

# How to Search in medical Literature

• Evidence-based medicine (EBM)—asking clear, relevant clinical questions, finding appropriate studies, critically appraising the literature, and implementing changes in practice behavior

### Definition

 EBM is the use of mathematical estimates of the risk of benefit and harm ,
 <u>derived from high –quality research</u> on population sample to inform <u>clinical decision –making</u>
 in the diagnosis ,investigation or management of individual patient

#### Only a tiny proportion of medical research breaks entirely new ground

### EBM: The science of trashing papers



# Primary care physicians identify 2.4 clinical questions for every 10 encounters (Barrie and Ward, 1997), but they spend less than 15 minutes on average with each patient

• Do not fail to use the many comprehensive sources of evidence-based information.



Sleep -deprived
Bleary- eyed
Punishment

**O** Jahezz

### **Evolving EBM**

- Pre EBM: Passive diffusion ("publish it and they will come")
- O Early EBM: Pull diffusion ("teach them to read it and they will come")
- O Current EBM: Push diffusion ("read it for them and send it to them")
- Future EBM: Prompt diffusion ("read it for them, connect it to their individual patients")

Sophistication
 OEfficiency in finding answers has not grown apace

### 1--What are looking for

 Keep current and satisfy intrinsic curiosity
 Looking for answer (clinic , patient)
 Before embarking on a research projects ,Surveying the existing literature

#### OEach approach involves searching in a very different way

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### Surveying the literature

 Preparing a detailed ,broad based and thoughtful literature review

• A simple PubMed search may not suffice

#### ONo stone has been left unturned

### Draw backs

#### • Lack of facilities

#### O Lack of searching skills

- O Lack of time
- Lack of motivation
- Information overload

### Which Database Should I Use?

PubMed EMBASE CINHAL Scopus Ovid TRIP Cochrane

### **Electronic Database**



Each record represent an article containing structured information (fields)
 A collection of records with structured information is called Database

#### O There are over 1000 websites dedicated to EBM

• Do not need to visit them all

### Web-based resources for EBM

- Oxford Center for evidence
- National institute for Health and Care Excellence
- National Health Service
- O Clinical Evidence

### PubMED --Medline

Flagship database for journal articles
Very conservative resource
Slow to pick up new journal
just USA
Jungle

### **2-Levels upon levels of evidence**

O To what degree that information can be trusted

**O** Do not apply the hierarchy of evidence mechanically

### Keep Sharp eye out

• For the believability of whatever information we find ,wherever we find it

### Boolean language

If you understand Boolean language and the difference between AND and OR then you are ready to conduct an electronic search

### **Boolean Logic "AND"**





## Identify the concept in your focused clinical question

- P Population of interest
- E the exposure being evaluated
- O outcomes expected
- M Methodological filter

#### • Focused question Link with Specific study designs

P=Among patients with osteoporosis

E=View Hoe effective are bisphosphonates

O=In preventing Fractures

M= Systemic review

• A powerful feature of electronic databases is the ability to make the computer carry out some of the critical appraisal

Type of question	Generic format	Method filter
Therapy	Among P, how effective is E in preventing O?	Systematic reviews or meta-analyses, RCTs, cohorts, case-control studies, case series or case reports
Diagnosis	Among P, how accurate is E in diagnosing O?	Studies that report 'sensitivity and specificity' or 'likelihood ratios', systematic reviews or meta-analyses
Harm	Among P, how much does E contribute to the causation of O?	Systematic reviews or meta-analyses, RCTs, cohorts, case-control studies, case series or case reports
Prognosis	Among P, by how much does E increase the risk of O?	Cohorts studies or systematic reviews or meta-analyses

Note: P = the population of interest (usually characterized by a disease or condition); E = the exposure being evaluated (either a treatment, a test, a harmful exposure or a prognostic factor); O = the outcome expected (a disease, complication or some measure of health).

### Tricky part

- Prioritize the concept from most to least important
- Each concept in the Venn
- If you intersect all sets straight away , you may end up with nothing
- One at a time

### intersect

### One at a time

### Ask yourself

- Which one is the most important ?
- If you were allowed only one term to search , which concept would you search For?

Focused clinical question	Identified concepts	Rank*
Among patients with osteoporosis, how effective are bisphosphonates in preventing fractures?	<ul> <li>P = patients with osteoporosis</li> <li>E = bisphosphonates</li> <li>O = fractures</li> <li>M = systematic reviews</li> </ul>	4 1 3 2
Among patients with diabetes, how effective are sulfonylureas in preventing usual complications?

- P = patients with diabetes
- E = sulfonylureas
- O = usual complications
- M = systematic reviews or RCTs



#### Examples of clinical qest., concepts how may be prioritiize

Among patients with diabetes, how effective are sulfonylureas in preventing usual complications?

₽	=	patients with diabetes	x
E	=	sulfonylureas	1
0	=	usual complications	3
M	=	systematic reviews or RCI	2

Among patients presenting with acute chest pain, how accurate is serum troponin-I determination in diagnosing acute myocardial infarction? P = patients with acute chest pain
 E = serum troponin-I determination
 O = acute myocardial infarction
 M = studies that report sensitivity,
 specificity, or likelihood ratios

Among patients presenting with acute chest pain, how accurate is serum troponin-I determination in diagnosing acute myocardial infarction? P = patients with acute chest pain x
 E = serum troponin-I determination
 O = acute myocardial infarction
 M = studies that report sensitivity,
 2

Bulk of the actual search : now touch the computer key

# (a) Expand (b) intersect each concept sequentially

• Till having manageable numbers

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Figure 7.3 PubMed history feature, enabling previous searches to be combined PubMed screen, displaying a portion of the MeSH tree

All MeSH Categories Diseases Category Musculoskeletal Diseases Bone Diseases Bone Diseases, Metabolic Bone Demineralization, Pathologic Decalcification, Pathologic Mucolipidoses Osteomalacia Osteoporosis Female Athlete Triad Syndrome Osteoporosis, Postmenopausal Pseudohypoparathyroidism Pseudopseudohypoparathyroidism Renal Osteodystrophy Rickets Hypophosphatemic Rickets, X-Linked Dominant Renal Osteodystrophy

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#### Figure 7.5 How a chosen MeSH term is used to search PubMed

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Figure 7.6 Use of PubMed history function to compare yield from a free text search (#5) and a MeSH search (#7)



Figure 7.7 Using PubMed Limits function to search for certain study types (in this case a meta-analysis)

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Figure 7.8 PubMed Clinical Queries feature, allowing articles to be searched for by type



Figure 7.9 The different articles found by our search strategy

### How to find current best evidence

### OHave current best evidence find us

O Problem –based learningO Learning by inquiry

- O The question we ask
- O How we ask questions
- O How well we use information resources
- How skilled we are in interpreting and applying these resources



### **O**Hands- on training



- O Do not know how to critically appraise
- O Do nor consistently apply the criteria
- O Do not have time



• You cant find what you want harder task do it yourself



1-a text have" in line "references to evidences that supports each of its key recommendations

2-date of publication of the references



- Comes from an explicit robust evidence process
- More important than "Named Chairs"

### How to perform a targeted search?

### Synthesized sources

#### '4S' evolution of services



#### Examples

Computerised decision support systems (CDSS)

Evidence-based journal abstracts

Cochrane reviews

Original published articles in journals

Reference:

Haynes RB (2001). Of studies, syntheses, synopses and systems: the '4S' evolution

# **Specialised resources**

### Primary studies-

### tackling the jungle

# BANGLe One stop shopping

O TRIP

• Get you the maximum bang for your buck

(احصل لك على أقصى قدر من الصخب لجهودك) •



# **Comparison Study**

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Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. Falagas ME <sup>1</sup> Pitsouri El, Matetzis GA, Parpas G	Final Version Lists
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Abstract The evolution of the electronic age has led to the development of numerous medical databases on the World Wide Web, offering search facilities or particular subject and the ability to perform citation analysis. We compared the content coverage and practical utility of PubMed. Scopus: Web of	n a Add to Favorites
Science, and Google Scholar. The official Web pages of the databases were used to extract information on the range of journals covered, search facilities and restrictions, and update frequency. We used the example of a keyword search to evaluate the usefulness of these databases in biomedical information retrieval and a specific published article to evaluate their utility in performing citation analysis. All databases were practical information retrieval and a specific published article to evaluate their utility in performing citation analysis. All databases were practical information retrieval and a specific published article to evaluate their utility in performing citation analysis.	Related citations in PubMed Three options for citation fracking. Google Scholar, Scopus and Wi (Biomed Digit Libr. 2008)
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#### Online tutorials for effective searching

- Finding the evidence cebm.net/index.aspx
- PubMed –searching medical literature www://research.library.gsu.edu/pubmed
- PubMed Tutorial
- www.nlm.nih.gov/bsd/disted/pubmedtutorial/





# PubMed

- **O** <u>PubMed</u> is a service of the US National Library of Medicine® that:
- Provides free access to <u>MEDLINE®</u>, the NLM® database of indexed citations and abstracts to medical, nursing, dental, veterinary, health care, and preclinical sciences journal articles
- Includes additional selected life sciences journals not in MEDLINE
- Adds new citations daily
- Was developed by the <u>National Center for Biotechnology</u> <u>Information (NCBI)</u> at the <u>National Library of Medicine (NLM)</u>

http://www.nlm.nih.gov/services/pubmed.html

# Medline fact sheet

- MEDLINE is the primary component of <u>PubMed®</u>
- Time coverage: generally <u>1946 to the present</u>, with some older material
- Source: Currently, citations from over 5,600 worldwide journals in about 40 languages; about 60 languages for older journals
- Updates: Since 2005, between 2,000-4,000 completed references are added each day. Beginning in June 2014, NLM began exporting citations 7 days a week. More than 750,000 total added in 2014
- Updates are suspended for several weeks during November and December as NLM makes the transition to a new year of <u>Medical</u> <u>Subject Headings (MeSH)</u> vocabulary used to index the articles

### Using PubMed (Providing targeted search)

Too much nontargeted information is being retrieved.

# **PubMed Home Page**

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# MeSH Database

<u>MeSH</u> (Medical Subject Headings) is the NLM controlled vocabulary thesaurus used for indexing PubMed citations

http://www.ncbi.nlm.nih.gov/books/NBK3827/#pubmedhelp.Searching\_by\_using\_t

### MeSH Database

- Terms are used in biomedical literature at NLM for indexing articles for Medicine
- Imposes uniformity to the indexing of literature
- MeSH terms: updated annually
#### MeSH facts

- O There are 27,149 descriptors in 2014 MeSH
- also over 218,000 entry terms that assist in finding the most appropriate MeSH Heading
- The MeSH thesaurus is used by NLM for indexing articles from 5,400 of the world's leading biomedical journals for the MEDLINE®/PubMED® database

#### How to use MeSH

Use the **MeSH database** to find MeSH terms:

- O Subheadings
- Publication Types
- Supplementary Concepts
- Pharmacological Actions

then build a PubMed search.

#### MeSH Database

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Webcasts and Videos:

#### Storytelling

• Anecdote has an important place in clinical practice

# **Systematic Review**

ALL evidence related to a particular field of research is collected via a systematic search of the literature and even unpublished sources, and evaluated using predefined criteria.

### **Meta-analysis: Definition**

A statistical analysis that combines or integrates the results of several independent clinical trials considered by the analyst to be 'combinable.'

### **Forms of Reviews**

#### **ONarrative reviews (traditional reviews)**

**OPooling of data** 

**O**Systematic reviews

Pearson K. Report on certain enteric fever inoculation statistics. BMJ <u>1904</u>;3:1243-6.:

"Many of the groups ... are far too small to

allow of any definite opinion being formed at all, having regard to the size of the probable

error involved."

Beecher HK. The powerful placebo. JAMA <u>1955</u>;159:1602-6:

The effectiveness of placebos in such diverse conditions as postoperative wound pain, cough, and angina pectoris was evaluated: the placebo was apparently effective in 35% of patients.

Glass G. Primary, secondary and meta-analysis of research. Educ Res <u>1976</u>;5:3-8:

The term meta-analysis was introduced in 1976 by the psychologist Glass,

#### The Cochrane Collaboration:

 Network of clinicians, epidemiologists, and other health professionals prepare, maintain and disseminate comprehensive and systematic reviews of the effects of health care.

 Since the foundation of the Cochrane Centre in Oxford in 1992, 15 further centres and hundreds of individuals are collaborating in review groups.

#### Meta-analysis vs. Narrative Reviews

#### Narrative reviews are not objective:

- O Controversies about which studies to include.
- Number of studies are considered more than the included patients in each study.
- O Reviewer's bias to his own opinion.
- **O** Reviewer's bias according to his speciality

#### Meta-analysis vs. a "Mega-study"

Single large studies are liable to:

- Type I error (false positive result)
- Type II error (false negative result):
  - O occur in 20% of research
  - a drug that reduces mortality by 10% mortality from myocardial infarction may need a study including 10.000 patient
- Generalizability of results can be questioned.

# **Meta-analysis and Guidelines**

# Repeated performance of meta-analysis whenever a new trial becomes available for inclusion is a cornerstone in formulating guidelines.

# Significance of Meta-analysis: Example

Mitchell JRA. Timolol after myocardial infarction: an answer or a new set of questions? BMJ <u>1981</u>;282:1565-70:

"despite claims that they reduce arrhythmias, cardiac work, and infarct size, we still have no clear evidence that ß blockers improve long-term survival after infarction despite almost 20 years of clinical trials."

#### Cumulative Meta-analysis: Example

Year	Trials	Cumulative odd	s ratios (95% GI)		
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**Detailed research protocol:** 

- O clear objectives hypotheses to be tested
- subgroups of interest
- **O** proposed methods of research
- criteria for identifying and selecting relevant studies and extracting and analyzing information

#### **Criteria for selecting a study:**

- Quality and design of study
- **O** Combinability of treatment, patients and outcome
- Duration of follow up
- Selection of studies should <u>not</u> be always restricted to published studies (to exclude publication bias)
- **O** Do <u>not</u> rely only on electronic databases, manual search is important!

#### Studies with following qualities should be included:

(scoring system out of 9)

- **O** Controlled trials
- Proper randomization
- Proper reporting on all included patients (intention to treat principle)
- **O** Objective (preferably blinded) outcome assessment

Data retrieval from included studies:

- Standardized record for data collection
- Preferably 2 independent observers for data extraction
- Blinding of observers to:
  - **O** Authors
  - **O** Institution
  - O Journal
  - O Source of funding
  - **O** acknowledgments

**Standardization of measures of outcome:** 

• If outcome is continuous (e.g. blood pressure or temperature): deviation.

units of standa

• If outcome is binary (cure or no cure, dead or alive):

odds ratios

relative risk.

108
Standardization of measures of outcome:

Odds and odds ratio

The odds is the number of patients who fulfil the criteria for a given endpoint divided by the number of patients who do not.

For example, the odds of diarrhoea during treatment with an antibiotic in a group of 10 patients may be 4 to 6 (4 with diarrhoea divided by 6 without, 0.66); in a control group the odds may be 1 to 9 (0.11). The odds ratio of treatment to control group would be 6 (0.66÷0.11).

Standardization of measures of outcome:

**Risk and relative risk** 

The risk is the number of patients who fulfil the criteria for a given end point divided by the total number of patients.

For example, the risk of diarrhoea during treatment with an antibiotic in a group of 10 patients may be 4 to 10; in the control group the risks may be 1 to 10. The relative risk of treatment to control group would be 4 ( $0.4\div0.1$ ).

#### Calculation of overall effect: principles

- Simple calculation of arithmetic average of results would be inappropriate: smaller studies (results more subject to play of chance) should be given less weight.
- Methods used for meta-analysis use a weighted average of the results: larger trials have more influence than smaller ones. The statistical techniques to do this can be classified into two models:
  - O "fixed effects" model
  - o "random effects" model

#### Statistical principles for calculation of overall effect:

#### • Fixed effects model:

considers, that variability in selected studies is exclusively due to random variation. Therefore, if all the studies were infinitely large they would give identical results.

#### • Random effects model:

assumes a different underlying effect for each study and takes this into consideration as an additional source of variation. 112



Sensitivity analysis

Recalculate the results after:

- Exclusion of lower quality studies ( $\leq$ 7)
- Exclusion of publication bias by examining the relation between sample size and magnitude of effect. With publication bias the larger the study the less the magnitude of the effect.
- Exclusion of studies stopped due to interim results.

If only a minimal changes occurs in the initial results, then the analysis is robust !

# Guidelines

Guidelines are systematically developed statements developed to assist practitioner decisions about appropriate health care for specific clinical circumstances

(Field and Lohr, 1990)

## Guidelines

#### Guidelines: "necessity driven"

#### Systematic Reviews: "evidence driven"

# **Appraisal of Guidelines**

- O Conflicts of interest
- O Clear topic-besed guidelines with objectives related to health
- O Multi-disciplinary approach (including EBM expert)
- O Comprehensiveness of collected data
- O Adapted to variations in clinical practice
- **O** Validity and reliability
- Clinical relevance and flexibility
- O Cost-effectiveness
- O Consideration of implementation strategies

## **Guidelines: Grade of Recommendation**

Grade A:	
Level of evide	nce: 1a: systematic review of RCTs
1	b: individual RCT
1	Ic: all or none
Grade B:	
Level of evidence: 2a: systematic review of cohort studies	
2	2b: individual cohort study
2	2c: outcomes research
3	Ba: systematic review of case-control studies
3	3b: individual case-control study
Grade C: 4	4: case series
Grade D: 5	5: expert opinion, bench research

# **Confidence** intervals

• An RR of 1.0 indicates no difference applicable

• Any 95% CI that includes RR = 1.0 indicates that there may be "no difference."

• Even though the 95% CI contains 1.0, there may still be a true difference, just not detected in this study



#### O E.g:

• a large study might find that a new antihypertensive drug lowered BP, on average, 1 mm Hg more than conventional treatments.

The results were statistically significant (P <.05)

 However, most clinicians would not find the 1 mm Hg difference in BP large enough to justify changing to a new drug.

# Controlled Trials

• In RCTs, study participants are randomly allocated to two or more groups and then assigned to receive an intervention

#### OBSTACLES TO EVIDENCE BASED MEDICINE in DEVELOPING COUNTRIES



when physicians own equipment (self-referral).

- Each review is prepared by an 'author team' with support from
- O specialist librarians
- O methodologists
- copy and content editors
- **O** peer reviewers

taking hundreds of hours of work from start to finish





#### Patient-Oriented Evidence that Matters



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- addresses a clinical problem or clinical question that primary care physicians will encounter in their practice
- uses patient-oriented outcomes
- has the potential to change our practice if the results are valid and applicable

# DOE "Disease-Oriented Evidence".

• are all too common in the medical literature, and they are often brought to our attention by pharmaceutical representatives eager to change our practice. However, this kind of evidence is often misleading and generally should be considered premature

#### When POEMs exist, forget the DOEs.

# At point of care

• resources are based on systematic evaluations of evidence and can provide clinicians with practical guidance at the point of care



If you put 4 colored marbles in a bag, 3 are red and 1 is green, then the odds of pulling a green marble out of the bag are: [(1/4) / (3/4)] = 1/3 (one in four times a green marble will be pulled)/(three in four times a red marble will be pulled) = 1/3, or the odds of pulling a green marble out of the bag are 1 to 3.

# THINK BIG!

start small.

ACT NOW