Introduction in clinical epidemiology and Evidence-Based Medicine

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Clinical Epidemiology

"helping smart doctors stop prescribing dumb treatments."

The 2009 Gairdner Awards for Medical Science lauded Dr. David Sackett for his leadership in the fields of clinical epidemiology and evidence-based medicine.
**Dr. David Sackett**  
*since 1960s*

- Sackett is the founder of the first clinical epidemiology department in Canada and led the move toward "evidence-based medicine," which he said has three components:
  - Being a good doctor with clinical skills to diagnose patients well.
  - Using evidence generated from proper research, such as randomized clinical trials in which similar groups of patients either receive or don't receive a given intervention and are then carefully followed up to see whether they fare better.
  - Incorporating a patient's expectations and values of health care.

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**Revolution of Evidence-Based Medicine (EBM)**

- Use (not just critical appraisal) of evidence in patient care.
Types of health care professional

Evidence Users

Evidence Generator

Evidence Finders

Evidence Ignorer

What EBM?

“Expertise in integrating
1. Best research evidence
2. Clinical Circumstance
3. Patient values
in clinical decisions”

Haynes, Devereaux, & Guyatt, 2002
Evidence-Based Medicine

Clinical Circumstance

Evidence-Based Medicine

Clinical Circumstance  Research evidence
Evidence-Based Medicine

Clinical Circumstance

Research evidence

Patient preference

Clinical expertise

Evidence-Based Medicine
Evidence alone is never sufficient to make a clinical decision

- Tread-off among
  - Benefit
  - Risk
  - Cost
  - Practicality
  - Patients’ value

What EBM is not:

- Cookbook medicine
- Overrules experience/expertise
- Always about RCT’s
- Always cost-minimizing
Why Evidence-Based Medicine Practice?

- Too many patients
- Too many problems
- Too many journals
- Information overload
- No time to read
- Read what I am familiar with
- Avoid difficult issues

Case scenario

- 54 years old
- Male
- Asymptomatic
- Unremarkable PE
- TC=210, LDL=170, HDL=42

WOULD YOU PRESCRIBE A STATIN?
The Evidence

6605 healthy patients with average cholesterol:

<p>| | |</p>
<table>
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<tr>
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<td><strong>Placebo</strong></td>
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WOULD YOU PRESCRIBE A STATIN?
### The Clinician

6605 healthy patients with average cholesterol:

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➤ No question. We’ll save lives.

### The Health Economist

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➤ It will cost 14,400,000 to buy the drug for 1000 pts.

➤ Will eat up funds for TB, pneumonia, diarrhea, etc.

➤ We could actually lose lives!!!
### SOCIO-ECONOMIC PREDICAMENTS

<table>
<thead>
<tr>
<th></th>
<th>CLINICAL MEDICINE</th>
<th>HEALTH ECONOMICS</th>
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<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>Maximize Effectiveness</td>
<td>Maximize Efficiency</td>
</tr>
<tr>
<td><strong>Philosophy</strong></td>
<td>Cumulative benefit</td>
<td>Opportunity Costs</td>
</tr>
<tr>
<td><strong>Assumption</strong></td>
<td>Infinite resources</td>
<td>Finite Resources</td>
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#### How to practice Evidence-Based Medicine?
How do we actually practice EBM?

5 A’s of EBM

- Step 1: Ask answerable question
- Step 2: Find Articles
- Step 3: Critical Appraisal the evidence
- Step 4: Apply
- Step 5: Assess patient preference

Type of question in clinical practice

- Diagnosis
- Etiology or causation
- Treatment
- Prognosis
Hierarchy of Evidence

Systematic reviews

Randomized Controlled Trials

Cohort studies

Case-control studies

Cross-sectional studies

Cases reports

Monitor the change

Monitor change

Identify Clinical Problem

Search for Evidence

Critically Appraise Evidence

Act on Evidence

Monitor change

Update Evidence

Store good Evidence

Discard
Six factors influence the uptake of innovations

1. Relative benefit – what’s in it for me?
2. (non)-Complexity – is it easy to learn?
3. Trialability – can I try it out easily?
4. Observability – can I see others do it?
5. Compatibility – fit with ideas and work
6. Reinvention – can I adapt it to me?

Rogers, Diffusion of Innovations
How can we improve the uptake of EBM?

- Consider the 6 factors
- How might you change each?

1. Relative Benefit – what’s in it for me?

- Evidence-Based Medicine can:
  - Reduce reading by quality filters
  - Better management of patients
  - Relieve anxiety about uncertainty
Review the World Literature

Most “interesting” research is wrong, but clinicians not skilled in appraisal

- Flawed studies
  - Hormone Replacement Therapy
  - Beta-carotene and cancer
  - MMR and autism
  - Folate and CHD
- Data mining
  - Genes for anything
  - Suppression of outcomes
- Small early studies

Ioannidis J. Why Most Published Research Findings Are False. PLoS 2005
EBM can reduce reading need

*How much is valid AND relevant?*

**PROCESS**
- 120+ journals scanned
  - 50,000 articles
- Is it **valid**? (<5%)
  - Intervention: RCT
  - Prognosis: inception cohort
  - Etc
- Is it **relevant**?
  - 6-12 GPs & specialists asked:
    Relevant? Newsworthy?
- < 0.5% selected

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2. Non-complexity – is it easy to use?

- How can we simplify EBM?
Simplifying critical appraisal
The two mnemonics method

- What question did the study address?
  - PICO

- Were methods valid?
  - RAMMbo

Using the PICO to orient us

- What is the question (PICO)?
  - Do by yourself first, then (2 minutes)
  - Get group agreement on answers
Appraisal checklist - RAMMbo

Was the Study valid?
1. Recruitment
   - Who did the subjects represent?
2. Allocation
   - Was the assignment to treatments randomised?
   - Were the groups similar at the trial’s start?
3. Maintainence
   - Were the groups treated equally?
   - Were outcomes ascertained & analysed for most patients?
4. Measurements
   - Were patients and clinicians “blinded” to treatment? OR
   - Were measurements objective & standardised?

Study statistics (p-values & confidence intervals)

User Guide. JAMA, 1993

Simplify searching

PubMed Clinical Queries
• Built in methods filters
• Systematic review filter
• Automated MeSH
EBM and Systematic Reviews

- **EBM**
  - Steps
    1. Ask Question
    2. Search
    3. Appraise
    4. Apply
  - Time: 90 seconds
  - < 20 articles
  - **This** patient survives!

- **Systematic Review**
  - Steps
    1. Ask Question
    2. Search ++++ x 2
    3. Appraise x 2
    4. Synthesize
    5. Apply
  - Time: 6 months, team
  - < 2,000 articles
  - **This** patient is dead

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3. Trialability – can I try it out?

- How can we make EBM easy to try?
3. Trialability – provide easy steps

1. Keep a paper question log
2. Answer a few important questions / week
3. Get help with searches
4. Simplify appraisal OR use pre-appraised topics
5. Focus on interpretation

Critical Elements of good Critical Appraisal Topics (CATS)

1. Student own choice of clinical topic
2. Keep it simple
3. Small group presentation
4. Keep time frame short (<1 week)
Six factors influence the uptake of innovations

1. Relative benefit – what’s in it for me?
2. (non)-Complexity – is it easy to learn?
3. Trialability – can I try it out easily?
4. Observability – can I see others do it?
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Rogers, Diffusion of Innovations
Is bed rest ever helpful?
A systematic review of trials*

- 10 trials of bed rest after spinal puncture
  - no change in headache with bed rest
  - Increase in back pain

- Protocols in UK neurology units - 80% still recommend bed rest after LP

Serpell M, BMJ 1998;316:1709–10

Many “Leaks” from research & practice

If 80% achieved at each stage then
0.8 x 0.8 x 0.8 x 0.8 x 0.8 x 0.8 x 0.8 = 0.21
Knowledge Gaps
between what is known and what is done

• What “gaps” between research and practice are you involved in?

• Why does the “gap” exist?
  – (list several possible causes)

1. Too much information
2. Too much information
3. Too much information
Knowledge Gaps
between what is known and what is done

• What “gaps” between research and practice are you involved in?

• Why does the “gap” exist?
  – (list several possible causes)

• What would you do to “fix” the gap?

“Just in Time” learning
The EBM Approach to Education

• Shift focus to current patient problems (“just in time” education)
  – Relevant to YOUR practice
  – Memorable – and behaviour changed!
  – Up to date

• Skills and resources for best current answers

Dave Sackett
3 skills for handling evidence:

- Forming answerable clinical questions
- Searching for the best evidence answer
- Critical appraisal
How can you recognize and formulate clinical questions as they occur?

- Pay careful attention to the questions that spontaneously occur to you.
- Listen for the question behind the question
  - What can I use for a sprain?
    Might become
  - Is a topical NSAID like aspirin more effective than paracetamol at enabling resumption of sport at 1 week?

What if too many questions arise?

- Patients may have several active problems
  - possible questions about diagnosis, prognosis, therapy for each problem
- What is the most important issue for this patient now?
- Which question, when answered, will help me most?
- then selecting from the many the few questions that are most important to answer right away.
4 parts of clinical question

- Patient or Problem \( P \)
- Intervention or exposure \( I \)
- Comparison \( C \)
- Outcome \( O \)

**PICO**

- Patient or Problem
- Intervention
- Comparison
- Outcome

“Patient” refers to the person presenting with the problem, or more simply, to the problem itself. Both concepts are important in searching.
“Intervention” refers to the action taken in response to the problem. This is often a drug or surgical procedure, but it can take many forms.

“Comparison” refers to the benchmark against which the intervention is measured. Often it refers to another treatment, no treatment, or a placebo.
**PICO**

Patient or Problem

Intervention

Comparison

Outcome

“Outcome” refers to the anticipated result of the intervention.

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**Scenario 2**

- You are a physician supervising a senior resident in a tertiary care hospital in Bangkok.
- Your 60-year-old uncle was admitted at your hospital due to congestive heart failure. His underlying diseases were DM, HT and HLP and he has treated with ASA already.
- After recovery from CHF, his EF was 25% with sinus rhythm so his son concerned about thromboembolic risk and ask you whether you will prescribe anti-coagulant for him or not.
Step 1 Converting a clinical problem into a clinical question

P: In 60-year-old man with heart failure, sinus rhythm
I: Warfarin
C: ASA
O: Mortality/death

Step 2 Search the evidence
How?

1. Formulate your PICO question
2. Try secondary sources
3. Choose primary database(s)
4. Combine textwords
5. Filter for the right type of study

Try secondary sources

- Uptodate
  http://www.uptodate.com
- Cochrane library
  http://www.thecochranelibrary.com
- TRIP database
  http://www.tripdatabase.com
Primary sources

- Choosing the right bibliographic database(s)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>MEDLINE</td>
<td>US database covering all aspects of clinical medicine, biological sciences, education and technology</td>
</tr>
<tr>
<td>EMBASE</td>
<td>European equivalent of MEDLINE, with emphasis on drugs and pharmacology</td>
</tr>
<tr>
<td>CINAHL</td>
<td>Nursing and allied health, health education, occupational and physiotherapy, social services</td>
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Search Engine and Database

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<td>MEDLINE</td>
</tr>
<tr>
<td>Ovid</td>
<td>MEDLINE, EMBASE, ...</td>
</tr>
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Combine textwords
Boolean Operators

- **Intersection (AND)**
  - only those citations that contain selected terms.
- **Union (OR)**
  - citations that contain at least one of the selected terms.
- **Difference (NOT)**
  - exclude citations with the selected term
MEDLINE searching skills

- Searched with keywords
- Applied “‘Limits’”
- Used “‘Related articles’” option
- Used “Clinical Queries”
- Used Medical Subject Headings (MeSH)

Step 3 Critical Appraisal of the evidence
Users’ Guide for an Article

Guyatt GH, Rennie D. Users’ guides to the medical literature. 2002

Critical appraisal

• Are the results of the study valid?
• What are the results?
• How can you apply the results to patient care?
Type of clinical questions

- Diagnosis
- Risk and causation
- Treatment
- Prognosis

The EBM Practitioner

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- Interviews patients
  - farmer
  - 5 kids
  - earns 4,000/mo

- Informs patient
  - NNT = 250
  - drug costs 14,400/yr
  - Need to take for yrs

- Allows patients to decide for himself.
EBM AS A CYCLE

- Decision
  - Clinical circumstance and patient values
  - Assessment of applicability
- Clinical Question
  - Systematic search for best evidence
  - Assessment of validity

EBM is a lifelong learning process that includes:

- Evaluating the performance of the information in clinical practice.
- Discovering areas where more research is needed.
- Applying the information in clinical practice with physicians.