## Systematic Reviews Application & Importance

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### Types of Medical articles

- Original Article
- Review Article
- Case Reports
- Editorial
- Short Communication (short papers)
- Letter to Editor
- Personal Views

#### Types of Studies

- Primary Studies
- Secondary Studies

#### Primary studies

- Experiments
- Clinical trials
- Surveys



#### Secondary studies

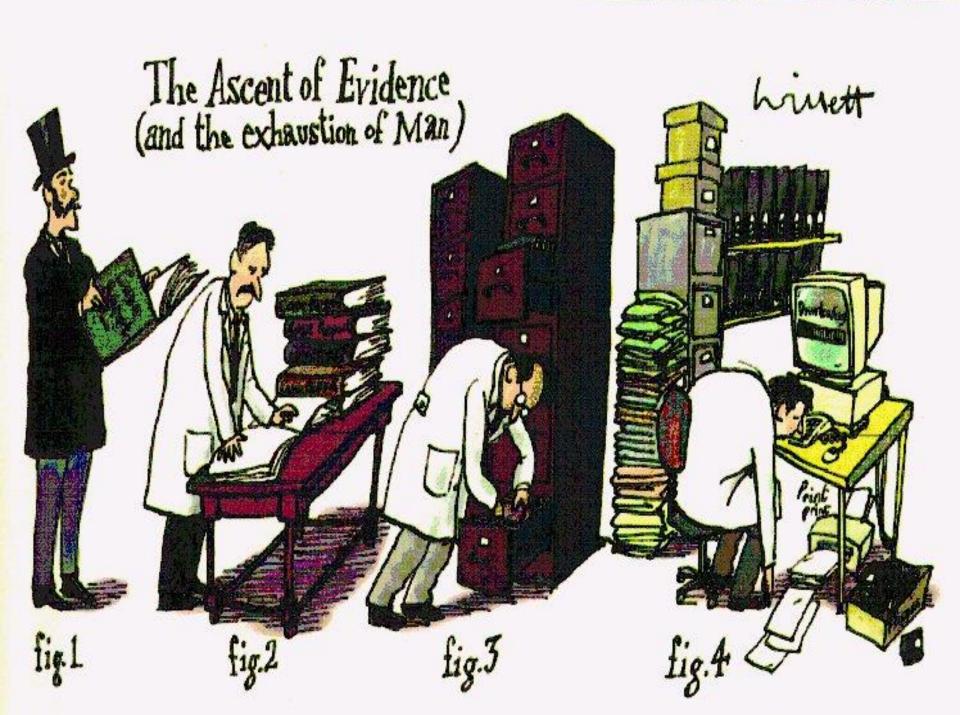
- Reviews (Overviews)
  - Narrative reviews
  - Systematic reviews & Meta-analyses
- Guidelines
- Decision analyses
- Economic analyses



- Traditional Review Articles (Narrative Review)
- Systematic Review (Meta-analysis)

■ مقالات مروری سنتی مرور روایتی

■ مقالات مروری نظاممند مرور ساختاردار



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#### Medical Publishing

#### **Annually:**

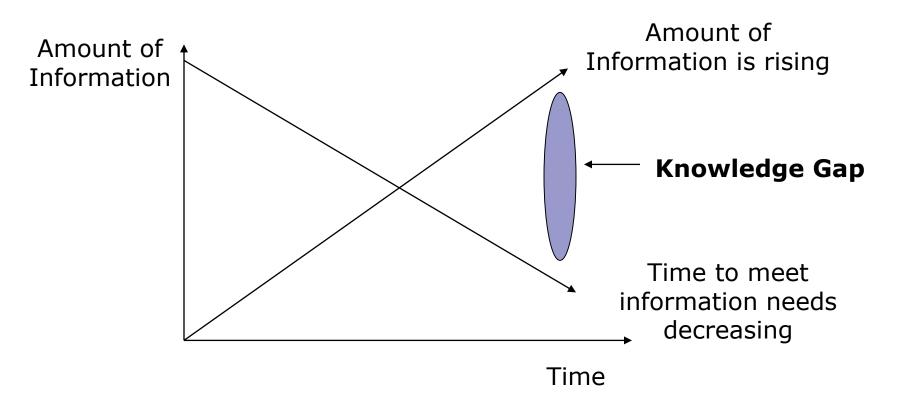
- 20,000 journals
- 17,000 new books

#### **MEDLINE:**

- +5,000 journals
- +30 Million references
- +2,00,000 new entries yearly



#### The Problem



The Knowledge Gap

# Half-time or Half-life of Clinical Medical Science is now

about 6 Month

## Doubling time of biomedical science was

about 19 years in 1991



about 20 months in 2001

#### So you work in a job which:

- Its half-time (half-life) is 6 months, &
- Its doubling-time is 20 month

You works in a ever-changing & evergrowing profession!

So you should keep updating!

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#### For General Physicians to keep current:

Read 19 new articles per day which appear in medical journals

19 x 2 hrs (Critical Appraisal) = 38 hrs per day

Davidoff F et al. (1995)

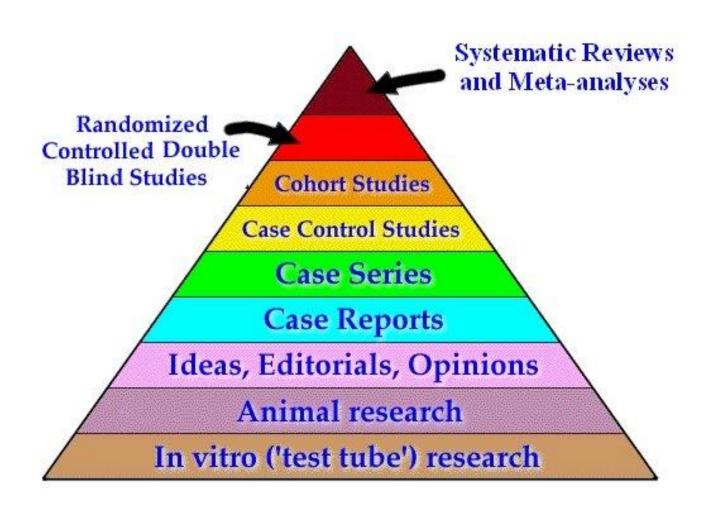
EBM; A new journal to help doctors identify the information they need. BMJ 310:1085-86.



#### What is 'level of evidence'?

The extent to which one can be confident that an estimate of effect or association is correct (unbiased).

#### Hierarchy of studies



#### **Evidence Pyramid**

Systematic Review

Randomized Controlled Trial

Cohort studies

Case Control studies

Case Series/Case Reports

Animal research



#### Levels of Evidence

Level of Evidence	Type of Study	
1a	Systematic reviews of randomized clinical trials (RCTs)	
1b	Individual RCTs	
2a	Systematic reviews of cohort studies	
2b	Individual cohort studies and low-quality RCTs	
3a	Systematic reviews of case-controlled studies	
3b	Individual case-controlled studies	
4	Case series and poor-quality cohort and case-control studies	
5	Expert opinion based on clinical experience	

Adapted from: Sackett DL et al. *Evidence-Based Medicine: How to Practice and Teach EBM*. 2nd ed. Churchill Livingstone; 2000.



#### Systematic reviews

- Postdam Consultation on Meta-analysis (Cook et al, 1995) defined a systematic review as
- "application of scientific strategies that limit bias to the systematic assembly, critical appraisal and synthesis of all relevant studies on a specific topic"



#### Systematic reviews

- Systematic review is a method of
  - □locating,
  - □ appraising,
  - □ and synthesizing evidence
  - while making explicit efforts to limit bias
- > a quarter of a century since Gene Glass coined the term "meta-analysis" to refer to the quantitative synthesis of the results of primary studies

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#### A 'systematic review', therefore, aims to be:

- Systematic (e.g. in its identification of literature)
- Explicit (e.g. in its statement of objectives, materials and methods)
- Reproducible (e.g. in its methodology and conclusions



#### Systematic Review

"Scientific tool which can be used to summaries, appraise, and communicate the results and implications of otherwise unmanageable quantities of research" (NHS CRD, 1996).



#### Systematic Review

the process by which similar studies, identified from a comprehensive trawl of numerous sources, are summarized in easy-to-read graphical or tabular form and then their collective message or "bottom line' presented, together with implications for practice and future research (Booth & Haines, 1998).



#### They are not conventional Reviews

- Follow a strict methodological and statistical protocol
  - more comprehensive
  - minimising the chance of bias
  - improves transparency, repeatability and reliability

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#### Stages of a systematic review

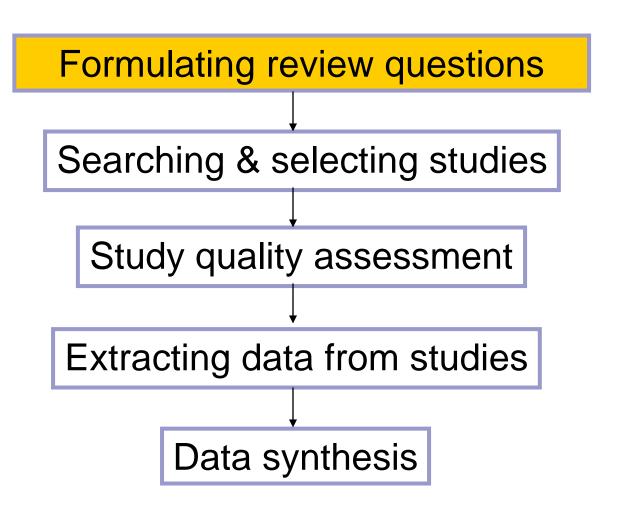
- Planning the review i.e. identifying the need for a review, and documenting the methodology
- Conducting the review i.e. finding, selecting, appraising, extracting and synthesizing primary research studies
- Reporting and dissemination i.e. writing up and disseminating the results of the review

### Differences Between Traditional and Systematic Reviews

(Adapted from Cook, D. J. et. al. (1997). Ann. Intern. Med. 126: 376-380)			
Feature	Traditional Review	Systematic Review	
Question	Often broad in scope	Focused question	
Sources & search	Not usually specified, potentially biased	Comprehensive sources & explicit search strategy	
Selection	Rarely specified, potentially biased	Criterion-based selection, uniformly applied	
Appraisal	Variable	Rigorous critical appraisal, uniformly applied	
Synthesis	Often a qualitative summary	Quantitative summary* when appropriate	
Inferences	Sometimes evidence-based	Evidence-based	
*A quantitative summary that includes a statistical synthesis is a meta-			

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#### Steps of Doing a Systematic Review





#### Formulating review questions

- The first and most important decision in preparing a review is to determine its focus
- This is best done by asking clearly framed questions.
- Define a four part clinical question, breaking the question down into its component parts



#### Question components: PICO

What types of Patients?

What types of nterventions?

What types of Comparison?

What types of Outcomes?



#### **Ask Clinical Questions**

#### **Components of Clinical Questions**

Patient/ Population

In patients with acute MI

In women with suspected coronary disease

In postmenopausal women Intervention/ Exposure

does early treatment with a statin

what is the accuracy of exercise ECHO

does hormone replacement therapy

Comparison

compared to placebo

compared to exercise ECG

compared to no HRT

Outcome

decrease cardiovascular mortality?

for diagnosing significant CAD?

increase the risk of breast cancer?



#### What types of participants?

- Disease or condition of interest
- Potential co-morbidity
- Setting
- Demographic factors



#### What types of intervention?

- Treatment
- Diagnostic test
- Causative agent
- Prognostic factor
- Exposure to disease
- Risk behavior



#### What types of outcomes?

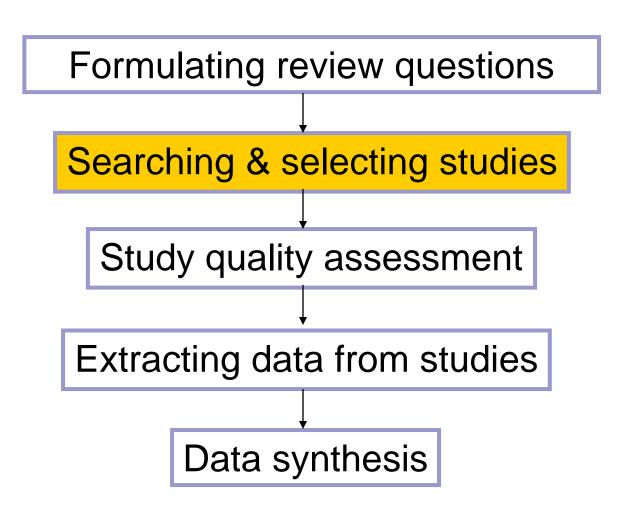
- Mortality/Survival
- Risk of disease
- Disease free period
- Quality of life
- Work absenteeism
- Disability/ Duration and severity of illness
- Pain
- Accuracy of diagnose



## Rationale for well-formulated questions

- Determining the structure of a review
- Determining Strategies for locating and selecting studies or data,
- Critically appraising the relevance and validity,
- Helping readers in their initial assessments of relevance.

#### Steps of Doing a Systematic Review





#### Selecting studies

- performing a comprehensive, objective, and reproducible search of the literature
- selecting studies which meet the original inclusion and exclusion criteria

can be the most time-consuming and challenging task in preparing a systematic review

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### Data sources for a systematic review

- Electronic databases
  - MEDLINE and EMBASE
  - □ The Cochrane Central Register of Controlled Trials (CENTRAL)
- Conference proceedings & abstract books
- Hand searching
- "Grey literature" (thesis, Internal reports, pharmaceutical industry files)
- Checking reference lists
- Unpublished sources known to experts in the specialty (seek by personal communication)
- Raw data from published trials



### Generating a search strategy

- Multiple electronic databases and the internet using a range of Boolean search-terms
- Foreign language searches
- Include grey literature to avoid publication bias (see subsequent slides)
- Search bibliographies and contact experts



### Developing a search strategy

It is always necessary to strike a balance between comprehensiveness and precision when developing a search strategy.



## An electronic search strategy generally has three sets of terms:

- 1) terms to search for the health condition of interest;
- 2) terms to search for the intervention(s) evaluated;
- 3) terms to search for the types of study design to be included (such as randomized trials)



### Literature Searching: Search terms

- Key words:
  - □ Reflect the population, intervention and outcome

Consider synonyms and alternative spellings

(e.g., colonise and colonize)

□ Foreign language translations



## Vitamin C for preventing and treating the common cold

- The following electronic databases were searched for reports of trials: the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2004); MEDLINE (January 1966 to June 2004); and EMBASE (1990 to June Week 23 2004).
- We ran the following search strings in combination with the search strategy developed by the Cochrane Collaboration for identifying randomised controlled trials (<u>Dickersin 1994</u>)
- MEDLINE and CENTRAL were searched using the following search strategy:

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- 1 exp Common Cold/
- 2 common cold\$.mp.
- 3 exp RHINOVIRUS/
- 4 rhinovir\$.mp.
- 5 or/1-4
- 6 exp Ascorbic Acid/
- 7 ascorbic acid.mp.
- 8 vitamin c.mp.
- 9 or/6-8
- 10 5 and 9
- EMBASE search strategy:
- 1 exp Common Cold/
- 2 common cold\$.mp.
- 3 exp Rhinovirus/
- 4 rhinovirus infection\$.mp.
- 5 or/1-4
- 6 exp Ascorbic Acid/
- 7 vitamin c.mp.
- 8 or/6-7
- 9 5 and 8



### Documenting a search strategy

The search strategy should be described in sufficient detail in a review that the process could be replicated:

- Title of database searched (e.g. MEDLINE)
- Date search was run (month, day, year)
- Years covered by the search
- Complete search strategy used, including all search terms

#### Exclude irrelevant citations

After screening all title & abstracts (n= #)

#### Exclude irrelevant studies

After detailed assessment of full text
(n= #)

#### Identify potentially relevant citations

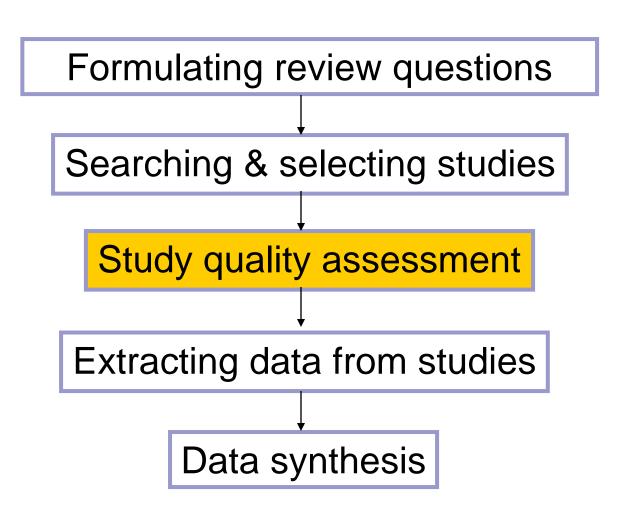
From wide searching of electronic databases & hand searching of other appropriate resources (n=#)

Retrieve hard copies of all potentially relevant citations

Identified through the above searches plus contact with experts, sifting through reference list & other resources

Include studies in systematic review (n= #)

### Steps of Doing a Systematic Review





### Appraising study quality

- There is no such thing as a perfect study, all studies have weaknesses, limitations, biases
- Interpretation of the findings of a study depends on design, conduct and analysis, as well as on the population, interventions, and outcome measures
- The researchers in a primary study did not necessarily set out to answer your review question

# What do we do with quality assessment results?

- Determine minimum quality threshold for inclusion
- Explore differences in quality as an explanation for heterogeneity in study results
- To weight individual study results in relation to their validity or the amount of information they contain
- Guide interpretation and overall recommendations



### Assessment of study quality

- Assess each study for:
  - □eligibility for inclusion
  - □study quality
  - reported findings

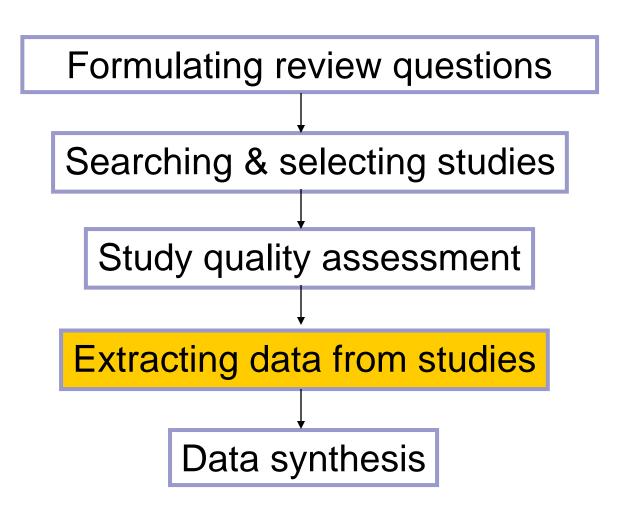
Ideally will involve two independent reviewers.



### Assessment of study quality

Validity: the degree to which the trial design, conduct, analysis, and presentation have minimized or avoided systematic biases.

### Steps of Doing a Systematic Review

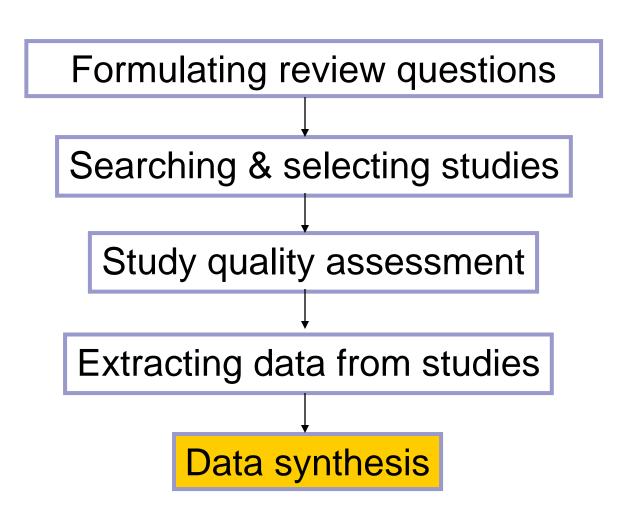




### Collecting data

- Data collection forms
  - Methods
  - Participants
  - Interventions
  - Outcome measures and results

### Steps of Doing a Systematic Review





### Meta-Analysis

when an overview incorporates a specific statistical strategy for assembling the results of several studies into a single estimate



# Systematic reviews & Meta-Analysis

 Systematic reviews do not have to have a meta-analysis

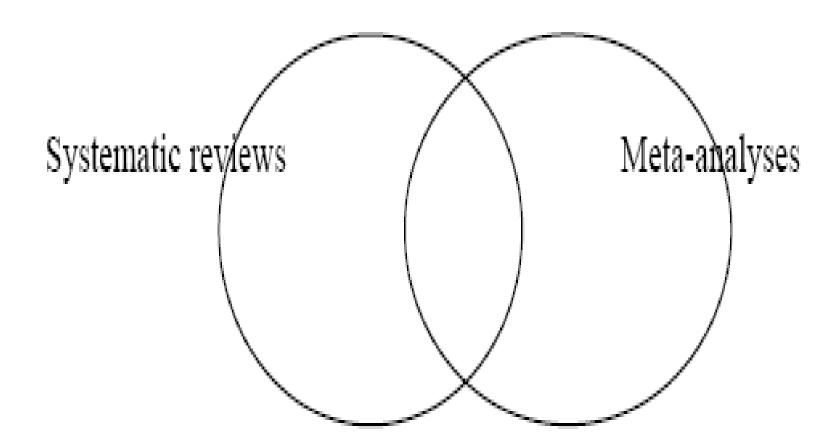
There are times when it is not appropriate or possible.



# Systematic reviews & Meta-Analysis

- The term 'meta-analysis' is often used interchangeable with 'systematic review'
- It is actually a statistical technique used to combine the results of several studies addressing the same question into a single summary measure (Khan et al., 2000).





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