Academic detailing to improve the appropriateness and contain the cost of prescribing

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The “telephone” problem

- Excellent basic and translational research
- Frequently irrelevant drug review
- Lack of head-to-head studies
- Inadequate post-marketing safety surveillance
- Distorted communication of data
- Flawed reimbursement policies
- Minimal prescriber accountability

- Irrational prescribing, resulting in:
  - suboptimal outcomes for patients
  - unaffordable costs
An informational vacuum

• In medical school
  – We do a poor job preparing students to manage drug information in the real world

• The house officer years
  – free lunches / infomercials
  – ‘product placements’ in teaching hospitals

• After training
  – few sources of non-commercial information
  – industry dominates CME / blurring of boundaries
  – no requirements for continuing pharmacologic competency

• Little comparative data is available to adequately weigh Rx alternatives
A bizarre marketplace

- Person choosing product isn’t the consumer
- Consumer can’t choose among products
- MDs don’t know what drugs cost
- We don’t know our patients’ drug coverage
- Some consumers are insulated against cost
- Data needed to ‘comparison shop’ don’t exist
- Manufacturer-dominated information flow
  - generic manufacturers lack both $$ and rationale
  - passivity of gov’t and most other payors
  - not a major goal for academia

>>>>>>>>>>>> market failure.
FDA lesions make things worse

• Anti-regulatory trends:
  – “Government is not the solution to our problem; government is the problem.”
    – President Ronald Reagan, 1st Inaugural Address
  – user fees have helped change FDA orientation
  – reliance on the marketplace to solve most social issues
  – the power of lobbying and $$ to shape policy
  – loosening of FDA limits on promotion
The rationale

- FDA has limited data when drugs are first approved
  - with limited relevance to many patients
- physician data overload
  - hundreds of important drug-related papers are published each month
- imbalanced communication
  - manufacturers provide much of the information
- the need for non-product-driven overviews
  - delivered in a relevant, user-friendly way
Limitations of pre-approval data

- The randomized controlled trial is the “gold standard” FDA uses for determining efficacy, BUT...
- how do the label and the ads relate to the patients seen in routine practice?
The trials that FDA evaluates…

• are funded and conducted by the drug’s manufacturer
• are generally designed to speed approval
• may last a short time, even for a drug to be taken for a lifetime
• often compare a new drug to a placebo
• are assessed by FDA reviewers whose salaries come from industry “user fees”
Drug approvals are based on:

- volunteer patients, usually healthier
- under-representation of important groups
  - especially the elderly
- small samples
- selected clinicians, settings
- protocolized care: compliance, monitoring
- short duration
- surrogate endpoints
- compared to what?
as a result……

- This usually doesn’t provide head-to-head comparative data about relevant prescribing choices.
  - example: hypertension Rx; ALLHAT
- A drug that achieved a surrogate outcome may not produce the expected clinical benefit.
  - example: Avandia (rosiglitazone) and M.I.
- Unanticipated adverse effects are likely.
  - example: Vioxx (rofecoxib)
- Use differs in actual practice vs. trials
  - by doctors
  - by patients
There is no requirement that a new drug be tested against the standard of care.

- The law states that a drug must be judged “effective” if it works better than placebo.
- FDA has no budget to conduct its own trials.
  - It must depend on studies conducted by the company that makes the drug.
  - NIH generally does not fund such studies either.
FDA faces major challenges

- severely understaffed
- has had no systematic way to follow up on problems once a drug is marketed
- may require years to get important new risk information into label and ads
- has had little clout to force manufacturers to follow up on adverse effect signals

Source: Institute of Medicine, 2006; Government Accountability Office, 2006; FDA Science Board, 2007
Drinking from a fire hose

• To stay abreast of all important new drug developments, a primary care doctor would have to regularly scan dozens of journals.

• Systematic overviews (Cochrane, DERP) cover selected fields, but…
  – are lengthy and hard to wade through
  – may not be recently updated

• Some important findings are not in journals
  – FDA alerts, ‘Dear Doctor’ letters
  – important trial data presented at clinical meetings
Limitations of promotional materials

• Industry-generated marketing messages are a dominant source of drug information.
  – often the only available source for new products
• Their main purpose is to increase sales.
• Industry sales reps can be a problematic source of drug education
  – most have little or no real scientific training
  – most are on commission
  – messages often skewed to favor the product they’re selling
Does promotion work? Yes!

• There is clear evidence that sales reps and samples change prescribing
  – otherwise industry wouldn’t spend >$30 billion per year doing it

• A large social science literature shows the persuasive effects of relationships, gifts
  – the symbolic power of even small presents

• Marketing promotes only the costliest products
Yeats said it well

“The center cannot hold; 
The best lack all conviction, 
while the worst 
are full of passionate intensity.”

— The Second Coming, 1920
Modeling evidence-based practice

• DOPE database of ~250,000 anonymized patients with data on all filled Rxs and all Dxs and medical encounters
• Identified all treated hypertensives
• Developed algorithm to ‘replace’ all meds with guideline-driven Rx, based on Dxs
• Estimated savings projected nationally: $1.2 billion

– Ref: Fischer MA, Avorn J, JAMA 2004
What we need: evidence-based, non-product-driven research and communication about drugs

This is a public good, not a marketplace solution
The goal of academic detailing

to close the gap
between the best available science
and actual prescribing practice,
so that each prescription is based
only on the most current and accurate
evidence about efficacy, safety,
and cost-effectiveness.
The logic of academic detailing

• Med school faculty have a solid grasp of the evidence about drug benefits and risks – *but we’re often terrible communicators.*

• Drug makers are superb communicators – *but do so only to increase product sales.*

• Can the **content** of the former be communicated to prescribers through a ‘**delivery system**’ based on the latter?
Two different worlds

• **Academia:**
  - MD comes to us
  - Didactic
  - Content ornate, not clinically relevant
  - Visually boring
  - No idea of MD’s perspective
  - Evaluation: minimal
  - Goal: ????

• **Drug industry:**
  - Go to MD
  - Interactive
  - Content is simple, straightforward, relevant
  - Excellent graphics
  - MD-specific data informs discussion
  - Outcome evaluated, drives salary
  - Goal: behavior change
The content of academic detailing

- Well trained clinicians (pharm, RN, MD) visit prescribers in their offices and offer a service that provides non-commercial, non-product-driven, evidence-based information about the comparative benefit, risk, and cost-effectiveness of drugs used for common clinical problems.
The method of academic detailing

• Information is provided **interactively**
  – generally in the doctor’s **own office**
• This enables the educator to
  – **understand** where the MD is coming from in terms of knowledge, attitudes, behavior
  – **modify** the presentation appropriately
  – keep the prescriber **engaged**
• The visit ends with specific practice-change recommendations.
• Over time, the relationship becomes more trusted and useful.
What academic detailing **is not**

- memos or brochures provided through the mail
- lectures delivered in the doctor’s office
- about formulary compliance
- about cost reduction primarily
The first academic detailing “un-ads”

- As used in the original New England Journal of Medicine randomized controlled trial
  - Avorn & Soumerai, NEJM, 1983
- The reverse side of each page contained concise clinical background and specific prescribing recommendations
  - with references

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Skeptical about “Vasodilator” therapy for Senile Dementia?

You have every reason to be.

Years ago, when neurologists believed that “sluggish” cerebral blood flow was the cause of senility, a number of drugs were marketed to dilate cerebral vessels and thus improve mental functioning. But more recent clinical evidence tells a very different story.

For the vast majority of senile patients, degeneration of neurons is the cause of their symptoms, not sluggish blood flow to the brain.¹,²

“Cerebral vasodilator” drugs do not reliably improve mental functioning or behavior in the elderly.³,⁴,⁶
Mrs. R is doing fine…

without vasodilators

Intermittent claudication is a familiar clinical problem facing physicians with large geriatric caseloads. "Peripheral vasodilators" nylidrin (Aridin), cycloedulat (Cyclospasmol), papaverine (Pavabid, Cerespan, etc.), isosuprime (Vasodilan) and others have long been promoted for use in the management of this condition. However, recent clinical evidence indicates that vasodilators are not effective in the treatment of intermittent claudication,¹ while regular exercise has been shown to improve symptoms somewhat.²,³
"Twenty-five dollars?"

Yes, that's what a course of cephalexin (Keflex) can cost—... a troublesome "side effect" for many patients.

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Patient education materials

• In focus groups, many physicians said they would be more willing to change their prescribing if they had an easier way of explaining to the patients why the change was necessary.

• So we created what might be the first “direct-to-consumer unadvertisements”
Common Sense About The Common Cold

With all the success that antibiotics like pencillin and other "wonder drugs" have had since World War II, it is natural for patients to want such a powerful "cure" to treat the annoying symptoms of the common cold. However, antibiotics, like other strong medications, can cause problems if they are used when not absolutely necessary. This brochure answers some common questions about colds and their treatment.
Why Your Doctor Recommended “Plain Aspirin”

Although it may be hard to believe, aspirin is one of the strongest and most reliable pain relievers yet discovered. In fact, for most cases of mild or moderate pain, science has yet to come up with a more powerful treatment than aspirin, short of narcotics. This brochure answers some common questions about aspirin’s pain-relieving abilities.
Initial results of the first study

• 92% MD acceptance rate from ‘cold calls’ to physicians

• Significant 14% reduction in inappropriate prescribing
  – Avorn & Soumerai, NEJM 1983

• Benefit-cost analysis based on actual expenditures: saved $2 for every dollar spent
  – Soumerai & Avorn, Medical Care 1987
Next target: nursing homes

• # of patients greater than in acute hospitals
• sickest pts, most meds, low MD/RN staffing
• a different social & clinical context
• heavy use of psychoactive drugs
• no data on baseline patterns of med use!
  – so we studied it
    • Beers et al, JAMA 1988
    • helped lead to better federal regulations
YOUR GENTLE TOUCH may be all she needs at bedtime

For many nursing home residents, bedtime is a lonely time. A moment or two with the nurse or aide can be reassuring, even if a sleeping pill is not given. Personal contact and a simple program of sleep-promoting routines (see other side) may help bring on rest without the risk of drug “hangover” or other adverse effects.
In the elderly, the side-effects of sedatives are all over the map.

**THE SIDE-EFFECTS** of tranquilizers can be much more frequent and severe in the elderly. Consider non-drug alternatives first. If drugs must be used, the shortest course is usually the safest course. Choose a medication with a brief half-life, and give it for only a few days or weeks to minimize adverse effects.
Outcomes of nursing home study

• significant reduction in use of targeted drugs
  – with no change in use of more acceptable drugs
• significant improvement in memory in pts taking antipsychotic drugs
• no increase in staff distress
  – all ‘un-ads’ are at www.PowerfulMedicines.org
Where we are now

• Academic detailing programs operating in Canada, Europe, Australia, developing world
  – public payment for drugs a spur to public action
  – programs funded by government, but controlled by profession
• HMO uptake in U.S.
  – rising drug costs drive payors to action
• State-funded programs in PA, MA, NY, SC, DC, New England
• 2008: Sen. Kohl introduces bill to create a federally funded national academic detailing program
Status of the evidence

• A cottage industry of literature has developed in last 25 years
• Cochrane Collaborative exhaustive review in 2007 confirmed efficacy
• Effectiveness varies with quality of execution
  – like brain surgery
  – it’s not a pill
The Pennsylvania program

• State pays > $3 billion / year in publicly funded drug benefits
  – constrained budgets, public health mission
  – motivation to improve prescribing
• The non-profit “Independent Drug Information Service” began visiting doctors in October ‘05
  – Wall Street Journal, March 2006
  – N.Y. Times, September 2006
• www.RxFacts.org
Balanced data about medications
Clinical topics

- coxibs/NSAIDs
- G.I. acid Sx (PPIs, H₂ blockers)
- anti-platelet drugs (clopidogrel, aspirin)
- hypertension
- cholesterol
- diabetes
- depression

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Materials

• materials prepared by Harvard Medical School clinical faculty members
• evidence documents  
  – review and assess all recent literature
• “un-advertisements”
• patient scenarios
• physician reference cards
• patient education materials  
  – help facilitate behavior change
• All materials available at www.RxFacts.org
Life after Vioxx...

The unexpected withdrawal of Vioxx in September 2004, followed by Bextra in April 2005, has led many physicians to reassess the place of selective cox-2 inhibitors in pain management. These concerns were heightened last spring when the FDA applied the same “black box warning” to all NSAIDs as well, cautioning that they each can increase the risk of cardiovascular events. What is really known about the comparative efficacy and safety of these drugs?
A patient’s guide to heartburn prevention and treatment

Over 60 million Americans experience heartburn—a burning pain in the middle of the chest that may move up to the neck. Some people have the feeling that food is “coming back up,” producing an acid or bitter taste. Heartburn is painful and unpleasant, but there are steps you can take to reduce or get rid of it.

Balanced data about medications
Patient name:

Three steps to end dependence on your acid-lowering drug ("PPI"):

- Aciphex (rabeprazole)
- Nexium (esomeprazole)
- Prilosec (omeprazole)
- Protonix (pantoprazole)
- Prevacid (lansoprazole)

1. For the first 2 weeks: ______ to ______
   Reduce your dose by half.
   - If you were taking one pill a day, take one pill every other day.
   - If you were taking two pills a day:
     - Take one pill a day for a week.
     - and then take one pill every other day for the following week.

2. For the next 2 weeks: ______ to ______
   Stop the PPI.
   If you have abdominal symptoms:
   - For immediate relief, take an antacid such as Maalox, Mylanta, Tums or a generic.
   - You can also take an over-the-counter H₂ blocker such as ranitidine (Zantac), famotidine (Pepcid), or cimetidine (Tagamet).

3. Over the next 2 weeks: ______ to ______
   Slowly decrease the dose of H₂ blocker or antacid to the lowest amounts needed to control your symptoms.

Contact your doctor if symptoms persist.

Physician signature:

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### Typical adult doses for common non-opioid analgesics

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Dose for pain</th>
<th>Dose for osteoarthritis (OA)</th>
<th>Maximum doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>naproxen</strong></td>
<td>220 mg p.o. q6-12h p.r.n.</td>
<td>220 mg p.o. b.i.d.</td>
<td>1000 mg/day (pain and OA)</td>
</tr>
<tr>
<td>(Naprosyn, Aleve,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaprox, Naprelan,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and generics)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ibuprofen</strong></td>
<td>200-400 mg p.o. q4-6h p.r.n.</td>
<td>300-800 mg p.o. t.i.d-q.i.d. (1200-3200 mg/day)</td>
<td>1200 mg/day (pain); 3200 mg/day (OA)</td>
</tr>
<tr>
<td>(Motrin, Advil,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuprin, Rufen, and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>generics)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>diclofenac</strong></td>
<td>50 mg p.o. b.i.d.-t.i.d. p.r.n.</td>
<td>50 mg p.o. b.i.d.-t.i.d. (delayed-release diclofenac is also available)</td>
<td>200 mg/day</td>
</tr>
<tr>
<td>(Catapres, Voltaren, and generics)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>acetaminophen</strong></td>
<td>650-1000 mg p.o. q4-6h p.r.n.</td>
<td>extended-release, 650-1300 mg p.o. q8h</td>
<td>4 g/day; 3 g/day for patients &gt;65 or with other co-morbidities</td>
</tr>
<tr>
<td>(Tylenol, Panadol,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tempra, and</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>generics)</td>
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<td></td>
</tr>
</tbody>
</table>

Note: These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition. December 2005
Physician reaction
<table>
<thead>
<tr>
<th>Survey item</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The program provides me with useful information about commonly used medications.</td>
<td>4.6±.5</td>
</tr>
<tr>
<td>2. The content represents unbiased and balanced information about drugs.</td>
<td>4.6±.6</td>
</tr>
<tr>
<td>3. The program provides a perspective on prescribing that is different from what I get from other sources.</td>
<td>4.4±.7</td>
</tr>
<tr>
<td>4. I find the patient materials useful in my practice.</td>
<td>4.3±.8</td>
</tr>
<tr>
<td>5. It makes sense for the Commonwealth of Pennsylvania to devote resources to this activity.</td>
<td>4.4±.7</td>
</tr>
<tr>
<td>6. My Drug Information Consultant is a well-informed source of evidence-based information about drugs I prescribe.</td>
<td>4.6±.6</td>
</tr>
<tr>
<td>7. Being able to get Continuing Medical Education credits from Harvard is a valuable component of the program.</td>
<td>4.1±1.2</td>
</tr>
<tr>
<td>8. I would like to see this program continue.</td>
<td>4.6±.6</td>
</tr>
</tbody>
</table>
Calculation of savings (PPI module)

• Design: We tracked prescribing by MDs offered the program, and compared it to prescribing by comparable MDs in other regions of PA
• “index date” = date of first visit, or frequency-matched date for controls
• interrupted time-series analysis
• used paid claims data from PACE program
### Prescribing stratum

<table>
<thead>
<tr>
<th>Prescribing stratum</th>
<th>Number of MDs</th>
<th>6-month PPI saving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low (≤ 19 PPI scripts in past year)</td>
<td>60</td>
<td>$23,436</td>
</tr>
<tr>
<td>Low (20 - 40 scripts)</td>
<td>68</td>
<td>$53,285</td>
</tr>
<tr>
<td>Medium (41 - 75 scripts)</td>
<td>71</td>
<td>$69,197</td>
</tr>
<tr>
<td>High (76+ scripts)</td>
<td>92</td>
<td>$139,983</td>
</tr>
<tr>
<td>6-mo total, weighted by MD distribution</td>
<td></td>
<td>$285,901</td>
</tr>
</tbody>
</table>
Implications of stratification

- Program is most cost-effective if targeted at high-volume prescribers
- They are easy to identify from paid claims data
- Economies of scale are possible if other payors can help defray costs
  - “free rider” issue
Summary of savings from PPI module

• $286,000 less PPI use in PACE by intervention physicians vs. comparable MDs
  – in 6 months following 1st visit
• $572,000 if changes persisted for a year
• Considers only savings to PACE program
  – does not include savings to Medicaid, state employees, other insurers
“How can we possibly afford this?!”

- The U.S. already spends more per capita on drugs than any other nation.
- Much of that is wasted.
- Government (federal, state, VA) is footing a big part of the bill.
  - e.g., Medicaid spent $1 billion a year on Vioxx
  - similar argument for Avandia, Zyprexa, etc.
- Providing evidence-based drug information probably saves more than it costs.
Drivers of change

- Growing awareness of need to use medications appropriately
- Escalating drug costs
- Heightened concern over side effects
- Rising skepticism by MDs, patients
- Greater sophistication in data accessibility, informatics
What lies ahead

“The lion and the lamb shall lie down together, but the lamb won’t get much sleep.”

-- Woody Allen
For much more information:

J. Avorn, “Powerful Medicines: the Benefits, Risks, and Costs of Prescription Drugs”

(Knopf 2004, Vintage 2005)

www.PowerfulMedicines.org
www.RxFacts.org
www.DrugEpi.org