Introduction to Evidence Based Medicine (EBM)

Objectives

* Define evidence based medicine
* Delineate the purpose of evidence based medicine
* Discuss sources and levels of evidence
* Introduce «grade» to assess quality of evidence
* Introduce 5As of evidence based medicine
* Formulate the PICOT clinical question

What is Evidence Based Medicine?

* Conscientious, explicit, judicious use of current best evidence in making decisions about care of individual patients.

David Sackett, Seminars in Perinatology, 1997

What is Evidence Based Medicine?

* 1990 McMaster University residency statement: An attitude of “enlightened skepticism” toward the application of research to day-to-day management of patients.

EBM is the integration of

Straus S. et al, Evidence-Based Medicine:
How to Practice and Teach EBM. 3nd Ed. Churchill-Livingstone. 2005.

A case vignette

* 88 year-old woman is admitted with the constriction of the right mainstem bronchus by primary lung cancer, leading to progressive dyspnea.
* Critical review of evidence suggests that bronchial stenting can relieve symptoms but does not prolong survival.
* What should we do?

A case vignette

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* Critical review of evidence suggests that bronchial stenting can relieve symptoms but does not prolong survival.
* What should we do?
* The patient does not want a procedure, and elects to go home on supplemental oxygen and morphine.

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* Critical review of evidence suggests that bronchial stenting can relieve symptoms but does not prolong survival.
* What should we do?
* The patient does not want a procedure, and decides to go home on supplemental oxygen and morphine.
* Evidence is never enough – it is necessary but not sufficient.

The Purpose of EBM

* Make the best possible decisions for and with our patients

The Purpose of EBM

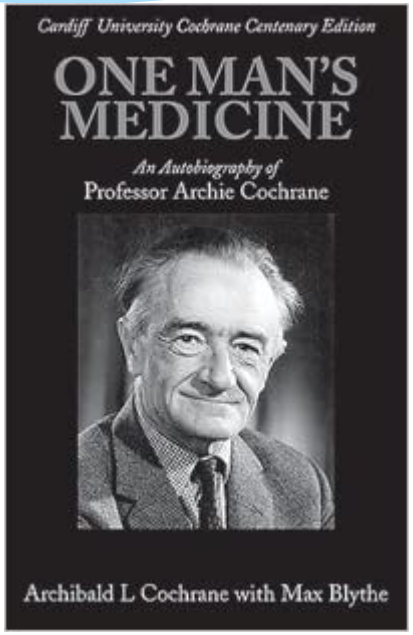
* Wide variations in practice are often not related to differences among patients
* Variation in clinical practice are due to
  * Variation in beliefs
  * Variation in interpretation of evidence
  * Variation in response when evidence is uncertain
* Minimizing variations in practice can improve
  * Quality of health care delivery
  * Patient outcomes

Lewis SJ and Orland BI. The importance and impact of Evidence-Based-Medicine. JMCP 2004

Cochrane Collaboration

* “It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials”

  Archie Cochrane (1979)



https://pubmed.ncbi.nlm.nih.gov/19730323/
https://de.wikipedia.org/wiki/Archie_Cochrane

What is EBM not?

* Algorithm-based ("cook-book") medicine
  * We'll see common themes, but every case is unique.
* Only RCT's and meta-analyses
  * For many clinical questions, these study designs are
    * Impossible
    * Inappropriate/unethical
    * Unavailable
* A sectarian obsession with criticizing papers
  * Although nothing we do should be free from investigation

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Abstract

Objectives To determine whether parachutes are effective in preventing major trauma related to gravitational challenge.

Design Systematic review of randomised controlled trials.

Data sources: Medline, Web of Science, Embase, and the Cochrane Library databases; appropriate internet sites and citation lists.

Study selection: Studies showing the effects of using a parachute during free fall.

Main outcome measure Death or major trauma, defined as an injury severity score > 15.

Results We were unable to identify any randomised controlled trials of parachute intervention.

Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.

https://www.bmj.com/content/327/7429/1459

EBM History

* James Lind, Salisbury
  * “On the 20th of May 1747, I took twelve patients … on board the Salisbury at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees … and had one diet common to all.”

https://en.wikipedia.org/wiki/James_Lind

EBM History

* Lind placed two sailors each on:
  * Cider
  * Elixir vitriol
  * Seawater
  * Vinegar
  * Oranges and lemons
  * Nutmeg/garlic/mustard seed/myrrh/barley water/tamarind purgative

EBM History

* “They continued six days under this course … The consequence was that the most sudden and visible good effects were perceived from the use of the oranges and lemons; one of those who had taken them being at the end of the six days fit for duty … The other was the best recovered of any in his condition; and now deemed pretty well, was appointed nurse to the rest of the sick.”
* Eventually, Englishmen became known as “Limeys”.

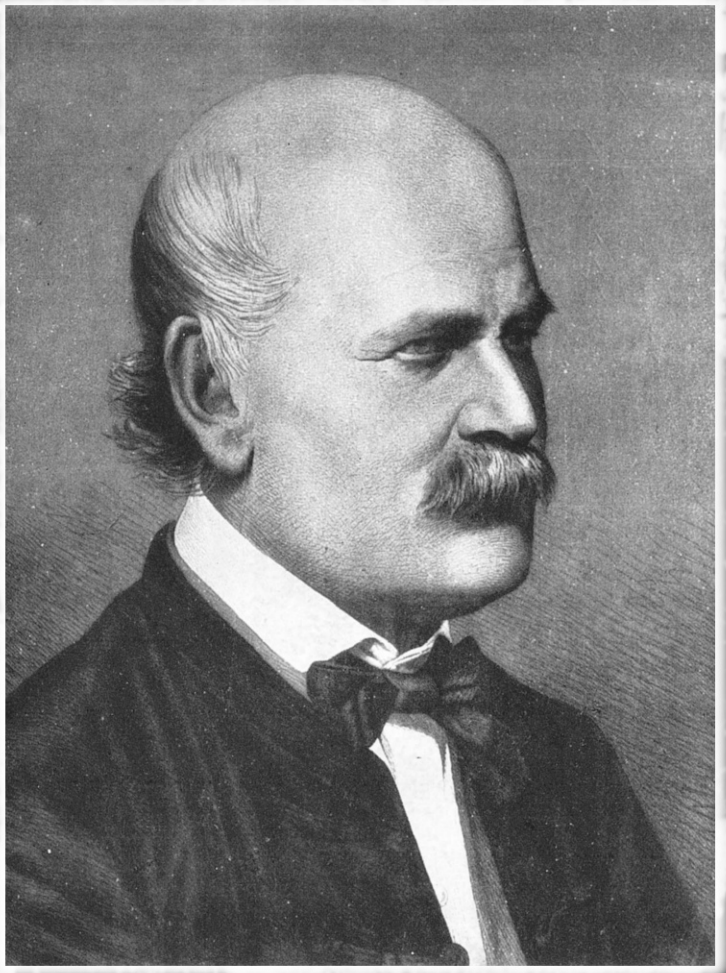
EBM History

* Puerperal fever
  * Postpartum condition often leading to death
  * Thought to be due to “miasma” (Greek mythology: a contagious power that has an independent life of its own
* **Semmelweis** noted that women whose babies were delivered by physicians at Vienna Charity developed puerperal fever far more often (12%) than those attended by midwives at the adjacent maternity hospital (2%).

EBM History

* Semmelweis noted that the medical students and physicians would move directly from autopsy dissection to patients, and also between patients, without changing clothes or washing hands.
* In 1847, he abolished this practice, instituted chlorine-based hand-washing, and within a year the rate of puerperal fever at Vienna Charity dropped to below 1%.

https://en.wikipedia.org/wiki/Ignaz_Semmelweis



EBM History

* 1980's
  * EC/IC bypass surgery to prevent stroke recurrence
  * Nonrandomized cohorts suggested surgical patients did better
* 1985 RCT showed the only actual effect was increased post-operative complications

The EC/IC Bypass Study Group: Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke: results of an international randomized trial. N Engl J Med 1985; 313:1191-1200. https://pubmed.ncbi.nlm.nih.gov/2865674/

EBM History

* David Sackett (1934 – 2015)
* Founded the Oxford Centre for Evidence-Based Medicine. https://www.cebm.ox.ac.uk/

https://en.wikipedia.org/wiki/David_Sackett

Sources of Evidence

Category	Sources and examples
Systems	Computerized decision support
Summaries	Evidence-based textbooks e.g. ACP med, Dynamed, PIER, CE, UTD
Synopsis of syntheses	Evidence-based journal abstracts e.g. ACPJC, EBM, EBN, DARE
Syntheses	Systematic reviews e.g. Cochrane, Evidence Updates
Synopsis of studies	Evidence based journal abstracts
Studies	Original journal articles

Strauss, Glasziou, Richardson & Hayes. Evidence Based Medicine. 4th edition

Who needs EBM?

* Do you plan to see patients?
* Do you plan to help patients make the best decisions for their health?
* Do you plan to teach?
* Do you plan to do research?
* Do you have family members who look to you for medical advice?

Types of Questions Related to Evidence

* This course will concentrate on evidence related to;
  * Diagnosis
  * Therapy
  * Harm
  * Prognosis

Does Methodological Quality Matter?

"Therapeutic reports with controls tend to have no enthusiasm….

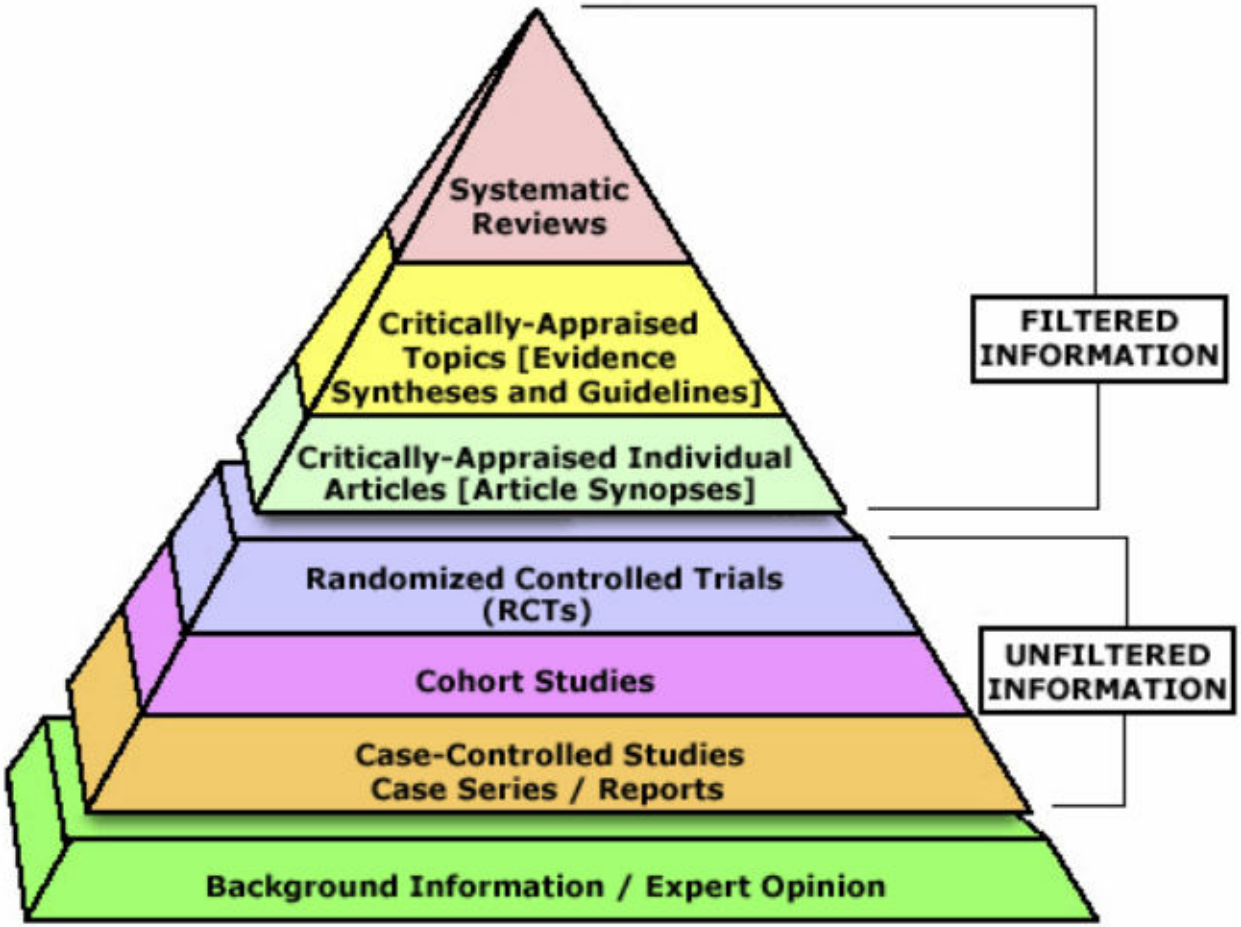
…and reports with enthusiasm tend to have no controls"

David Sackett 1986

Letterie, G. S. (2005). *Surgery, assisted reproductive technology and infertility: diagnosis and management of problems in gynecologic reproductive medicine*. CRC press.

Hierarchy of Evidence

* RCT
* Cohort
* Case Control
* Case Series
* Case Report
* Animal Research
* Editorials
* In vitro research



https://s4be.cochrane.org/blog/2013/02/14/the-ebm-pyramid/

Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009)

What are we to do when the irresistible force of the need to offer clinical advice meets with the immovable object of flawed evidence? All we can do is our best: give the advice, but alert the advisees to the flaws in the evidence on which it is based.

The CEBM 'Levels of Evidence 1' document sets out one approach to systematising this process for different question types.

(For definitions of terms used see our **glossary**)

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR" validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR" with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval"¡)	Individual inception cohort study with > 80% follow-up; CDR" validated in a single population	Validating** cohort study with good" " " reference standards; or CDR" tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses

https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

Grades of Recommendation

* A: consistent level 1 studies
* B: consistent level 2 or 3 studies or extrapolations from level 1 studies
* C: level 4 studies or extrapolations from level 2 or 3 studies
* D: level 5 evidence or troublingly inconsistent or inconclusive studies of any level

https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009

Understanding the Changing Landscape of Evidence

"Half of what you are taught as medical students will in 10 years have been shown to be wrong.

And the trouble is, none of our teachers know which half"

Dr. Sydney Burwell, Dean of Harvard Medical School

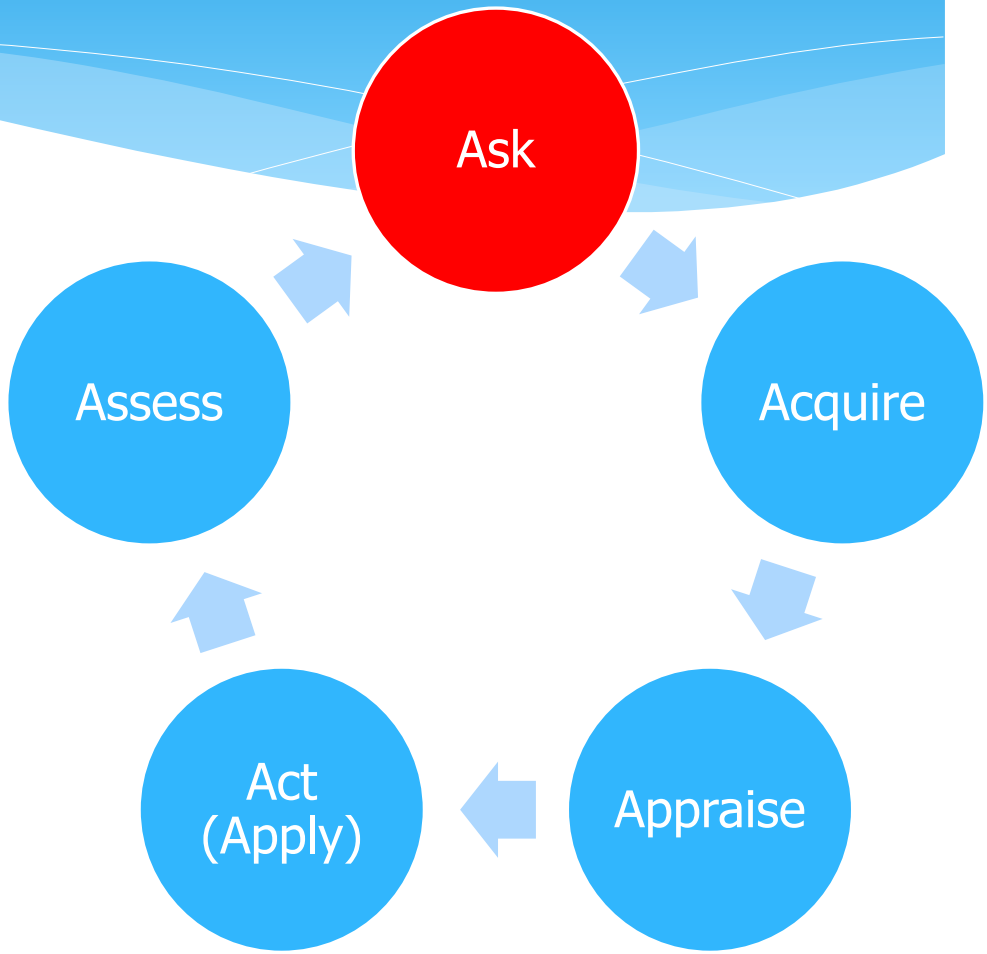
The Controversial History of Hormone Replacement Therapy

* The history of hormone replacement therapy (HRT) started in the 1960s, with very high popularity in the 1990s.
* In 2002, it was shown that HRT had more detrimental than beneficial effects.
* In the following years, new studies showed that the use of HRT in younger women or in early postmenopausal women had a beneficial effect on the cardiovascular system, reducing coronary disease and all-cause mortality.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6780820/

Steps of Evidence Based Practice: 5As

* Ask the right question
* Acquire the best evidence
* Appraise the evidence critically
* Act or Apply the evidence
* Assess



Users' Guides to Medical Literature. Essentials of Evidence-Based Clinical Practice 3rd Ed. McGraw Hill. 2015.

Ask the Right Question (PICOT/PECOT)

* **P**atient, Problem or Population
* **I**ntervention or Exposure
* **C**omparison (control vs. intervention)
* **O**utcome/s of interest
* **T**ype of study or **T**ype of Question (diagnosis, therapy, harm, prognosis)

Ask the Right Question (PICOT)

You are caring for a 25 week preterm infant, 750 g birthweight who is 6 days old, in the NICU.

The infant is ventilated and has an oxygen requirement of 60%.

Mild to moderate cardiomegaly on X-ray.

A murmur was investigated with an echocardiogram which shows a hemodynamically significant Patent Ductus Arteriosus.

What is the evidence that in preterm infants at < 1000 g birth weight with a hemodynamically significant patent ductus arteriosus **(P)**, treatment with indomethacin **(I)** compared to no treatment **(C)** will result in closure and avoid surgical ligation **(O)** from randomized controlled trials **(T)**?

Ask the Right Question (PICOT)

* Scenario 1: In the patient on the previous slide, you and cardiology colleagues confer that this PDA should be treated with a course of indomethacin.
* The infant is on 80 ml/kg/day of feeds, feeding well.
* You consider the options of continuing or discontinuing feeding while on indomethacin treatment.
* How will you frame your PICOT question?

Ask the Right Question (PICOT)

* Scenario 2: You are about to discharge a former 25-week preterm infant, who is currently 36 corrected weeks of gestation and who has had apneic episodes in the past.
* You stopped his caffeine a week ago because his apnea was getting better and the last apnea was 2 weeks back.
* Mother is still very worried and requests you to send them home with an apnea monitor so that she has some peace of mind.
* The baby has no heart disease, bronchopulmonary dysplasia or severe intraventricular hemorrhage and is feeding well.
* You want to query if sending apnea monitors home is evidence based.

* Early-Onset Sepsis risk calculation: https://neonatalsepsiscalculator.kaiserpermanente.org/
* We can use this to illustrate the concept of pre-test and post-test probabilities.

Limitations of EBM

* Time consuming
* Access to medical literature
* Knowledge of epidemiology and statistics
* Publication bias
* Conflict of interest
* There might be no evidence available
* Practicing medicine bears uncertainty

Summary Questions

* What is EBM?
* Delineate the purpose of evidence based medicine
* What are the levels of evidence and grade of recommendation?
* What are the 5As of EBM?
* How do you formulate the PICOT clinical question?

Summary

* What is evidence based medicine.
* What are the sources of evidence?
* Explain the levels of evidence?
* List the grades of evidence.
* Explain the 5As of evidence based medicine.
* Formulate the PICOT clinical question.