Academic detailing and the emerging crises of drug regulation, communication, and cost

Jerry Avorn, M.D.
Professor of Medicine, Harvard Medical School
Chief, Division of Pharmacoepidemiology and Pharmacoeconomics
Department of Medicine
Brigham and Women’s Hospital
Conflicts of interest

• Most of the research in my Division is funded by NIH, FDA, AHRQ, and PCORI.

• Neither I nor anyone in my division accepts personal compensation of any kind from any pharmaceutical manufacturers.

• Our unit also receives research support for drug safety studies from drug companies through unrestricted grants to the Brigham and Women’s Hospital.

• My external work on academic detailing is done through the non-profit Alosa Foundation; I receive no payment of any kind for it.
The times they are a-changin’

- ...for the worse, in some ways, for the healthcare system
- ...but creating greater need, demand, and opportunities for evidence-based, proactive educational outreach programs.
Loosening regulation

• of drug approval
• of drug promotion
“Who[m] do You Trust?”

“In my decades of practice as an internist, I have taken comfort that drugs on the market were there because their manufacturers had provided the FDA with at least some evidence that they worked and that their known risks were depicted in the product labeling. I did not need to review on my own all of the available evidence about efficacy and safety for each drug I prescribed. Even if I had the time and acumen to do so— and what busy practitioner has hundreds of hours to assess each new medication?—I knew that the FDA had additional thousands of details about these drugs I could never see, because they were the private property of the companies that had paid for the clinical trials.”

Avorn J. “In opposition to liberty: We need a ‘Sovereign’ to govern drug claims.” Ann Intern Med, 2015.
The growing pressure to approve drugs with lower standards (and faster)

- mis-identification of the problem
- The “21st Century Cures Act”
  - More surrogate outcomes, greater speed
  - Avorn, Sarpatwari, Kesselheim on 21st Century Cures Act, *NEJM* 2015
  - Darrow, Avorn, Kesselheim on new approval pathways, *NEJM* 2014
- Face validity of the appeal of many ‘reforms’
  - even a Congressperson can relate to this
  - arcane nature of the scientific details
- Power considerations, industry vs. FDA
- Likely outcome: more drugs approved with questionable clinical usefulness
- more need for academic detailing programs
Rx promotion = “commercial free speech”

• **Basic [bad] idea:** Corporations have the same rights as people, and their promotional statements are protected by the U.S. Constitution.
  – *Citizens United* decision, 2010
  – *Sorrell vs. IMS*, 2011
    • pharma marketing ‘speech’ is protected as a form of ‘expression’

• Libertarian rationale: “Big Government” shouldn’t restrict the freedom of prescribers, companies, patients to do as they please.

• **Caronia case:** Kesselheim, Mello, Avorn, *JAMA* 2013
Worrisome developments of 2014-2015

• Government chose not to appeal Caronia decision

• FDA draft guidances issued last year:
  – Loosening rules for off-label promotion
  – Loosening rules for depicting risk

• The triumph of commercial free speech arguments
  • Amarin fish oil case of May-Oct 2015
  • Injunction against FDA, and the ghost of Frances Kelsey
    • Avorn, Sarpotwari, Kesselheim, *NEJM* 2015: “Forbidden and permitted statements...”
Why this should trouble us

• Prescribing is already shaped by promotion more than by evidence-based medicine
  – BP, DM, lipids, etc., etc.
• Conventional CME is already skewed by industry funding, influence.
• Worrisome precedents of off-label marketing
  – antipsychotics in elderly, antidepressants in children, etc., etc.
• Likely consequence: more aggressive promotion for sketchy indications, now protected.
• → more need for academic detailing programs
Costs:
The return of the vampire
New drug affordability problems

• Blockbusters → generics → “Pharmageddon”
  – Nexium, Lipitor, Plavix, Prozac, Fosamax, etc.
    • now all are generic
• But now: hep C drugs, PCS-K9 inhibitors, oncology drugs
  • and recent slimy scandals (e.g., Daraprim’s 5,000% rise)
• ‘Bending the cost curve’ by shifting payments to patients
  – especially for drugs
  – growing numbers of patients can’t afford the meds we prescribe
  – → reduced adherence, worse clinical outcomes
The drug marketplace will become more chaotic

• It will be even harder for prescribers to choose among treatments of varying efficacy and safety
  
  – “The center cannot hold...the best lack all conviction, while the worst are full of passionate intensity.”
  
  -- W. B. Yeats, 1920

• Gresham’s Law (16\textsuperscript{th} Century English financier):
  
  – “Bad money drives out good money.”

• Avorn’s Third Law:
  
  – “Good information doesn’t disseminate itself.”

• What will this Hobbesian ‘State of Nature’ look like?
  
  – pre-1962 drug approvals & promotion
  
  – the supplements industry
Other developments relevant to AD

• Transformation of health care delivery systems to encompass all components of service more universally. More and more....
  – someone will be responsible for prescribing patterns
    • quality as well as cost
  – someone will be responsible for the quality of practice
  – someone will be responsible for clinical outcomes
• e.g., Medicare stars, HEDIS, penalties for readmission, other preventable bad outcomes
• We’re all looking more like Kaiser/NHS/Australia
How our approach is broadening

• Focus is on **optimal management** of a **clinical problem**
  – Dx, non-drug treatments, community resources
  – not just which drugs to use or avoid

• **Learning about the practitioner’s perspective and needs** informs the discussion content
  – baseline data on practice sure helps
  – prior focus group research is key in developing modules

• Emphasis on **behavioral change**, not just transfer of knowledge
Managing pain without overusing opioids
Implementing safe, effective, and less risky analgesic strategies
Restrained use of antipsychotic medications: Rational management of irrationality

These drugs are commonly prescribed in conditions for which there is little evidence of benefit, but considerable risk of harm.
**Costs vary widely, and can be significant**

**FIGURE 7. Average monthly price of commonly used medications for COPD**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol (Proventil HFA)</td>
<td>$58</td>
</tr>
<tr>
<td>Ivalbuterol (Xopenex HFA)</td>
<td>$53</td>
</tr>
<tr>
<td>Ipratropium (Atrovent HFA)</td>
<td>$43</td>
</tr>
<tr>
<td>Combination short-acting β-agonist/anticholinergic</td>
<td>$277</td>
</tr>
<tr>
<td>Albuterol/Ipratropium (Combivent Respimat)</td>
<td>$275</td>
</tr>
<tr>
<td>Albuterol/Ipratropium (generic vials for nebulizers)</td>
<td>$211</td>
</tr>
<tr>
<td>Formoterol (Foradil Aerolizer)</td>
<td>$288</td>
</tr>
<tr>
<td>Ipratropium (generic, vials for nebulizers)</td>
<td>$238</td>
</tr>
<tr>
<td>Salmeterol (Serevent Diskus)</td>
<td>$220</td>
</tr>
<tr>
<td>Afamiflortol (Bronva via)</td>
<td>$521</td>
</tr>
<tr>
<td>Ipratropium (generic, vials for nebulizers)</td>
<td>$223</td>
</tr>
<tr>
<td>Budesonide 180 mg (Pulmicort Flexhaler)</td>
<td>$291</td>
</tr>
<tr>
<td>Ipratropium (generic, vials for nebulizers)</td>
<td>$248</td>
</tr>
<tr>
<td>Budenoside 180 mg (Advair)</td>
<td>$236</td>
</tr>
<tr>
<td>Beclomethasone 90 mg (Qvar)</td>
<td>$129</td>
</tr>
<tr>
<td>Fluticasone 250 mg (Florn Diskus)</td>
<td>$223</td>
</tr>
<tr>
<td>Combination ICS/long-acting β-agonists</td>
<td>$192</td>
</tr>
<tr>
<td>Budenoside 180 mg/formoterol 4.5 mg (Symbicort)</td>
<td>$276</td>
</tr>
<tr>
<td>Roflumilast (Daliresp 0.5 mg tablet)</td>
<td>$227</td>
</tr>
</tbody>
</table>

*Prices from goodrx.com and ePharmacy. October 2013. Solutions for nebulizers are often significantly less expensive than the metered dose inhalers. See medicare.com/health-conditions/asthma-apnea/nebulizers.html

**References:**

Topics at [www.AlosaFoundation.org](http://www.AlosaFoundation.org)

- G.I. acid Sx
- anti-platelet drugs
- hypertension
- cholesterol
- diabetes
- depression
- osteoporosis
- HIV for the PCP

- COPD
- cognitive impairment
- incontinence
- gait impairment, falls
- sleep meds
- atrial fibrillation
- chronic pain/opioids
- anti-psychotics
What we need more of

• Continuing evolution of the health care system to create **organizations with accountability**
• Mandated **access** to prescribers to present clinical evidence on optimal prescribing
  – [and perhaps also to feed back their Rx’ing data]
  – presented in a way that is user-friendly and engaging
• Encouragement of prescribers to **make time** for this, and to pay attention
• **Motivation** for prescribers to improve practice
  – financial incentives?
• “The future cannot be predicted, but futures can be invented.”
  • Dennis Gabor, Nobel Laureate in Physics

• “When you get to a fork in the road, take it.”
  • Yogi Berra, recently deceased baseball hero
Some useful links

Research on medications from the BWH Division of Pharmaco-epi and Pharmaco-eco (“DoPE”):

www. DrugEpi.org

Academic detailing resources:

www. NaRCAD.org

www. AlosaFoundation.org

“Powerful Medicines: the Benefits, Risks, and Costs of Prescription Drugs” (Knopf):

www. PowerfulMedicines.org