The advantages of CER: clinical, methodological, and political considerations

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Conflicts of interest

- Neither I nor any of my faculty accept any personal compensation of any kind from any drug or device manufacturer.
- Most of the research in my Division is funded by NIH / AHRQ / FDA.
- The Division occasionally accepts unrestricted research grants from industry to conduct specific drug-epi studies.

Subtitle of the talk:

"Pharmaco-epistemology and the politics of knowledge"

What is “pharmaco-epistemology”?!

- definition: ***How we know what we know*** about drug benefits, risks, side effects, and cost-effectiveness.

- How can drug ***knowledge*** have ***politics***?
  - What we study and what we learn about medications is shaped by economic, cultural, and political factors as well as purely scientific ones.

What doctors, payers, patients, and policymakers need to know about a drug

- Its benefits, safety, and value (cost-effectiveness) ***in relation to other reasonable prescribing choices for a given condition.***
- How well the drug actually works in ***typical populations*** (effectiveness), not just in randomized controlled trials (efficacy).

What the FDA approval process tells us

- How well a new product works when prescribed by **atypical doctors** treating a **small sample** of **volunteer patients** that **under-represents** several key populations in a **highly protocolized** trial design that is usually **brief**, may compare the new drug only to **placebo**, and may use a **surrogate measure** rather than actual clinical outcomes as its measure of efficacy.

Generating the additional knowledge we need

- Historical impotence of FDA's "mandated post-market commitment" requirements
  - FDAAA should help remedy this
- Failure of the marketplace assumption
  - decades of experience that this doesn't produce the data we need
- Re-discovery of the concept of Public Goods
  - things that benefit all, funded by society
  - like highways, fire departments, clean air, police, education, defense

“Poster child” examples of seminal CER studies

- ALLHAT
  - NHLBI-funded study of >30,000 patients with high blood pressure
  - found inexpensive thiazide-type drugs work as well as or better then more costly products
  - revolutionized how we treat hypertension
- Women’s Health Initiative
  - NIH-funded study of estrogens and heart disease
  - demonstrated that some of the most widely used drugs in US were harmful

We are now entering a new era of expanded CER research

- $1.1 billion in 2009 stimulus package
- promise of hundreds of millions more from Medicare on an ongoing basis
  - PCORI
- most stakeholders understand the need for this

Clinical and methodological issues

- Picking the right comparator(s)
  - may include drug vs. device vs. surgery
    - as well as “watchful waiting” for some conditions
- Studying ***typical*** care
  - in terms of patients, clinicians, settings
- Observational studies vs. randomized controlled trials
  - strengths, weaknesses of each
  - important methods issues in obsvl studies

    - See Avorn & Fischer, and Chokshi, Avorn, & Kesselheim, *Health Affairs, October 2010*

Politics vs. science in CER

The “death panel” disinformation strategy

- No real basis for this in any law or regulation
- Generating new knowledge never denied needed care to anyone.
- Most denial of services results from lack of access…
  - …which is largely caused by the unaffordability of care
  - …which is largely the result of inefficient use of available resources.

-- Avorn, NEJM 2009

The politics of individual differences

- Based on currently hot topics in therapeutics:
  - pharmacogenomics
    - (aka pharmacograndiomics?)
  - “personalized medicine”
  - individual differences in treatment response
  - racial, gender age disparities in drug effects

Putting this into perspective

- Yes, there are some important examples of genetic variation driving drug response.
  - e.g., Herceptin, some other oncology drugs
  - less responsiveness of blacks to ACE inhibitors
- These differences can be accommodated in rational, science-driven policies.
- This is ***not*** a major issue in the vast majority of clinical prescribing decisions.

Once comparative effectiveness studies are completed…

…there's still a lot of work to do to transform these findings into improved patient care decisions.

Implementation issues

- Must avoid CER-based policies that are ham-handed, clinically obtuse, or unethical:
  - motivation based on stinginess or profit rather than appropriate care
  - excessively rigid formularies
  - lack of respect for individual patient differences
  - contempt for physician's clinical acumen
  - manipulative and sadistic "prior authorization" requirements

Lost in translation?
Two more missing ingredients

- Effective ***communication*** of CER findings to practitioners and policymakers
  - it won't disseminate itself

- **Motivation** for clinicians and systems to take up these findings and use them to transform practice
  - to replace current incentives that are absent or perverse

"Academic detailing": one way to get CER into practice

- interactive, clinically relevant ***educational outreach***, based on social marketing and pharma approach
- Proof of concept in RCTs
  - Avorn & Soumerai, NEJM 1983; Avorn et al, NEJM 1992
  - evidence of cost-effectiveness
  - Cochrane Collaborative review of 69 RCTs in 2007
- Growth of programs
  - Europe, Australia, Canada
  - U.S. HMOs

Current status of academic detailing in U.S.

- The "Independent Drug Information Service" (iDiS):
  - impartial, evidence-based review of CER literature
  - production of user-friendly educational materials for MDs, patients
  - runs academic detailing programs in PA, DC, MA
  - trains educators for other programs, incl. VA
- Other state programs in NY, SC, VT, ME, etc.
- Pending federal programs

Education can take us pretty far… but not all the way

- Most physicians would rather prescribe wisely than poorly.

  …it's just that most of us don't have access to the information we need.

- Better communication alone can't combat the perverse incentives of fee-for-service medicine
  - *"It is difficult to get a man to understand something when his salary depends on his not understanding it."* -- Upton Sinclair

Conclusion

- Much of the care Americans receive is suboptimal and/or very overpriced.
- Methodologically rigorous CER can help us move toward improved quality and affordability.
- To do this, it will have to be effectively deployed throughout a health care system that is re-engineered to make proper use of it.

For more information….

"Powerful Medicines: the Benefits, Risks, and Costs of Prescription Drugs"

(Knopf, 2005):

www.PowerfulMedicines.org

The BWH Division of Pharmaco-epi and Pharmaco-eco ("DoPE"):

www. DrugEpi.org

Academic detailing program:

www. RxFacts.org