the menu creating commands



# STATA meta-analysis commands

---

- ❑ Finally the **STATA meta-analysis commands** will be active under “user menu”
- ❑ The profile.do file will launch itself automatically each time you open STATA.



# Basic principles of meta-analysis

---

- Meta-analysis is typically a two-stage process:
  - A summary statistic is calculated for each study, to describe the observed intervention effect
  - The summary statistics are usually
    - risk ratios
    - odds ratios or
    - risk differences for event data,
    - differences in means for continuous data
    - hazard ratios for survival time data

# Basic principles of meta-analysis

---

- In the second stage the overall (pooled) treatment effect is calculated as a weighted average of these summary statistics
- The weights are chosen to reflect the amount of information that each trial contains

$$\text{Weighted average} = \frac{\text{sum of (estimate} \times \text{weight)}}{\text{sum of weights}}$$

- In practice the weights are often the inverse of the variance (the square of the standard error) of the treatment effect, which relates closely to sample size
- The precision (confidence interval) and statistical significance of the overall estimate are also calculated

# Objectives of meta-analysis

---

- There are different, legitimate objectives for a meta-analysis:
  - to improve statistical power to detect a treatment effect
  - to increase precision
  - to provide the closest estimate of an unknown real effect
  - to identify subsets of studies (sub-groups) associated with a beneficial effect
  - to explore if there are differences in the size or direction of the treatment effect associated with study-specific variables

# Meta-analysis using Stata

---

- Any systematic review, whether it includes meta-analysis or not, should include all the procedures and results mentioned so far
  - Introduction
  - Methods
  - qualitative synthesis
- Following Meta synthesis, aggregate data or data from set of individual studies may be pooled quantitatively
- The rationale for a meta-analysis is that
  - By combining studies, the overall sample will increase
  - Improve the statistical power and precision of estimates of treatment effects

# Meta-analysis

---

- Meta analysis will be appropriate when:
  - the outcome variable is either a **binary** or **continuous** data
  - we have more than one study with estimated measures
  - the study characteristics that could potentially affect outcome variable are **homogeneous** in the **two groups**
  - the outcome is measured in **a similar way**
- Only appropriate when studies are considered similar enough from a clinical and methodological point of view
- Using meta analysis , we can combine measures like
  - risk ratio, odds ratio, risk difference,
  - mean difference (standardized) , p-values, correlation coefficient, and sensitivity & specificity of a diagnostic test

# Models of Meta-Analysis

---

- There are two models used in meta-analysis,
  - the **fixed effect model** and
  - the **random effects model**.
- Main difference is in the calculation of standard errors associated with the combined effect size
  - **Fixed effects** models only assume within-study variability
  - **Random effects** model assume within and between study variability

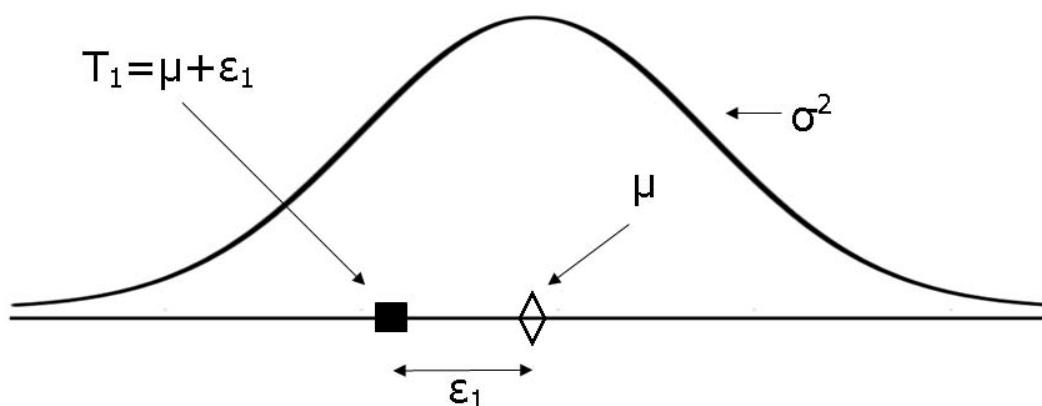
## Fixed and random effect estimate

---

- **Fixed effect model** assumes that there is **one true effect size** which is shared by all the included studies.
- It follows that the combined effect is our estimate of this common effect size
- **Random effects model** we allow that the true effect could vary from study to study.
  - effect size might be a little higher if the subjects are
    - older,
    - or more educated,
    - or healthier, and so on.
- The studies included in the meta-analysis are assumed to be a **random sample** of the relevant distribution of effects
- The combined effect estimates the mean effect in this distribution

## Fixed and random effect estimate

- **Under the fixed effect model** all studies are estimating the same effect size
- we can assign weights to all studies based entirely on the amount of information captured by that study.
- A **large study** would be given the **lion's share** of the weight, and a small study could be largely ignored



$$T_i = \mu + e_i$$

# Interpreting a fixed effects model

---

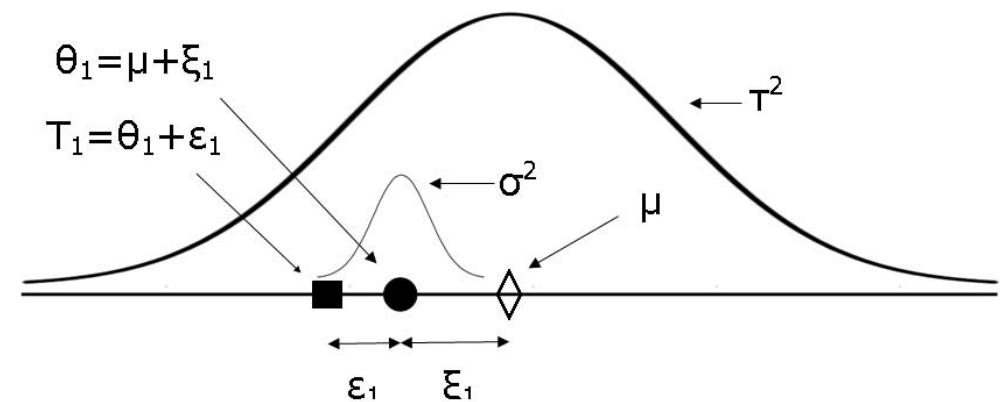
- In the fixed effects model the summary effect computed in meta-analysis is the best estimate of the common treatment effect
- In the fixed effects model the summary treatment effect is a weighted summary of the study-specific effect sizes
- The weights assigned to each study depend on the study's precision; more specifically each study's weight is equal to the inverse of its variance
- Study weights are functions of within-study variance; and confidence intervals are relatively narrow (**conservative**)

(Nikolakopoulou et al, 2014)

## Fixed and random effect estimate

- **under the random effects model** we are trying to estimate the mean of a distribution of true effects.
- Large studies may yield more precise estimates than small studies
- We want to be sure that all of these effect sizes are included in our estimate of the mean.
- The **weights assigned** under random effects are more **balanced**.
- Large studies are less likely to dominate the analysis and small studies are less likely to be ignored.

$$T_i = \theta_i + e_i = \mu + \xi_i + e_i$$



## Random effects model

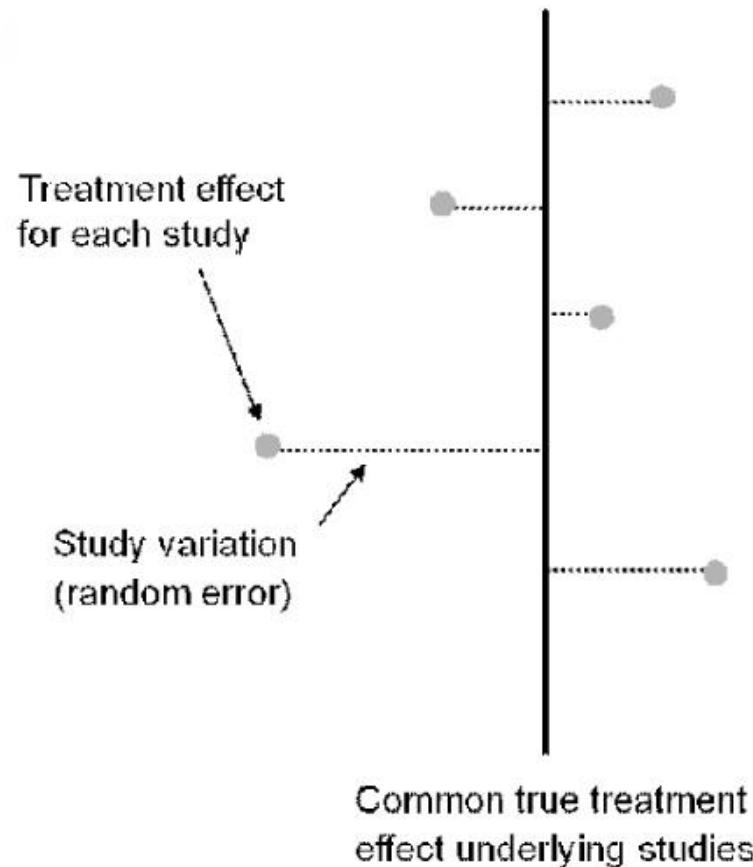
---

- Each study's effect size is a random draw from some underlying population of effect sizes and that within each study, we use a different sample of individuals so our estimate of each study's effect size will vary from its study mean by the sampling variance
- In the random effects model the summary effect computed in meta-analysis is not the estimate of a common overall effect, but the average of a collection of possible treatment effects
- Random effects gives more weight to smaller studies
- Results in **wider confidence intervals** (Liberal)
- Similar (almost identical) where heterogeneity is not present

(Khan et al, 2012; Pigott, 2012)

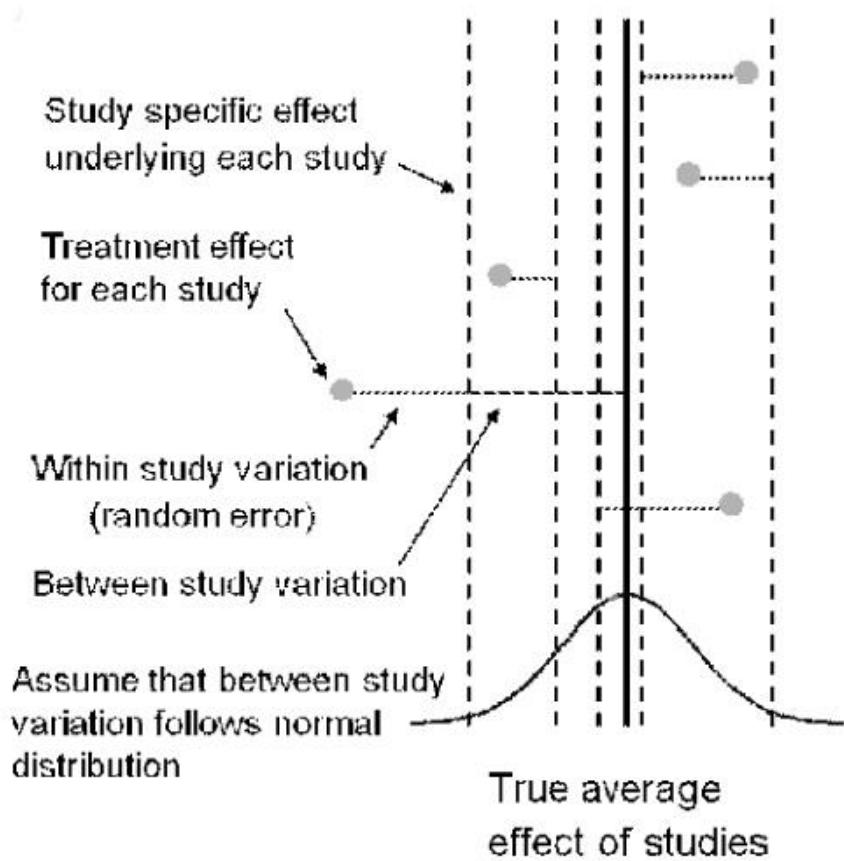
## ► Fixed effects model

A



## ► Random effects model

B



- The two meta-analysis models may yield similar or contradicting results

## Analyses on Meta data

---

- To perform meta analysis using stata, the common data structure should contain the variables:
  - Study ID
  - Study name (surname of first author followed by eta al and year of publication)
  - Year
  - Size of population 1
  - Event of from population 1
  - Non-Event of from population 1
  - Size of population 0
  - Event of from population 0
  - Non-Event of from population 0
  - **Effect size with measures of precision**
  - And other possible covariates

# Methods in meta analysis

---

- We use stata to:
  - Estimate the magnitude of true heterogeneity and test it
  - Perform Random and Fixed effect main meta analysis
  - Perform subgroup analysis (based on  $I^2$  and Q)
  - Perform Meta regression
  - Produce funnel plot and Egger's or Begg's test to explore publication bias
  - Perform sensitivity analysis

# Example 1: cholesterol reduction

Variables

Filter variables here

|    | id | trialname        | intervention | ihdentry            | cholreduc | sc  | fc   | nc   | se  |
|----|----|------------------|--------------|---------------------|-----------|-----|------|------|-----|
| 1  | 1  | WHO              | Drug         | Without known IHD   | .55       | 210 | 5086 | 5296 | 173 |
| 2  | 2  | Newcastle        | Drug         | With IHD            | .68       | 85  | 168  | 253  | 54  |
| 3  | 3  | Scottish         | Drug         | With IHD            | .85       | 75  | 292  | 367  | 54  |
| 4  | 4  | CDP              | Drug         | With IHD            | .55       | 936 | 1853 | 2789 | 676 |
| 5  | 5  | VA drug-lipid    | Drug         | With IHD            | .59       | 69  | 215  | 284  | 42  |
| 6  | 6  | Stockholm        | Drug         | With IHD            | .84       | 101 | 175  | 276  | 73  |
| 7  | 7  | LRC              | Drug         | Without known IHD   | .65       | 193 | 1707 | 1900 | 157 |
| 8  | 8  | NHLBI            | Drug         | With IHD            | .85       | 11  | 61   | 72   | 6   |
| 9  | 9  | Upjohn           | Drug         | With or without IHD | .49       | 42  | 1087 | 1129 | 36  |
| 10 | 10 | McCaughan        | Drug         | With or without IHD | .68       | 2   | 28   | 30   | 2   |
| 11 | 11 | Helsinki w/o IHD | Drug         | Without known IHD   | .69       | 84  | 1946 | 2030 | 56  |
| 12 | 12 | CLAS             | Drug         | With IHD            | 1.35      | 5   | 89   | 94   | 1   |
| 13 | 13 | Minnesota        | Diet         | Without known IHD   | .7        | 121 | 4395 | 4516 | 131 |
| 14 | 14 | Los Angeles      | Diet         | Without known IHD   | .87       | 65  | 357  | 422  | 52  |
| 15 | 15 | MRC              | Diet         | With IHD            | .95       | 52  | 142  | 194  | 45  |
| 16 | 16 | Oslo             | Diet         | With IHD            | 1.13      | 81  | 148  | 229  | 61  |
| 17 | 17 | Sydney           | Diet         | With IHD            | .31       | 24  | 213  | 237  | 37  |
| 18 | 18 | St Mary's        | Diet         | With IHD            | .61       | 11  | 41   | 52   | 8   |
| 19 | 19 | London Hospitals | Diet         | With IHD            | .57       | 50  | 84   | 134  | 47  |
| 20 | 20 | POSCH            | Surgery      | With IHD            | 1.43      | 125 | 292  | 417  | 82  |
| 21 | 21 | EXCEL            | Drug         | With or without IHD | 1.08      | 20  | 1643 | 1663 | 62  |
| 22 | 22 | FATS             | Drug         | With IHD            | 1.48      | 0   | 52   | 52   | 2   |
| 23 | 23 | Gross            | Drug         | With IHD            | .56       | 0   | 29   | 29   | 1   |
| 24 | 24 | STARS            | Diet         | With IHD            | 1.06      | 5   | 25   | 30   | 3   |
| 25 | 25 | DART             | Diet         | With IHD            | .26       | 144 | 871  | 1015 | 132 |
| 26 | 26 | Wales            | Drug         | With IHD            | .76       | 24  | 202  | 217  | 25  |

Variables

Filter variables here

| Name                                             | Label                            |
|--------------------------------------------------|----------------------------------|
| <input checked="" type="checkbox"/> id           | ID in Stat Med 1999              |
| <input checked="" type="checkbox"/> trialname    | Trial name                       |
| <input checked="" type="checkbox"/> intervention | Intervention type                |
| <input checked="" type="checkbox"/> ihdentry     | Ischaemic heart disease on entry |
| <input checked="" type="checkbox"/> cholreduc    | Cholesterol reduction (mmol/l)   |
| <input checked="" type="checkbox"/> sc           | Control group Events             |
| <input checked="" type="checkbox"/> fc           | Control group No events          |
| <input checked="" type="checkbox"/> nc           | Control group total              |
| <input checked="" type="checkbox"/> se           | Treated group Events             |
| <input checked="" type="checkbox"/> fe           | Treated group No events          |
| <input checked="" type="checkbox"/> ne           | Treated group total              |
| <input checked="" type="checkbox"/> or           | Odds ratio                       |
| <input checked="" type="checkbox"/> logor        | Log-odds ratio                   |
| <input checked="" type="checkbox"/> selogor      | SE of Log-odds ratio             |
| <input checked="" type="checkbox"/> varlogor     | Variance of Log-odds ratio       |
| <input checked="" type="checkbox"/> _SS          | Sample size                      |
| <input checked="" type="checkbox"/> _ES          | RR                               |
| <input checked="" type="checkbox"/> _selogES     | se(logRR)                        |
| <input checked="" type="checkbox"/> _LCI         | Lower CI (RR)                    |
| <input checked="" type="checkbox"/> _UCI         | Upper CI (RR)                    |
| <input checked="" type="checkbox"/> _WT          | M-H weight                       |

Properties

Variables

| Name | Type | Format | Value label | Notes |
|------|------|--------|-------------|-------|
| id   | byte | %9.0g  |             |       |

Data

| Filename   | Label    |
|------------|----------|
| stata_exar | Serum ch |

## Example 2: Consider the following review question

---

### □ Observational studies

- Among HIV infected adults who initiated ART (**Population**), were adult initiated with EFV regimen (**Exposure/ intervention**) at higher risk of treatment failure (**Outcome**) as compared to those who initiated with NVP regimen (**comparison**)?

**Population**

**Intervention**

**Comparison**

**Outcome**

# Data processing

---

## □ The data in to excel

| study | Author               | Year | design                             | country                  | Event2             | N     | EFVcases | EFV    | NVPcases | NVP  | EFVnoncases | NVPnoncases |
|-------|----------------------|------|------------------------------------|--------------------------|--------------------|-------|----------|--------|----------|------|-------------|-------------|
| 6     | Stringer JS, et al   | 2010 | Prospective Cohort                 | Multicenter              | Treatment Failure  | 878   | 15       | 58     | 231      | 820  | 43          | 589         |
| 7     | Kwobah CM, et al     | 2012 | case-control                       | Kenya                    | Treatment Failure  | 3233  | 155      | 427    | 894      | 2633 | 272         | 1739        |
| 8     | Nachega JB, et al    | 2008 | Cohort                             | South Africa             | Treatment Failure  | 2817  | 251      | 1822   | 203      | 995  | 1571        | 792         |
| 9     | Boulle A, et al 2007 | 2007 | Cohort                             | South Africa             | NNRTI substitution | 2679  | 25       | 1612   | 63       | 1067 |             |             |
| 10    | Shearer K, et al     | 2014 | Cohort                             | South Africa             | Treatment Failure  | 8854  | 307      | 8211   | 43       | 643  | 7904        | 600         |
| 10    | Shearer K, et al     | 2014 | Cohort                             | South Africa             | Death              | 12840 | 1006     | 11,962 | 55       | 878  | 10956       | 823         |
| 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana                    | Treatment Failure  | 3990  | 633      | 2369   | 495      | 1621 | 1733        | 1126        |
| 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana                    | Death              | 3990  | 208      | 2369   | 110      | 1621 | 2161        | 1511        |
| 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana                    | NNRTI Substitution | 3990  | 219      | 2369   | 254      | 1621 | 2150        | 1367        |
| 13    | Shearer K2, et al    | 2013 | Cohort                             | South Africa             | Treatment Failure  | 2385  | 101      | 2,254  | 16       | 131  | 2153        | 115         |
| 13    | Shearer K2, et al    | 2013 | Cohort                             | South Africa             | Death              | 2385  | 107      | 2,254  | 5        | 131  | 2147        | 126         |
| 14    | Barth RE, et al      | 2011 | Retrospective observational cohort | South Africa sub-Saharan | Treatment Failure  | 735   | 204      | 426    | 133      | 309  | 222         | 176         |
| 16    | Gsponer T, et al     | 2012 | Collaborative analysis             | Africa                   | Treatment Failure  | 2404  | 25       | 186    | 298      | 2218 | 161         | 1920        |
| 23    | Sarfo FS2, et al     | 2014 | Retrospective cohort study         | Ghana sub-Saharan        | NNRTI Substitution | 3999  | 123      | 2,378  | 158      | 1621 | 2255        | 1463        |
| 24    | Keiser O, et al      | 2010 | Case control                       | Africa                   | Treatment Failure  | 4281  | 295      | 1,951  | 370      | 2325 | 1661        | 1955        |
| 25    | Anlay DZ, et al      | 2016 | Retrospective follow up            | Ethiopia                 | NNRTI Substitution | 410   | 28       | 289    | 60       | 121  | 261         | 161         |
| 26    | van Zyl GU, et al    | 2011 | Cross-sectional                    | South Africa             | NNRTI Substitution | 167   | 69       | 82     | 68       | 85   | 13          | 15          |
| 27    | Abah IO, et al       | 2015 | Cohort                             | Nigeria                  | NNRTI Substitution | 6309  | 443      | 558    | 4183     | 5751 | 115         | 1568        |
| 29    | Bock P, et al        | 2013 | Multicentre cohort                 | South Africa             | NNRTI Substitution | 27350 | 1631     | 19441  | 1277     | 7909 | 17810       | 6629        |
| 29    | Bock P, et al        | 2013 | Multicentre cohort                 | South Africa             | Death              | 27350 | 1294     | 19441  | 299      | 7909 | 18147       | 7610        |
| 30    | Tirfe ZM, et al      | 2013 | Retrospective cohort study         | Ethiopia                 | Treatment Failure  | 492   | 91       | 246    | 82       | 246  | 154         | 164         |

# Data processing

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## □ Import or export data to STATA

|    | study | author               | year | design                             | country            | event2             | n     | efvcases | efv    |
|----|-------|----------------------|------|------------------------------------|--------------------|--------------------|-------|----------|--------|
| 1  | 6     | Stringer JS, et al   | 2010 | Prospective Cohort                 | Multicenter        | Treatment Failure  | 878   | 15       | 58     |
| 2  | 7     | Kwobah CM, et al     | 2012 | case-control                       | Kenya              | Treatment Failure  | 3233  | 155      | 427    |
| 3  | 8     | Nachega JB, et al    | 2008 | Cohort                             | South Africa       | Treatment Failure  | 2817  | 251      | 1822   |
| 4  | 9     | Boulle A, et al 2007 | 2007 | Cohort                             | South Africa       | NNRTI substitution | 2679  | 25       | 1612   |
| 5  | 10    | Shearer K, et al     | 2014 | Cohort                             | South Africa       | Treatment Failure  | 8854  | 307      | 8211   |
| 6  | 10    | Shearer K, et al     | 2014 | Cohort                             | South Africa       | Death              | 12840 | 1006     | 11,962 |
| 7  | 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana              | Treatment Failure  | 3990  | 633      | 2369   |
| 8  | 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana              | Death              | 3990  | 208      | 2369   |
| 9  | 11    | Sarfo FS, et al      | 2014 | Retrospective Observational        | Ghana              | NNRTI Substitution | 3990  | 219      | 2369   |
| 10 | 13    | Shearer K2, et al    | 2013 | Cohort                             | South Africa       | Treatment Failure  | 2385  | 101      | 2,254  |
| 11 | 13    | Shearer K2, et al    | 2013 | Cohort                             | South Africa       | Death              | 2385  | 107      | 2,254  |
| 12 | 14    | Barth RE, et al      | 2011 | Retrospective observational cohort | South Africa       | Treatment Failure  | 735   | 204      | 426    |
| 13 | 16    | Gsponer T, et al     | 2012 | Collaborative analysis             | sub-Saharan Africa | Treatment Failure  | 2404  | 25       | 186    |
| 14 | 23    | Sarfo FS2, et al     | 2014 | Retrospective cohort study         | Ghana              | NNRTI Substitution | 3999  | 123      | 2,378  |
| 15 | 24    | Keiser O, et al      | 2010 | Case control                       | sub-Saharan Africa | Treatment Failure  | 4281  | 295      | 1,951  |
| 16 | 25    | Anlay DZ, et al      | 2016 | Retrospective follow up            | Ethiopia           | NNRTI Substitution | 410   | 28       | 289    |
| 17 | 26    | van Zyl GU, et al    | 2011 | Cross-sectional                    | South Africa       | NNRTI Substitution | 167   | 69       | 82     |
| 18 | 27    | Abah IO, et al       | 2015 | Cohort                             | Nigeria            | NNRTI Substitution | 6309  | 443      | 558    |
| 19 | 29    | Bock P, et al        | 2013 | Multicentre cohort                 | South Africa       | NNRTI Substitution | 27350 | 1631     | 19441  |
| 20 | 29    | Bock P, et al        | 2013 | Multicentre cohort                 | South Africa       | Death              | 27350 | 1294     | 19441  |
| 21 | 30    | Tirfe ZM, et al      | 2013 | Retrospective cohort study         | Ethiopia           | Treatment Failure  | 492   | 91       | 246    |

## Example 3: Diagnostic test accuracy

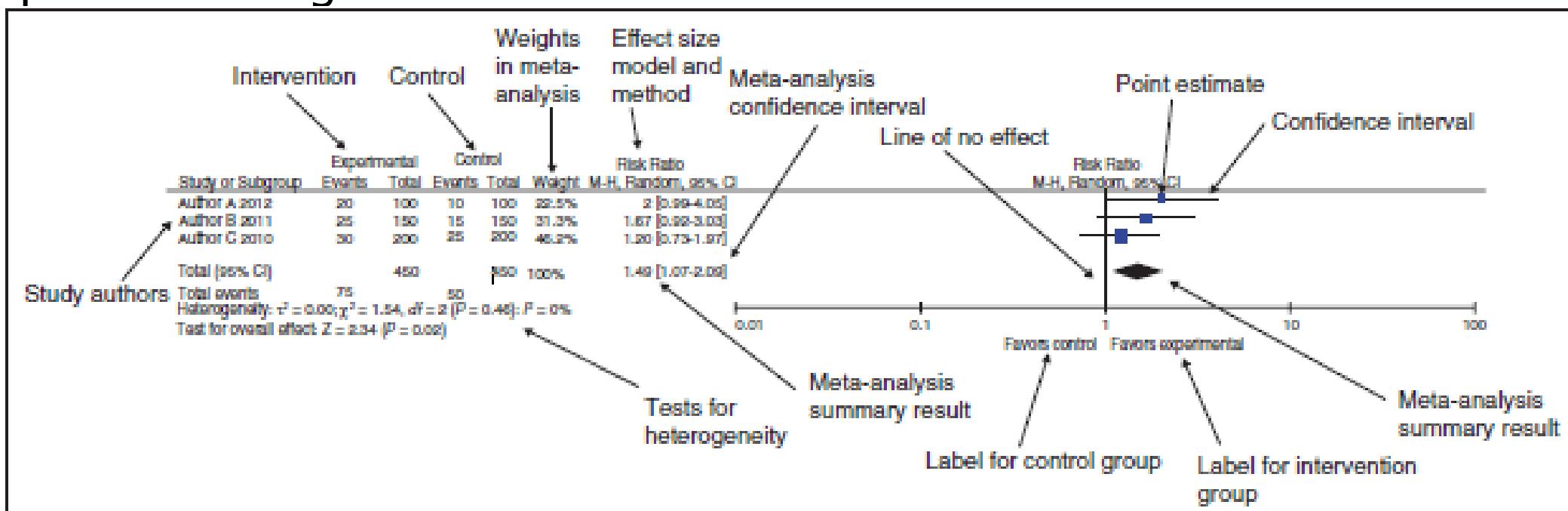
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- Data from 17 studies of lymphangiography for the diagnosis of lymph node metastasis in women with cervical cancer. The total number of patients in each study ranges from 21 to 300.

| studyid | author          | year | tp | fp | fn | tn  | ndis | nnondis | sens     | spec     |
|---------|-----------------|------|----|----|----|-----|------|---------|----------|----------|
| 1       | Kindermann      | 1970 | 19 | 1  | 10 | 81  | 29   | 82      | .6551724 | .9878049 |
| 2       | Lecart & Lefant | 1971 | 8  | 9  | 2  | 13  | 10   | 22      | .8       | .5909091 |
| 3       | Piver           | 1971 | 41 | 1  | 12 | 49  | 53   | 50      | .7735849 | .98      |
| 4       | Piver & Barlow  | 1973 | 5  | 1  | 2  | 18  | 7    | 19      | .7142857 | .9473684 |
| 5       | Kolbenstvedt    | 1975 | 45 | 58 | 32 | 165 | 77   | 223     | .5844156 | .7399103 |
| 6       | Leman           | 1975 | 8  | 6  | 2  | 32  | 10   | 38      | .8       | .8421053 |
| 7       | Brown           | 1979 | 5  | 8  | 1  | 7   | 6    | 15      | .8333333 | .4666667 |
| 8       | Lagasse         | 1979 | 15 | 17 | 11 | 52  | 26   | 69      | .5769231 | .7536232 |
| 9       | Kjorstad        | 1980 | 16 | 11 | 8  | 24  | 24   | 35      | .6666667 | .6857143 |
| 10      | Ashraf          | 1982 | 4  | 8  | 2  | 25  | 6    | 33      | .6666667 | .7575758 |
| 11      | de Muylder      | 1984 | 8  | 12 | 10 | 70  | 18   | 82      | .4444444 | .8536586 |
| 12      | Smales          | 1986 | 10 | 4  | 4  | 55  | 14   | 59      | .7142857 | .9322034 |
| 13      | Feigen          | 1987 | 2  | 5  | 6  | 23  | 8    | 28      | .25      | .8214286 |
| 14      | Swart           | 1989 | 7  | 10 | 7  | 30  | 14   | 40      | .5       | .75      |
| 15      | Heller          | 1990 | 44 | 50 | 12 | 135 | 56   | 185     | .7857143 | .7297297 |
| 16      | La Fianza       | 1990 | 8  | 3  | 1  | 37  | 9    | 40      | .8888889 | .925     |
| 17      | Stellato        | 1992 | 4  | 3  | 0  | 14  | 4    | 17      | 1        | .8235294 |

# Graphical displays for meta-analysis

- Forest plots are the most familiar method for presenting results of meta-analyses
- Forest plots display effect estimates and their confidence intervals for each study and the results of the meta-analysis. They are plotted along a vertical line of no effect



# When is meta-analysis appropriate?

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- Only appropriate when studies are considered similar enough from a clinical and methodological point of view (homogenous studies) and
- There is no publication bias
  
- If studies are heterogeneous from a clinical
  - e.g. population, intervention, comparator and outcome)
- Methodological (i.e. study design and risk of bias point of view)
- If there is significant publication bias
  - 
  - Then it is uncertain if it is appropriate to synthesize the respective studies with meta-analysis

# Heterogeneity

---

- **Clinical heterogeneity** refers to differences between studies in the characteristics of their populations, interventions and outcomes
- **Methodological heterogeneity** refers to differences between studies in their study designs and quality
- **Statistical heterogeneity** refers to the variation of effects between studies. It may be due to clinical heterogeneity or methodological heterogeneity or chance

(Khan et al, 2012)

# Test of heterogeneity

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- Clinical and methodological heterogeneity
  - Common sense: are the patients, interventions and outcomes in each of the included studies sufficiently similar?
    - are study designs and quality similar?
- Statistical heterogeneity
  - Graphic aid (visually)
    - Forest plot, overlapping confidence intervals
  - Statistical tests
    - chi-squared test (Cochran Q test)
    - I square statistic ( $I^2$ )

## Standard chi-squared test (Cochran Q test)

---

- Tests the statistical hypothesis that the true treatments effects (the effect size parameters) are the same in all the primary studies included in meta-analysis
- If results of the test are statistically significant (P-value <0.05)
  - the statistical hypothesis that the true treatments effects are the same in all the primary studies included in meta-analysis (the hypothesis of homogeneity) is rejected
  - Therefore, it is considered that there is statistical heterogeneity

## Standard chi-squared test (Cochran Q test)

---

- The statistical power of the test is in most cases very low due to the small number of studies;

$$Q = \sum_{i=1}^k W_i (Y_i - M)^2$$

- Where  $W_i$  is the study weight,  $Y_i$  is the study effect size,  $M$  is the summary effect, and the  $k$  is number of studies.
  - heterogeneity may be present even if the  $Q$  statistic is not statistically significant at conventional levels of significance such as 0.05.
- It is not appropriate to decide the meta-analysis model based only on the results of the Chi-squared statistical test ( $Q$  test) for heterogeneity

## Between-studies variance (tau-square)

---

- Is defined as the variance of the true effect sizes
- To yield this estimate we start with the difference ( $Q - df$ ) which represents the dispersion in true effects on a standardized scale

$$\tau^2 = \frac{Q - df}{C}, \text{ Where } c = \sum w_i - \frac{\sum w_i^2}{\sum w_i}$$

- Where  $df = \text{number of studies} - 1$
- With a p-value less than 0.05 leading us to reject the null, and conclude that the studies do not share a common effect size

## I-square statistic ( $I^2$ )

---

- A statistic used for quantifying inconsistency in meta-analysis
- $I^2$  is a percentage and its value lies between 0% and 100%

$$I^2 = \left( \frac{Q - df}{Q} \right) \times 100\%$$

- A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity . If  $I^2 = 0\%$  this means that all variability in effect size estimates is due to sampling error within studies
- If  $I^2= 50\%$  it means that half of the total variability among effect sizes is caused not by sampling error but by true heterogeneity between studies
- With a small number of studies (< 20), the  $I^2$  test should be interpreted very cautiously

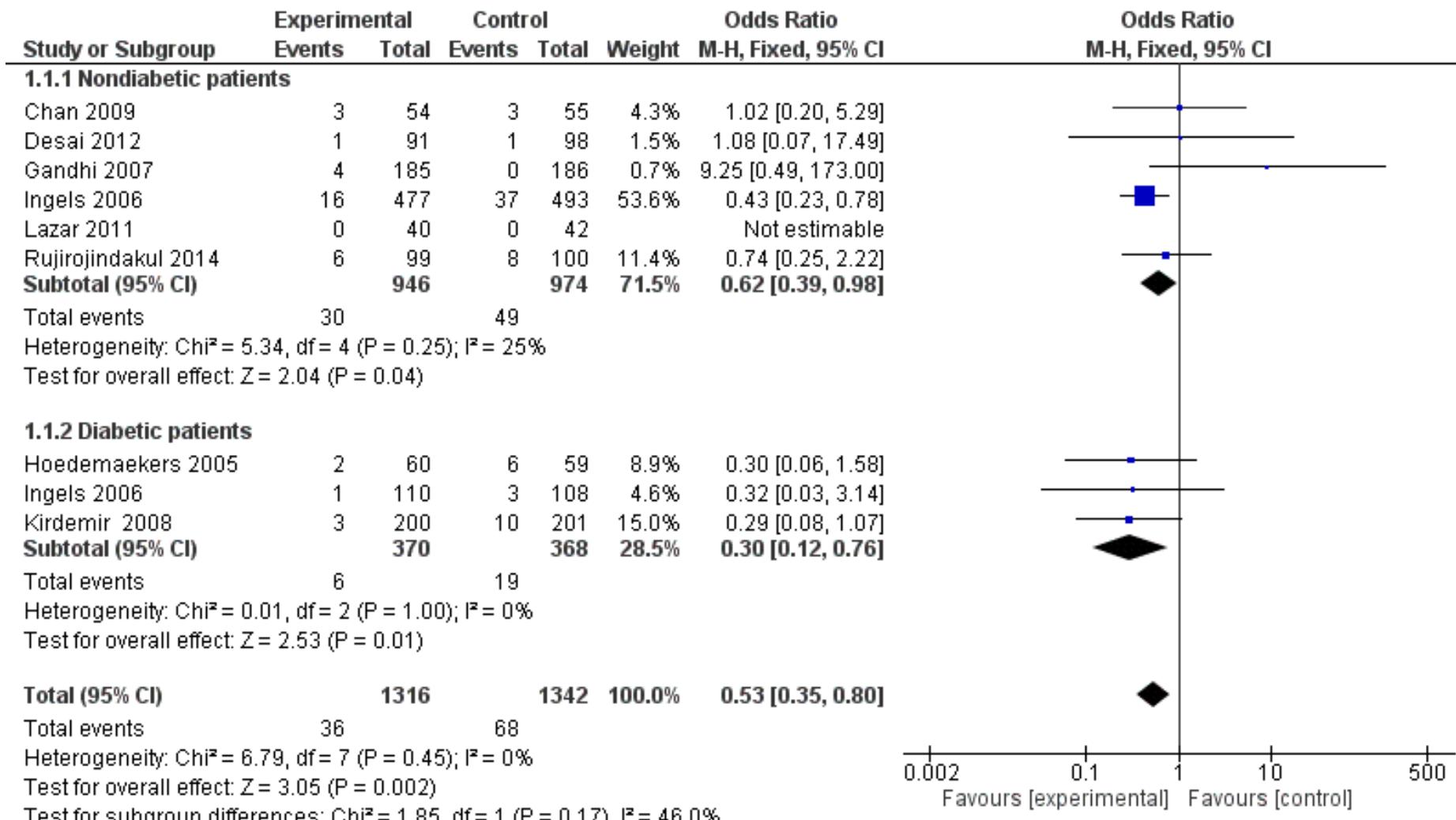
## Subgroup analysis

---

- Subgroup analyses may be done for subsets of participants or for subsets of studies
- Subgroup analyses involve splitting the data or the studies into subgroups, often so as to make comparisons between them
- False negative and false positive significance tests increase in likelihood rapidly as more subgroup analyses are performed

(Higgins & Green, 2011)

# Example: Subgroup analysis



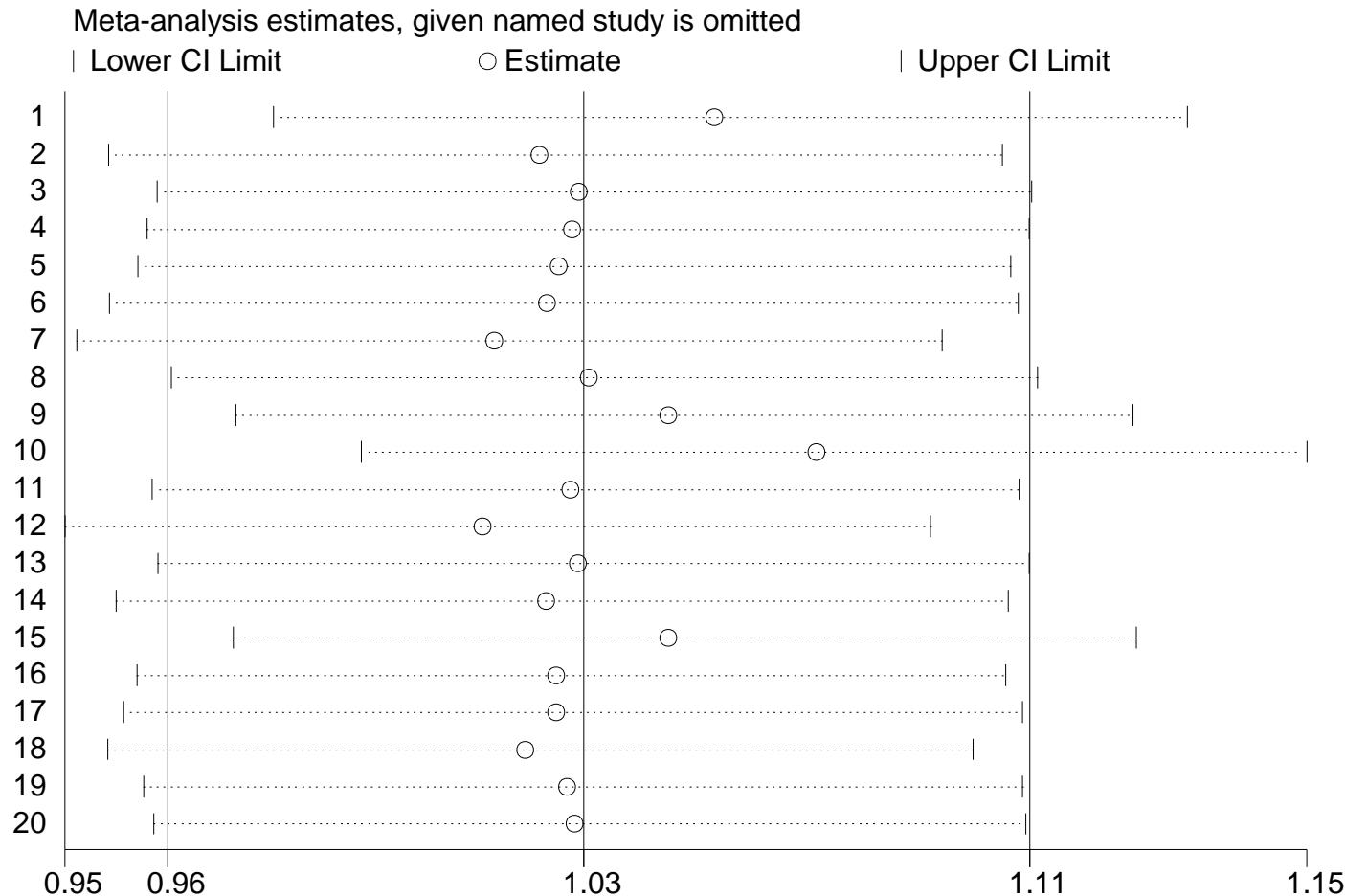
# Sensitivity analysis

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- Sensitivity analysis refers to the repetition of an analysis under different assumptions to examine the impact of these assumptions on the results (Khan et al, 2012)
- Test impact of decisions made during the review process
  - ▣ use both models
  - ▣ compute meta-analysis with and without the inclusion of poor quality studies
  - ▣ use both RR and OR for meta-analysis
  - ▣ compute meta-analysis with and without the inclusion of small sample size studies
  - ▣ compute meta-analysis with and without the inclusion of a mega-trial
- If findings remain consistent across analyses, this means they are more robust and we can be more confident in the result

# Example: Sensitivity analysis

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# Assessing publication biases

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- The model (for publication bias)
  - Large studies are likely to be published regardless of statistical significance because these studies involve large commitments of time and resources
  - Moderately sized studies are at risk of being lost, but with a moderate sample size even modest effects will be significant, and so only some studies are lost here
  - Small studies are at greatest risk for being lost. Because of the small sample size, only the largest effects are likely to be significant, with the small and moderate effects likely to be unpublished
  - The combined result of these three items is that we expect the bias to increase as the sample size goes down.

# Sources of funnel plot asymmetry

---

- Selection biases
  - Publication bias and other reporting biases
  - Biased inclusion criteria
- True heterogeneity: size of effect differs according to study size
  - Intensity of intervention
  - Differences in underlying risk
- Data irregularities
  - Poor methodological design of small studies
  - Inadequate analysis
  - Fraud
- Artifact: heterogeneity due to poor choice of effect measure
- Chance

# Egger test

---

```
. metabias logor selogor, egger graph
```

Note: default data input format (theta, se\_theta) assumed.

Tests for Publication Bias

Begg's Test

```
adj. Kendall's Score (P-Q) =      12
    Std. Dev. of Score =      50.62
    Number of Studies =      28
        z =      0.24
    Pr > |z| =      0.813
        z =      0.22 (continuity corrected)
    Pr > |z| =      0.828 (continuity corrected)
```

Egger's test

| Std_Eff | Coef.     | Std. Err. | t     | P> t  | [95% Conf. Interval] |
|---------|-----------|-----------|-------|-------|----------------------|
| slope   | -.1497183 | .0776855  | -1.93 | 0.065 | -.3094031 .0099665   |
| bias    | -.3014327 | .4370127  | -0.69 | 0.496 | -1.199725 .5968598   |

# Functions in Stata

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- For proportion study:
  - *Metaprop x n* (x is event of interest and n is the total sample)
  - Metaprop takes the outcome of interest and the total population
- For prevalence study
  - *Metan ES seES*
  - Metan takes prevalence with standard error of prevalence
- To see the trend, we can use metacum
  - *Metacum* can be also used to update meta-analysis

## Functions in stata

---

- For diagnostic test accuracy
  - *Metandi tp fp fn tn* (for diagnostic test accuracy)
- For two groups means (intervention and control)
  - *Metan n<sub>1</sub> m<sub>1</sub> sd<sub>1</sub> n<sub>2</sub> m<sub>2</sub> sd<sub>2</sub>*
- For binary outcome variable when the 2X2 table is given (i.e. a, b, c, d)
  - *Metan a b c d*
- For binary outcome variable when no 2X2 table
  - *Metan SE seSE*

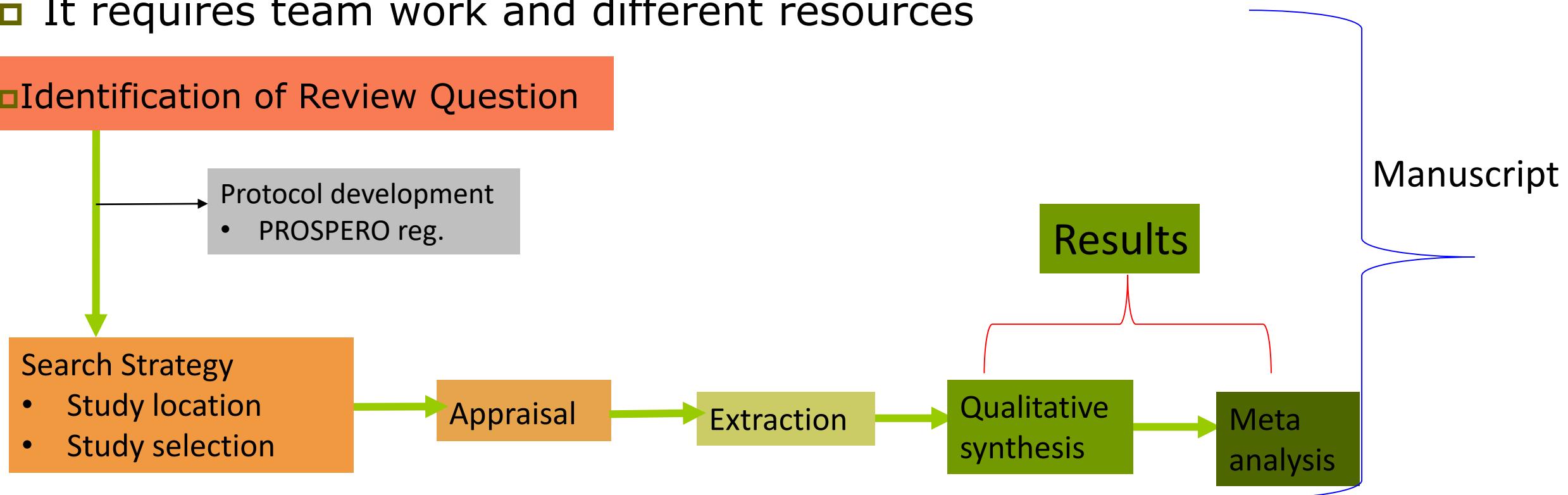
## Activity 8

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- Consider the example given above
  - Undertake a meta-analysis
  - Were results statistically significant?
  - Test homogeneity assumption
  - Test if there is publication bias

# Summary

- SR&MA is a long process which requires hard work and patience
- Through practice you will know many more things
- It requires team work and different resources
- Identification of Review Question



# Summary

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- My proposal:
- I need you to continue the review process and our plan is:
  - Study selection and critical appraisal will be completed by Aug. 2021
  - Data extraction completed by September 2021
  - Data analysis and synthesis (qualitative & quantitative) by October 2021
- Knowledge is **perishable**, which requires continuous update

# Thank you!

