Evidence-Based Medicine for clinical years
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“Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values”
Why do we need EBM?
Fifty years ago Frances Kelsey transformed the way prescription drugs are regulated. As a new FDA employee she was assigned to review Kevadaon, better known as its brand name drug thalidomide.

Kelsey at the time questioned the drugs safety. “It just came with so many extravagant claims that I didn’t believe.”
Types of study evidence affects the quality
Expert opinion - Lowest level of evidence

Would you ever have put babies to sleep on their tummies?
Expert opinion

Baby and Child Care” has actually sold more that 50 million copies, only outmatched in sales by the Bible
Over four fold increase risk of sudden infant death syndrome

Types of study evidence affects the quality

- Systematic Reviews
- Randomized Controlled Trials
- Cohort Studies
- Case-Control Studies
- Case Series, Case Reports
- Editorials, Expert Opinion
Papers

Mortality in relation to smoking: 50 years’ observations on male British doctors
Richard Doll, Richard Peto, Jillian Boreham, Isabelle Sutherland

Abstract

Objective  To compare the hazards of cigarette smoking in men who formed their habits at different periods, and the extent of the reduction in risk when cigarette smoking is stopped at different ages.

Design  Prospective study that has continued from 1951 to 2001.

Setting  United Kingdom.

Participants  34 439 male British doctors. Information about their smoking habits was obtained in 1951, and periodically thereafter; cause specific mortality was monitored for 50 years.

Main outcomes measures  Overall mortality by smoking habit, cause specific mortality by smoking habit, and occurrence of lung cancer.

Results  Smoking was associated with an increased risk of death from all causes, heart disease, and lung cancer. Smoking stopped at any age, provided a reduction in risk. Risk was proportional to the amount smoked, and the duration of smoking.

Conclusion  The results of this study, and other studies, have provided strong evidence that smoking is a major cause of death. More recently, smoking has been shown to be a cause of death in women and in most countries of the world where smoking is common.

1951 prospective study
This discovery stimulated much further research into the effects of smoking (not only on lung cancer but also on many other diseases), including a UK prospective study of smoking and death among British doctors born in 1951 and observed to 2001.

Cite this article as: BMJ, doi:10.1136/bmj.38142.554479.AE (published 22 June 2004)
Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age.

Doll R et al. BMJ 2004;328:1519
Types of study evidence affects the quality
Why we need RANDOMIZED CONTROLLED

In the early 1980s newly introduced antiarrhythmics were found to be highly successful at suppressing arrhythmias.

Not until a RCT was performed was it realized that, although these drugs suppressed arrhythmias, they actually increased mortality.

The CAST trial revealed Excess mortality of 56/1000.

By the time the results of this trial were published, at least 100,000 such patients had been taking these drugs.
Types of study evidence affects the quality

- Systematic Reviews
- Randomized Controlled Trials
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• For every 1000 patients treated **65 more** will be alive at **1 month** if treatment is administered in the **first hour** – the ‘golden hour’ – after symptom onset.

• **37 lives** are saved for every 1000 patients treated in the **1–2 hour interval**

• 26 lives are saved for every 1000 patients treated in the **2–3 hour interval**

• 29 lives are saved for every 1000 patients treated in the **3–6 hour interval**

• **20 lives** are saved for every 1000 patients treated in the **7–12 hour interval**
EBM as a medical student?
Be aware that treatment options should be based on clinical need and the effectiveness of treatment options, and that decisions should be arrived at through assessment and discussion with the patient.
Must be aware of their responsibility to maintain their knowledge and skills throughout their careers.

Students are expected to keep up to date and to apply knowledge necessary for good clinical care.
Steps of practicing EBM

1. Ask a focused question.
2. Track down some evidence.
3. Critically appraise evidence for its validity and effect.
4. Apply the evidence in practice.
1. General Questions

General knowledge about a condition such as heart attack. These types of questions typically ask who, what, where, when

- What are the risk factors for an MI?
- What are the symptoms and sign of someone presenting with MI?
- What are the diagnostic tests for MI?
- What are the treatments of MI?
- What are the complications of an MI?
Patient presenting with MI

Specific Questions about actual patient care decisions and actions

For treatment
4 (or 3) components:

In Patients with a heart attack
Does (I) cholesterol lowering therapy
Compared to placebo
reduce mortality (O)
Types of study evidence affects the quality
Heart Attack evidence

1999
HOPE trial published on ramipril in the NEJM

2000
Lancet: publishes effect of low dose β-blockers in the elderly

2001

2002
Lancet: HPS study shows benefit of statins independent of baseline level

2003
Lancet: primary PTCA more effective than thrombolysis

2005
Bmj calls for aspirin for everyone

2005
Lancet: 2005 COMMIT trial beta blocker should be withheld if the patient is unstable

2005
Lancet: cholesterol trialist collaboration 90,056 participants in 14 RTCs

2005
Lancet: COMMIT trial of early metoprolol in 45,852 participants

2009
Lancet: aspirin is of uncertain net benefit for primary prevention

2010
In hospital mortality 5%

2013
Routine use of Oxygen questioned in a Cochrane review

2015
American College of Physicians guidelines warn against screening asymptomatic individuals

2015
Paramedic 2 Trial tests effectiveness of adrenaline in cardiac arrest

2000
Lancet: COMMIT trial of early metoprolol in 45,852 participants
questions to ask

1. How common is the problem  
   Prevalence

2. Is early detection worthwhile  
   Screening

3. Is the diagnostic test accurate  
   Diagnosis

4. What will happen if we do nothing  
   Prognosis

5. Does this intervention help  
   Treatment

6. What are the harms of an intervention  
   Treatment
Specific Questions about actual patient care decisions and actions

General Questions about a condition. These types of questions typically ask who, what, where, when, how

Experience with the condition

Knowledge requirements
Keeping up to date
Size of Medical Knowledge

- **NLM MetaThesaurus**
  - 875,255 concepts
  - 2.14 million concept names

- **Diagnosis Pro**
  - 11,000 diseases
  - 30,000 abnormalities (symptoms, signs, lab, X-ray,)
  - 3,200 drugs (cf FDAs 18,283 products)

1 disease per day for 30 years

*To cover the vast field of medicine in four years is an impossible task.*
- William Olser
Median minutes/week spent reading about my patients

Self-reports at 17 Grand Rounds:

- Medical Students: 90 minutes
- House Officers (PGY1): 0 (up to 70%=none)
- SHOs (PGY2-4): 20 (up to 15%=none)
- Registrars: 45 (up to 40%=none)
- Sr. Registrars 30 (up to 15%=none)
- **Consultants:**
  - Grad. Post 1975: 45 (up to 30%=none)
  - Grad. Pre 1975: 30 (up to 40%=none)
Steps of practicing EBM

1. Ask a focused question.
2. Track down the evidence
3. Critically appraise evidence for its validity, effect size, precision
4. Apply the evidence in practice:
Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial

The DREAM (Diabetes REDuction Assessment with ramipril and rosiglitazone Medication) Trial Investigators

FINDINGS:

Background Rosiglitazone is a thiazolidinedione that reduces insulin resistance and might preserve insulin secretion.

The aim of this study was to assess prospectively the drug's ability to prevent type 2 diabetes in individuals at high risk of developing the condition.

At the end of study, 59 individuals had dropped out from the rosiglitazone group and 46 from the placebo group. 306 (11.6%) individuals given rosiglitazone and 686 (26.0%) given placebo developed the composite primary outcome (hazard ratio 0.40, 95% CI 0.35-0.46; p<0.0001); 1330 (50.5%) individuals in the rosiglitazone group and 798 (30.3%) in the placebo group became normoglycaemic (1.71, 1.57-1.87; p<0.0001).

Cardiovascular event rates were much the same in both groups, although 14 (0.5%) participants in the rosiglitazone group and two (0.1%) in the placebo group developed heart failure (p=0.01).

Interpretation Rosiglitazone at 8 mg daily for 3 years substantially reduces incident type 2 diabetes and increases the likelihood of regression to normoglycaemia in adults with impaired fasting glucose or impaired glucose tolerance, or both.
Furthermore, despite the population being at low risk of heart failure (10 year risk 0.33%) a significant increase (0.4%) in heart failure was seen in the rosiglitazone group compared with placebo (7.03, 1.60 to 30.9, number needed to harm at three years 250).
In the next 4 weeks

• Try to ask for one patient you have seen:

1. What causes the disease?
2. How was the disease diagnosed?
3. How was the patient treated?
4. What is the natural history of the disease?
5. Consider formulating a PICO

And try to find some evidence
Tracking switched outcomes in clinical trials

The team

We are a team of academics, medical students and programmers, based at the Centre for Evidence-Based Medicine, at the University of Oxford.
Thank you

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