Evidence-Based Medicine

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What is Evidence-Based Medicine?

- The use of current best evidence in conjunction with clinical expertise and patient values to make decisions about individual patients' care

What's the basic idea?

- A response to the bad old days of medical decisionmaking
  - Expert opinion
  - Personal clinical experience with its confirmation bias
  - Old textbooks
  - Received wisdom from the graybeards
- If a treatment works, the balance of quality evidence should support, not contradict it
- Evidence provides a reasonable/justifiable expectation of success, which is more ethical
- It's a way to arrive at the likely-best decisions for patients

What is it *not*?

- A way to denigrate clinical experience
- An excuse to ignore patient preferences/goals
- Checklist robot care or cookbook medicine
  - Every patient is different; EBM acknowledges this
- Profane worship of randomized controlled trials
  - RCTs are not the only source of "evidence" to consider
- A "brand"

Early applications of science in medicine

- James Lind, scurvy, 1750s
  - 12 scorbutic sailors- those given citrus recovered
  - Findings weren't acted on for 50 years
- Pierre Louis, cholera, 1830s
  - Kept survival/mortality data on cholera patients
  - Doing nothing was better than venesection or leeches
  - Bloodletting had never actually been tested
- Ignaz Semmelweis, postpartum sepsis, 1840s
  - Not a good idea to go straight from cadaver lab to OB
    - Unless you wash your hands

Motivating factors for EBM

- Daily need for valid info on diagnosis, prognosis, treatment, and prevention
- Traditional info sources are inadequate:
  - Textbooks go out of date quickly
  - Experts are frequently wrong
  - Didactic CME isn't particularly effective
  - Journals: very high volume, extremely variable validity
- Disparity: diagnostic skills and clinical judgment increase with experience; currency of knowledge and clinical performance tend to decline
- Time pressures

Developments that made it possible

- Adoption of indicators of evidence quality
  - Structured abstracts, names for types of studies, etc
- Creation of systematic reviews, meta-analyses
- Creation of evidence-based secondary-publication journals and collections
  - Cochrane
  - BMJ Clinical Evidence
  - The Campbell Collaboration
  - Evidence-Based Medicine, other journals, best-evidence sections in longstanding journals
- Information systems, internet, PubMed, UpToDate, etc.

How it's Done

Steps in an EBM approach

- Convert the need for information to an answerable question
- Find the best evidence to answer that question
- Evaluate the evidence for validity, effect size, and applicability
- Integrate this evaluation with clinical expertise and the patient's particular situation

An answerable question

- Define the patient or problem
- Define the intervention of interest
- Define the control/comparison intervention
- Define the outcome of interest

For example…

- A 65-yr-old male is scheduled for radioactive brachytherapy for prostate cancer. He reports taking aspirin daily, and notes that his GP and surgeon seem to disagree about whether he should continue taking it through surgery.
- What should you recommend?
- Note: "Ask Gerstein" will get an evidence-based answer, but we're learning to do it ourselves

Getting that question: PICO

- The **P**atient
  - 65 yo male
  - Primary or secondary prevention, or some other reason?
- The **I**ntervention
  - Perioperative ASA
- The **C**ontrol/comparison intervention
  - Withhold perioperative ASA
- The **O**utcome(s) of interest
  - Thrombosis (or maybe death) prevented with use
  - Perioperative bleed (or required transfusion) caused by use
  - Extended hospital stay- either way

So…

- In a 65 yo pt with history of thrombosis, does perioperative ASA reduce the risk of perioperative thrombosis compared to withholding it?
- In a 65 yo pt, does perioperative ASA increase the risk of perioperative major bleed compared to withholding it?

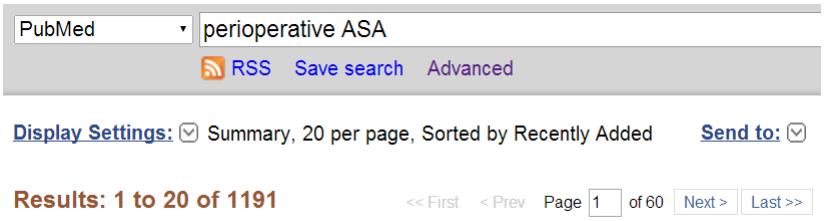
Next

- Hit the literature
  - PubMed
  - Cochrane Collaboration
  - Etc
- Evaluate what you find
  - Are the studies valid?
  - What is the effect size: big difference, or little one?
  - Applicability: are the study populations similar to my patient?
- For both expected benefits and expected harms

Still more

- Integrate your evaluation of the evidence with…
- Your clinical expertise
  - Any drug interactions expected?
  - Any other reason why you'd think twice one way or the other?
- This pt's unique situation
  - GERD + Barrett's esophagus?
  - Pt's degree of concern for thrombosis vs. bleed?
  - Any Hx of bleed?
  - Other cardiovascular comorbidities?

But there's so much!



EBM's prioritization of info

- 1. Systematic review of randomized trials
- 2. Randomized trial or observational study with dramatic effect
- 3. Nonrandomized controlled cohort / followup study
- 4. Case series, case-control studies, or historically controlled studies
- 5. Mechanistic reasoning

- Level may be graded down if study is poor quality, small size, imprecise, indirect for your situation, etc
- Systematic reviews are generally better than individual studies

It's hard to argue with that.

Does EBM improve patient outcomes?

- Hard to say
- Irony: EBM itself hasn't been directly tested
- Control group: doctors without access to information? Or maybe who ignore pt wishes?
- Indirect evidence (yeah, yeah): pts who receive treatments with a strong evidence basis tend to do better; same for those who are screened more carefully

All in all, a pretty good idea

But…

Limitations

- The evidence isn't always coherent or consistent
- Much evidence relates to efficacy (tightly controlled) instead of effectiveness (real life)
- Can be difficult to apply population-based results to individual patients
- Institutional inertia
- Need new skills- evidence search, critical appraisal
- Not all practices have access to many journals

Even then…

- EBM emphasizes the communications/clinical skills to get useful pt info and learn their values/goals/expectations
- Fosters generic evidence skills (obtain/analyze)
- Good model for self-directed learning
- Helps identify fruitful research questions
- Provides a common language for interdisciplinary teams

It grows…

US Preventive Services Task Force: www.uspreventiveservicestaskforce.org

- A grading system for strength of recommendations on various preventive services

Grade	Definition
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

GRADE working group: www.gradeworkinggroup.org

- Quality of evidence is graded as:
  - High
  - Moderate
  - Low
  - Very low

National Guideline Clearinghouse: www.guideline.gov

- A compendium of professional societies' published guidelines
- At least 131 in anesthesiology alone
- Also provides a way to compare these guidelines

Choosing Wisely: choosingwisely.org

- ABIM Foundation effort
- Goal: evidence-based lists of unnecessary tests/treatments in all medical specialties

American Society of Anesthesiologists

Five Things Physicians and Patients Should Question

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1 **Don't obtain baseline laboratory studies in patients without significant systemic disease (ASA I or II) undergoing low-risk surgery – specifically complete blood count, basic or comprehensive metabolic panel, coagulation studies when blood loss (or fluid shifts) is/are expected to be minimal.**

Performing routine laboratory tests in patients who are otherwise healthy is of little value in detecting disease. Evidence suggests that a targeted history and physical exam should determine whether pre-procedure laboratory

Cochrane Collaboration: www.cochrane.org

- Collection of systematic reviews and meta-analyses

The Cochrane Collaboration
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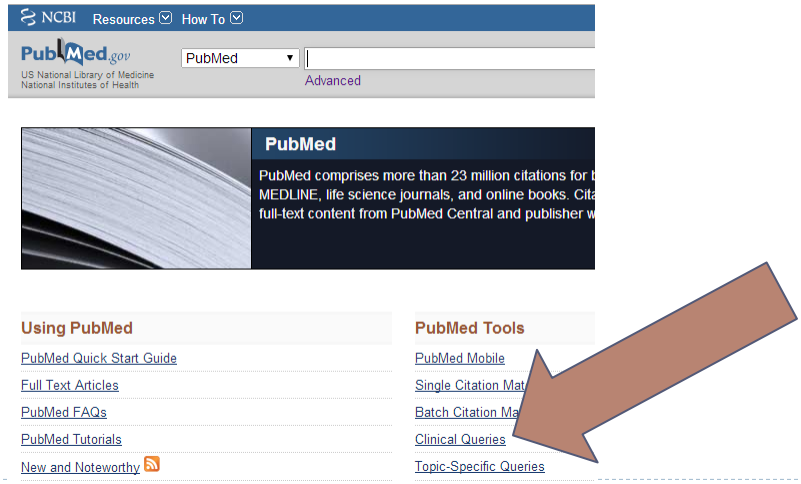
Oxycodone for neuropathic pain and fibromyalgia in adults

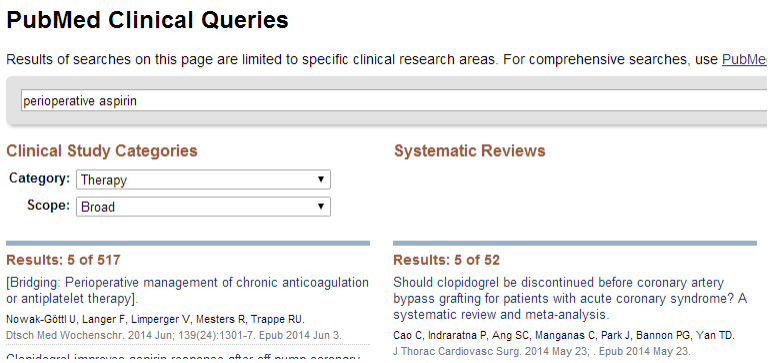
Neuropathic pain is pain coming from damaged nerves. It differs from pain messages carried along from damaged tissue (as in a fall, a cut, or an arthritic knee). Neuropathic pain is treated by differe pain from damaged tissue. Medicines such as paracetamol (acetaminophen) and ibuprofen are no neuropathic pain, while medicines that are sometimes used to treat epilepsy or depression can be some people with neuropathic pain. Fibromyalgia is a widespread pain disorder characterised by symptoms including poor sleep, fatigue and cognitive impairment. The cause, or causes, are not

Good old PubMed

- Especially its "Clinical Queries" service



What it does



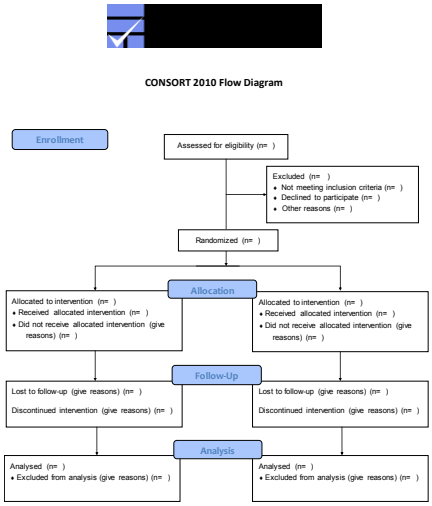
Some help as you evaluate the literature

Systematic reviews and meta-analyses

- Before beginning, they set forth rules for the search (including gray literature, unpublished, and non-English)
  - Define study inclusion/exclusion criteria
  - Define outcome of interest
  - Define measure of study quality
- Conduct the review and synthesize the findings
- If the data can be meaningfully merged in an effort to quantify an overall effect size, it becomes a meta-analysis

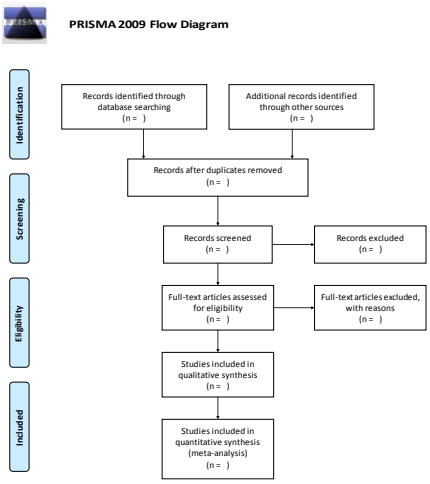
CONSORT: consort-statement.org

- Often required for publication
- Checklist and flow diagram for reporting clinical trials' design, analysis, and interpretation as well as subject enrollment



PRISMA: www.prisma-statement.org

- Same idea, but now meta-analyses and systematic reviews



Some ways to describe effect sizes

- If P% of exposed pts get a condition, and Q% of unexposed…
- Odds Ratio = P/(1-P) / Q/(1-Q)
  - If = 1, no difference
- Relative Risk = P/Q
  - If = 1, no difference
- Absolute Risk Reduction (Increase) = P-Q
- Relative Risk Reduction (Increase) = (P-Q)/Q
- Patient's Expected Event Rate (PEER) = Q
- Number Needed to Treat (Harm) = 1/(P-Q)

Intention-to-treat vs. Per-protocol

- ITT
  - Analysis is based on all enrolled subjects
  - Dropouts count as failures, etc
  - Gives a real-world view of effectiveness
- PP
  - Analysis is based on subjects who complete 100% of the trial
  - Dropouts not counted
  - Gives an ideal-world view of efficacy

But can we trust the literature?

The literature is imperfect

- Biases
  - Publication bias: positive results, large effect sizes, surprising results, etc
  - Selection bias
  - Performance bias
  - Detection bias: screening catches more
  - Attrition bias
  - Recall bias
  - Confirmation bias

A systematic review of flawed studies is…

- If the only literature available contains obvious and subtle bias, what are we to do?
- Just be thoughtful
- Do your own study, and get it published

Critical Responses

Not every doctor-scientist likes EBM as described

- All of science describes the same reality.
  - Claims that violate a large body of established knowledge should have an extraordinarily high threshold to acceptance
  - With EBM guidelines as stated, false claims can gain acceptance at rate p (statistical significance level).
- Unintended consequence of overemphasis on RCTs: calls to spend $ on more research of questionable value
  - Cochrane has only **one** review that declines to call for more research

Profoundly unlikely treatments

- Homeopathy
- Reiki
- Distance healing
- Crystals
- At $p \leq 0.05$, 5% of these studies will show they "work."
- For treatments like this, published RCTs tend to be equivocal… just as expected for ineffective treatments with publication bias.

The pioneers of EBM…

- Were doing a good thing.
- They relegated established scientific knowledge to the lowest level in EBM (…) to emphasize its insufficiency to determine safety and effectiveness.

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- Yes, scientific plausibility is insufficient. But it is **necessary**.

So how best to use EBM?

- Keep a scientific mindset
- Consider scientific plausibility as well as RCT results
- Get the best evidence available to inform your decisions, but be prepared to acknowledge that it may not be that great
- Don't forget to include your clinical judgment and the patient's particular situation
- Lack of RCTs does **not** automatically mean zero evidence