Inverting the Pyramid: A Reassessment of the Roles of Experiment in Evidence-Based Medicine

SPSP Biennial Conference 2009

20th June 2009

University of Minnesota

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UCL

Outline

1. What is EBM, and what's it for?
2. How does EBM work?
3. Pyramids and mountains
4. Are all forms of evidence created equal?
5. Causation and EBM…

What is EBM?

Evidence-based medicine (EBM) is the "*conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients*"

[Sackett, 1996]

How does EBM work?

- Frame a clinical scenario
- Systematically retrieve relevant evidence
- Appraise evidence
  - Applicability
  - Validity

How does EBM work?

- Frame a clinical scenario
- Systematically retrieve relevant evidence
- Appraise evidence
- Apply conclusions to practice
- Evaluate response
  - Repeat process…


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A clinical scenario…

- 61 year old man
- High blood pressure
- No improvement with diet and lifestyle interventions
- No current treatment
- No other ongoing health problems
- No significant past medical history

...becomes a clinical question

- What's the best drug treatment to prolong his life?
- Applicability criteria
  - Hypertension
  - Thiazide diuretic
  - Mortality

Retrieving and appraising evidence

- Hypertension (300381)
- Thiazide (14767)
- Mortality (600436)
- Hypertension AND thiazide AND mortality (464)

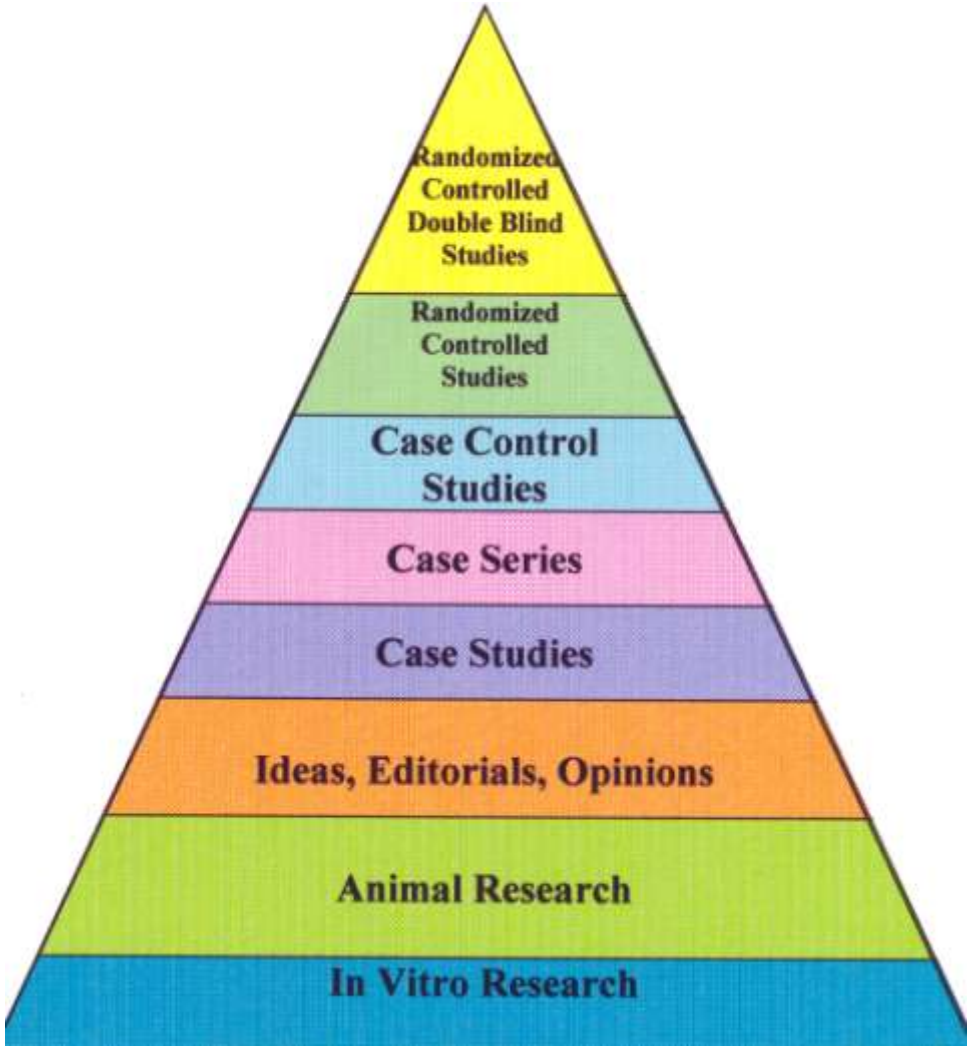
Pyramids and mountains…

- We still have a (small) mountain of information
- How can we hone this down?
- The Evidence Pyramid

http://library.downstate.edu/EBM2/2100.htm

Pyramids and mountains…

- We still have a mountain of information
- How can we hone this down?
- The Evidence Pyramids…



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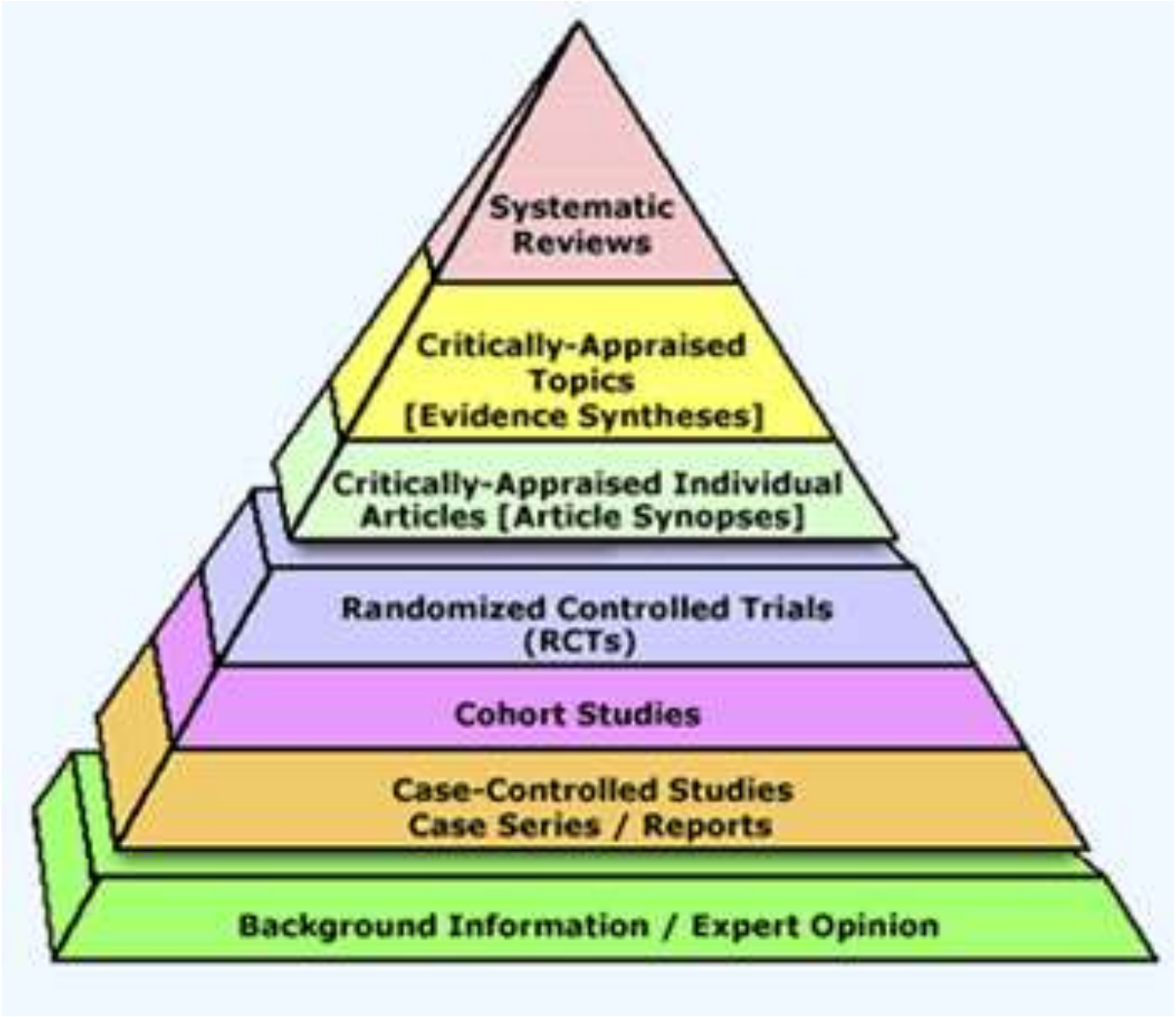

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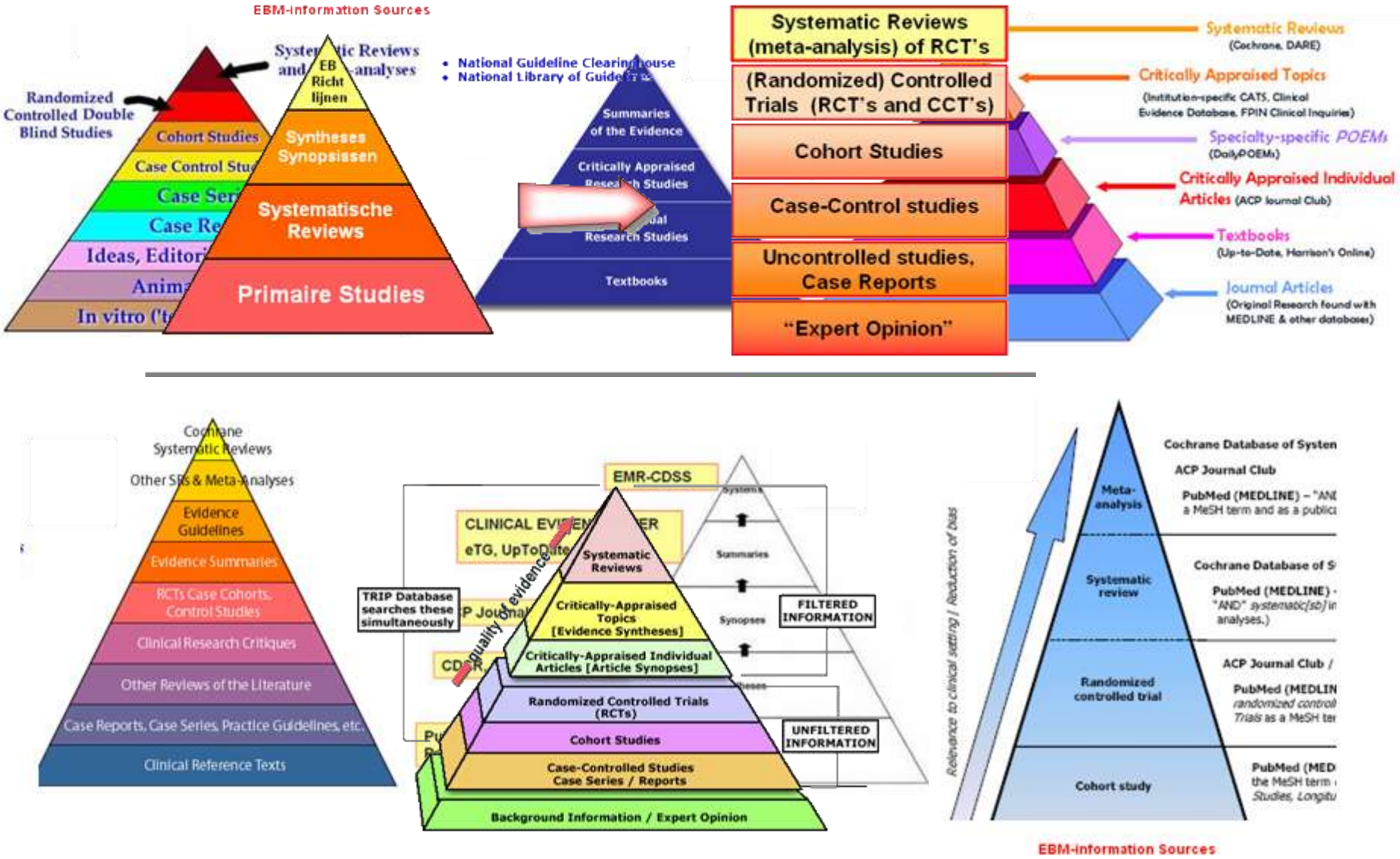

http://laikaspoetnik.wordpress.com/2008/09/26/time-to-weed-the-ebm-pyramids/

Pyramids and mountains…

- We still have a mountain of information
- How can we hone this down?
- The Evidence Pyramid
  - (or some sort of hierarchy of evidence)
  - Gives us a broad idea about validity

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1: Beta-blockers for hypertension.
Wiysonge CS, Bradley H, Mayosi BM, Maroney R, Mbewu A, Opie LH, Volmink J.
Cochrane Database Syst Rev. 2007 Jan 24;(1):CD002003. Review.
PMID: 17253471 [PubMed - indexed for MEDLINE]
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2: Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care.
Vijan S, Hayward RA.
Ann Intern Med. 2003 Apr 1;138(7):593-602. Review.
PMID: 12667032 [PubMed - indexed for MEDLINE]
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3: J-shaped relationship between blood pressure and mortality in hypertensive patients: new insights from a meta-analysis individual patient data

The mountain..

- Hypertension (300381)
- Thiazide (14767)
- Mortality (600436)
- Hypertension AND thiazide AND mortality (464)
  - meta-analyses (7)

Ann Intern Med. 1997 May 15;126(10):761-7.

Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators.

Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, Ekbom T, Fagard R, Friedman L, Perry M, Prineas R, Schron E.

Claude Bernard University, Lyon, France.

BACKGROUND: Trials of drug therapy for hypertension have shown that such therapy has a clear overall benefit in preventing cardiovascular disease. Although these trials have included slightly more women than men, it is still not clear whether treatment benefit is similar for both sexes. OBJECTIVE: To quantify the average treatment effect in both sexes and to determine whether available data show significant differences in treatment effect between women and men. DESIGN: Subgroup meta-analysis of individual patient data according to sex. Analysis was based on seven trials from the INDANA (INdividual Data ANalysis of Antihypertensive intervention trials) database and was adjusted for possible confounders. PATIENTS: 20,802 women and 19,975 men recruited between 1972 and 1990. INTERVENTIONS: Primarily beta-blockers and thiazide diuretics. RESULTS: In women, treatment effect was statistically significant for stroke (fatal strokes and all strokes) and for major cardiovascular events. In men, it was statistically significant for all categories of events (total and specific mortality, all coronary events, all strokes, and major cardiovascular events). The odds ratios for any category of event did not differ significantly between men and women. In absolute terms, the benefit in women was seen primarily for strokes; in men, treatment prevented as many coronary events as strokes. Graphical analyses suggest that these results could be completely explained by the difference in untreated risk. CONCLUSIONS: In terms of relative risk, treatment benefit did not differ between women and men. The absolute risk reduction attributable to treatment seemed to depend on untreated risk. These findings underline the need to predict accurately the untreated cardiovascular risk of an individual person in order to rationalize and individualize antihypertensive treatment.

The mountain..

- Hypertension (300381)
- Thiazide (14767)
- Mortality (600436)
- Hypertension AND thiazide AND mortality (464)
  - meta-analyses (7) – but none really applicable
  - RCTs (94)

And so on…

- In practice, good EBM methodology is often unfeasible
- Instead, other factors influence evidence choice:
  - Publication
  - Expert/peer opinion
  - Chance
- This leads to sub-optimal outcomes
- Pyramids present philosophical problems

Causation and EBM: A suggestion…

- Can we side-step these issues?
- Enter causation
  - Mechanism plus statistics (RWT)
  - Incorporates pluralistic evidence
  - Avoids blindly favouring certain forms of evidence
  - Still allows broad selection by validity

The Russo-Williamson thesis

- Russo and Williamson, 2007
- Monistic causation dependent on both mechanistic and statistical evidence
- Broadly
  - basic science gives us mechanism
  - trials give us statistics
- Uses existing evidence more effectively

Evidential pluralism

- Strong HPS case to be made for a mixture of types of evidence being important in causal decisions
- Avoids epistemological privilege, pyramids
- Driver for research programmes

Validity by evidence-base, not just by methodology

- Good trials tend to evaluate basic scientific findings
- Good basic science tends to investigate statistical findings
- Laboratory and clinical sciences are already interdependent

Conclusion

- Problem: Selecting evidence by methodology alone can be problematic
- Proposal: A reconsideration of evidential support for clinical decision-making by broadening the evidence-base in a causal fashion

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- Russo, F. and Williamson, J. 2007. “Interpreting Causality in the Health Sciences,” *International Studies in the Philosophy of Science.* **21**(2): 157—170.
- Sackett, D.L. 1996. “Evidence Based Medicine: What it is and what it isn't,**”** *British Medical Journal*. **312**(7023): 71—2.