

Ethics and Evidence at All Stages of Life

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Overview

1. Framing case: Mrs. Smith
2. A few facts
3. Case-based questions
4. Evidence can help us
5. Evidence can't help us as much as we'd like
6. Acknowledging uncertainty
7. The relationship between research and practice
8. What to do now

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Chronicity and complexity

Is what's good for the diseases always good for the patients?

Ross E.G. Upshur MD MSc CCFP FRCPC Shawn Tracy

Mrs Smith is an 83-year-old woman living independently in the community. She has the following active medical problems: congestive heart failure secondary to ischemic heart disease, atrial fibrillation, osteoarthritis, osteoporosis, urinary incontinence, and depression. She is taking 11 prescribed medications on a regular basis. She is seen regularly in the clinic for management of her anticoagulation and multiple chronic conditions.

Case-based Questions

What challenges do health care providers face in caring for Mrs. Smith?

What can be done to improve the evidence base for such decisions?

What should health care providers do in the face of uncertainty about the best evidence?

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Evidence-based Medicine

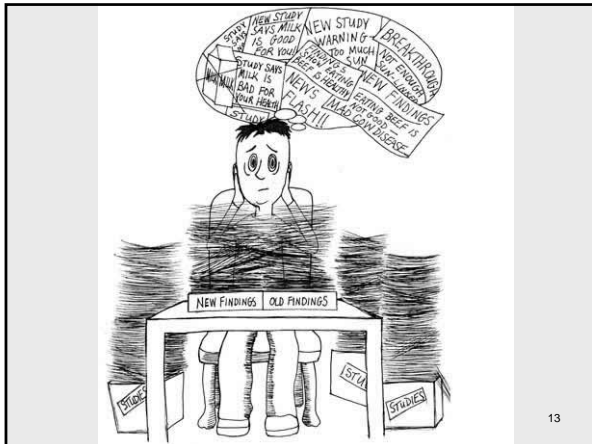
"Evidence-based Medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients"

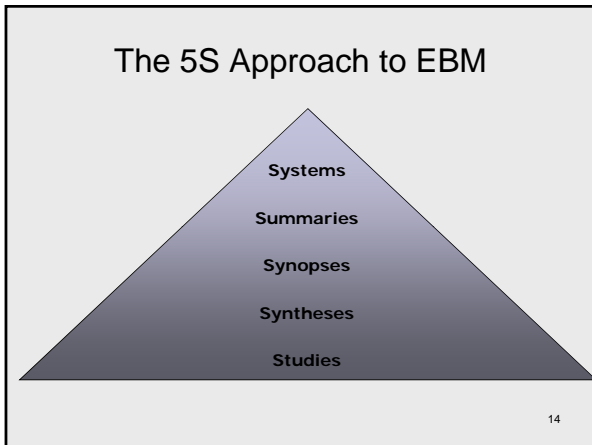
- Sackett, *JAMA* 1996

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The screenshot shows a Cochrane Review page. At the top, there are navigation tabs: 'Explore', 'New + Updated', 'Other languages', and 'Full Text: The Evidence Library'. Below these are search and filter options. The main content area has a sub-heading 'Routine perineal shaving on admission to hospital in labour' by Savaei V, Lavein T. The text discusses the benefits and risks of perineal shaving for women in labor. At the bottom of the page, there is a small image of a blue safety razor.

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“[I]n some circumstances, the title [of a review] provides enough information.” (38)

Source: Straus et al. (2005)

Clinicians are advised to “begin the search for evidence to guide clinical decisions at the highest possible level” and once evidence has been found, they “don’t have to look any further.”

Haynes, RB. (2006)

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A Few Selected Concerns

Contamination

Critical Thinking

Certainty and Consent

Context

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Contamination



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A few of the biases in RCTs

Allocation bias	Too early bias	Personal habit bias	Geography bias
Selection bias	Too late bias	Moral bias	Language of publication bias
Ascertainment bias	Learning curve bias	Values bias	Trial design bias
Choice of question bias	Complexity bias	Clinical practice bias	Favoured design bias
Hidden agenda bias	Comparison choice bias	Institution bias	Large trial bias
Cost and convenience bias	Placebo bias	Territory bias	Multicentred trial bias
Funding availability bias	Outcome choice bias	Tradition bias	Small trial bias
Secondary gains bias	Withdrawal bias	Do something bias	Complementary Medicine bias
Regulation bias	Dropout bias	Technology bias	Flashy title bias
IRB bias	Selective reporting bias	Resource allocation bias	Substituted question bias
Bureaucracy bias	Social desirability bias	Printed word bias	Vested interest bias
Wrong design bias	Optimism bias	Prestigious journal bias	Bankbook bias
Population choice bias	Data dredging bias	Non-prestigious journal bias	Overinflated belief bias
Age bias	Interesting data bias	Peer review bias	Reader attitude bias
Gender bias	Fraud bias	Prominent author bias	Belligerence bias
Pregnancy bias	Publication bias	Unknown author bias	Empiricism bias
Special circumstances bias	Language of publication bias	Who is s/he? bias	I am an epidemiologist bias
Recruitment bias	Country of publication bias	Famous institution bias	Careless reading bias
Informed consent bias	Time lag bias	Credential bias
Literacy bias	Reader bias	Professional background bias	
Language bias	Relation to author bias	Esteemed author bias	
Severity of illness bias	Rivalry bias	Friendship bias	
Intervention choice bias	I owe him one bias		

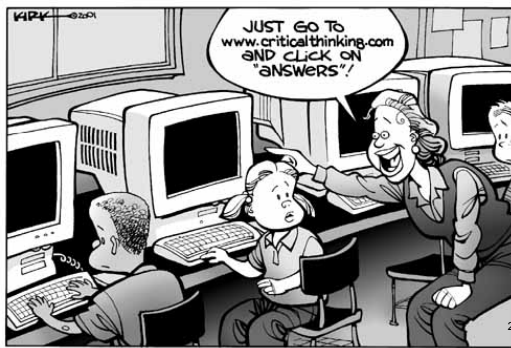
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Lesson Two

The importance of *not being too responsive* to research evidence in clinical practice

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Critical Thinking



Critical Thinking

"[M]any medical schools and training programs, in a form of premature closure, are moving away from teaching the fundamentals of careful evidence appraisal to emphasize the implementation of evidence."

Source: Montori and Guyatt (2008)

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Certainty and Consent

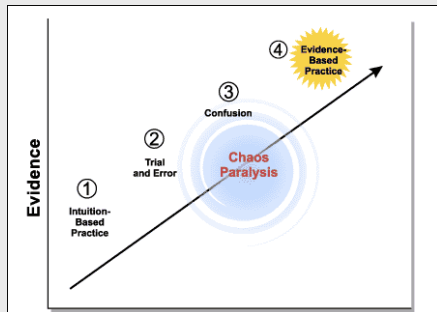


Figure 2. Evidence-Based Practice

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Certainty and Consent

Evidence-based Medicine "deals directly with the uncertainties of clinical medicine"

Source: EBM Working Group (1992)

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Combination Therapies and the Theoretical Limits of Evidence-Based Medicine

Neuroepidemiology 20(2):57-64, 2001

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Background: Advances in molecular pharmacology and surgical, endovascular, and radiation techniques have yielded multiple effective or promising, and potentially complementary, classes of treatments for virtually every major medical disorder. Consequently, determining the optimum combination of therapies for a condition is a burgeoning challenge to clinical trialists and practicing physicians. **Methods:** General phase III trial strategies for testing combination regimens are described, and then applied to two illustrative conditions, Alzheimer disease and ischemic stroke. **Results:** Strategies for testing combination regimens include: head to head trials of all combinations, which lead to unwieldy trial numbers; very large multi-arm trials, which impractically delay interval information on regimen utility; and hierarchical, serial clinical trials. Systematic literature review revealed seven classes of agents already approved or in late phase III testing for preventing the development or slowing the progression of Alzheimer disease and five for ischemic stroke prevention. Possible combination regimens number 128 (2^7) for Alzheimer disease and 32 (2^5) for ischemic stroke. Hierarchical, serial clinical trials would permit identification of the optimum combination of these agent classes for Alzheimer disease through 127 trials, enrolling 63,500 patients, requiring 286 years, for ischemic stroke through 31 trials, enrolling 188,000 patients, requiring 155 years. **Conclusions:** Marked limitations in the ability of clinical trials to interrogate varied treatment combinations to determine the most effective ensemble exist, and their scope is widely underappreciated. Steps that may attenuate, though not eliminate, the challenge of a surfeit of combination treatment regimens include preclinical testing to identify the most promising regimens, use of surrogate outcome measures in exploratory clinical trials, and use of hierarchical, serial and factorial phase III trials.

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Lesson Three

The importance of identifying and acknowledging uncertainty

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Context

"Is our patient so different from those in the study that its results cannot apply?"

Source: Straus et al. (2005)

(Original statement: "[A]sk whether there is some compelling reason why the results should not be applied to the patient. A compelling reason usually won't be found, and most often you can generalize the results to your patient with confidence.")

Guyatt, G.H., D.L. Sackett and D.J. Cook. (1994)

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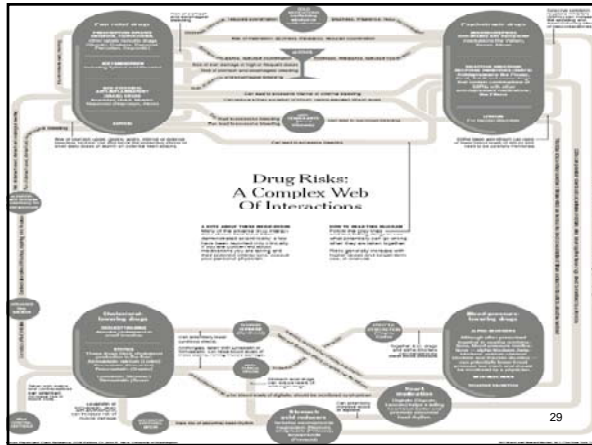
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Who is the “standard” research subject? Who is left out?



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The importance of building the relationship between research and practice

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Practical Progress?



“Health Canada might consider revisiting their regulations and encouraging the use of pragmatic designs to support their decision-making.”

Zwarenstein, Merrick and Shaun Treweek, “What kind of randomized trials do we need?” *Journal of Clinical Epidemiology* 62 (2009): 462.

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Case-based Questions

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Discussion

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