Division of
Pharmacoepidemiology & Pharmacoeconomics
Department of Medicine, Brigham & Women's Hospital, Harvard Medical School

Communicating CER Findings: The Role of Academic Detailing

Aaron Kesselheim, M.D., J.D., M.P.H.
Assistant Professor of Medicine, Harvard Medical School

February 9, 2012

Background information

- I am a full-time faculty member in the Division of Pharmacoepidemiology, within the Department of Medicine at Brigham and Women's Hospital and Harvard Medical School
- Other faculty in Division contribute to Independent Drug Information Service
  - I am not involved in the management of the program; provide occasional content, paid de minimis amount
  - Program is run by a non-profit organization
  - Jerry Avorn (head of program) does not receive compensation for his work

Agenda

- Review of academic detailing
- Comparison with industry-based promotion
- Goal: evaluate reasons for regulators viewing the two modes of communication differently

What is academic detailing?

- Provision of education by well-trained clinicians (pharm, RN, MD)
- Offer a **service**
- **Non-commercial, non-product-driven, evidence-based** information
- Treatment of common clinical problems
- **Comparative** benefit, risk, and cost-effectiveness of drugs, devices
- **Supported by** a public health agency or a non-profit health care system like Kaiser that is interested in improving clinical outcomes

Goal of academic detailing

- **To close the gap between:**
  - the best available evidence
  - actual clinical practice

- **…so that clinical decisions are based only on the most current and accurate evidence on:**
  - Efficacy
  - Safety
  - Cost-effectiveness

Rationale for academic detailing

- **FDA has limited data when treatments or tests are first approved**
  - with limited relevance to many patients
  - based on surrogate outcomes, often compared to placebo (e.g., Avandia)
- **Physician data overload**
  - hundreds of important clinical papers published each month
- **Imbalanced communication**
  - manufacturers provide much of the information as part of marketing programs
- **Need for non-product-driven overviews**
  - delivered in a relevant, user-friendly way

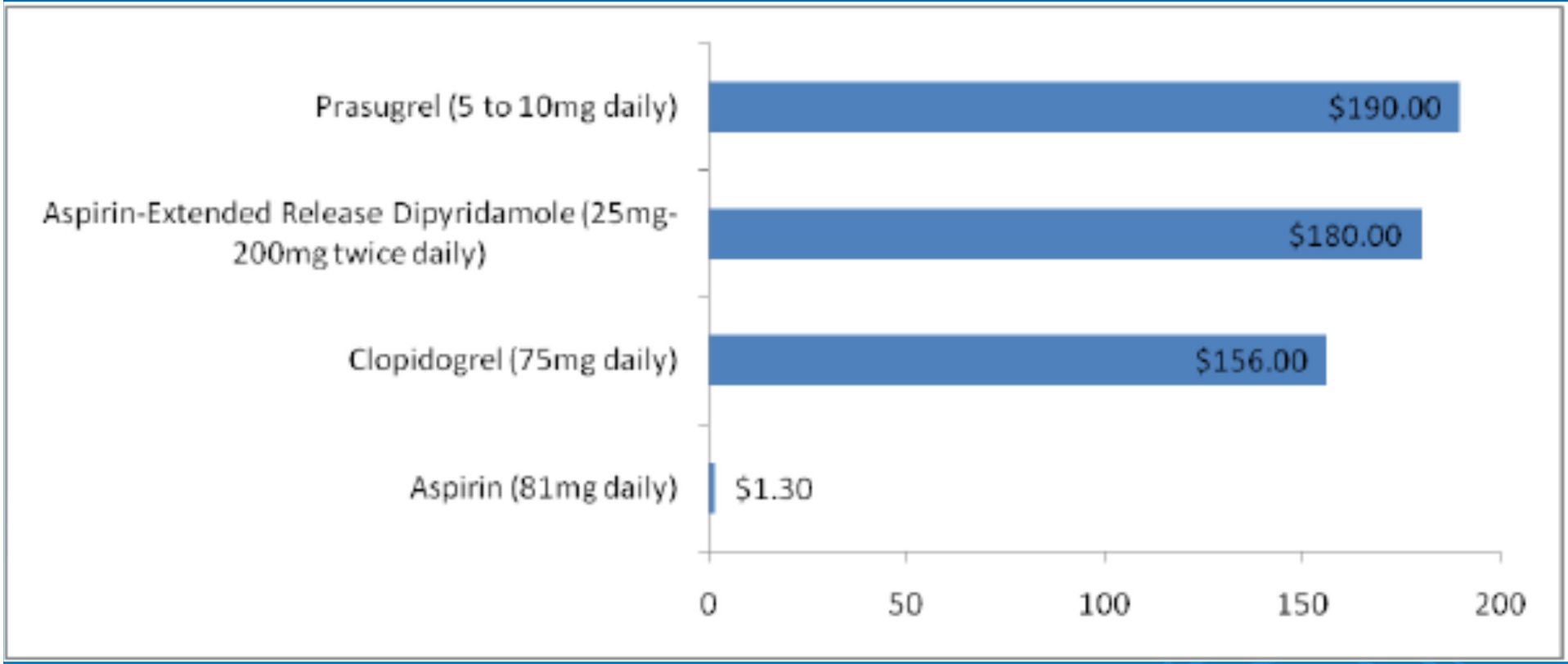
What academic detailing is NOT

- Memos or brochures provided through the mail
- Lectures delivered in the doctor's office
- About formulary compliance
- About cost reduction primarily
- About drugs only

Academic detailing: Example #1

Trial Name	Who was enrolled?	What was studied and for how long?	What was the primary outcome?	What were the main results?					
				Prevention of vascular events			Risk of major bleeding		
				Aspirin alone	Clopidogrel plus aspirin	Absolute difference	Aspirin alone	Clopidogrel plus aspirin	Absolute difference
CURE (NEJM 2001)	NSTEMI/UA (n=12,562)	clopidogrel + aspirin v. aspirin alone (for 3-12 months)	Death from cardiovascular causes, non-fatal MI, non-fatal stroke	11.4%	9.3%	2.1%	2.7%	3.7%	1%
CLARITY-TIMI 28 (NEJM 2005)	STEMI (n=3,491)	clopidogrel + aspirin v. aspirin alone (until angiography, day 8 or hospital discharge)	Occluded infarct-related artery on angiography, death, or recurrent MI	21%	15%	6%	1.3%	1.1%	not significant
COMMIT (Lancet 2005)	STEMI (n=45,852)	clopidogrel + aspirin v. aspirin alone (until discharge or up to 4 weeks in hospital)	Death, re-infarction or stroke	10.1%	9.2%	0.9%	0.58%	0.55%	not significant

Antiplatelet drug costs (average monthly price)



Antiplatelet drug recommendations

BOTTOM LINE: Several antiplatelet regimens have demonstrated efficacy in reducing cardiovascular events in patients with acute coronary syndromes. More potent regimens are more effective at preventing recurrent events but are also more likely to cause bleeding. Dual therapy with clopidogrel and aspirin for at least one year is the currently recommended treatment for all ACS patients. For many ACS patients who have undergone PCI, a recent trial suggests that prasugrel and aspirin for 15 months is likely the appropriate choice. However, the benefit-risk relationship did not demonstrate an advantage in patients with low body weight, age ≥ 75 years, or who have a history of stroke or transient ischemic attack.

http://www.rxfacts.org/pdf/Antiplatelet%20evidence%20document%20FINAL%20120109%20(1).pdf

Academic detailing: Example #2

- "Preventing falls and enhancing mobility in the community-dwelling elderly" (Dec 2008)
  - Screening for falls risk
  - Multifactorial assessment
  - Specific interventions
    - Patient and caregiver involvement and education
    - Strength and balance training
    - Mobility and gait improvement
    - Home hazard assessment and modification
    - Treat orthostatic hypotension
    - Reduce fear of falling

http://www.rxfacts.org/pdf/Falls%20and%20mobility ev%20doc 2009.02.18.pdf

Flexible uses of academic detailing

- Improve knowledge
  - New guidelines
  - Health threats
- Change in treatment
  - More effective/cost effective or safer
  - Decrease misuse and overuse
- Improve patient education
  - Use of materials
  - Communication of vital information
- Increase diagnosis/screening
  - What to look for
  - What to do when found
- Increase utilization of complementary resources
  - Public health programs
  - Referral resources

Some positive aspects of industry-funded promotion

- In-depth knowledge of particular drug, including reports about recent trials, nuances of label
- Superb communicators
- Substantial resources to commit to dissemination of information

Regulation of industry-funded promotion

- Not allowed to be deceptive/fraudulent, lacking in fair balance, or otherwise misleading (21 CFR 201.2), defined as:
  - Contains favorable information from a study that is not designed to make such conclusions
  - Uses statistical analyses and techniques on a retrospective basis to discover and cite findings not soundly supported by the study
  - Fails to provide sufficient emphasis for information relating to side effects
- Must relate to approved uses
  - Exceptions: Can respond when receive unsolicited request, can engage in “bona fide” scientific dialogue, can proactively distribute peer-reviewed journal articles

Why regulate industry promotion?

- Promotional statements strongly drive prescribing behavior
  - Use of targeted prescriptions increases after sales rep visits
  - Increase in requests by physicians to add drugs to their hospital formularies
  - Strong, consistent, specific, and independent association between physician prescribing and exposure to drug reps
- … But in ways that may not match evidence-based practice guidelines or the medical literature

See, e.g., Avorn et al. AJM 1982; Lurie et al JGIM 1990; Wazana JAMA 2000; Manchanda & Honka YJHPLE 2005; etc.

Why regulate industry promotion? (cont'd)

- Numerous examples of companies promoting their products by touting benefits that don't exist or inappropriately downplaying side effects
  - Vioxx: Divert attention away from cardiac risks ("Dodgeball")
  - Antipsychotics in children/elderly: Widespread promotion despite lack of efficacy and known risks of harm
  - Antibiotics: Approved for one type of infection, promoted for many more where no evidence of efficacy, don't mention risk of antibiotic resistance
  - Antiepileptics: Promotion of gabapentin for numerous conditions for which it was conclusively shown not to work, contributing to billions in annual sales for drug approved as add-on

See, e.g., Steinman et al. AIM 2006; Spielmans SSM 2009; Krumholz et al BMJ 2007; Kesselheim et al. PLoS Med 2011; etc.

Off-label marketing settlements (2004-2010)

Year	Company	Civil settlement	Criminal fines
2004	Warner Lambert	$189 million	$240 million
2005	Serono	$567	$137
2006	InterMune	$37	
2007	Bristol Myers Squibb	$515	
2007	Cell Therapeutics	$11	
2007	Orphan Medical	$21	$5
2007	Medicis	$10	
2008	Cephalon	$375	$50
2009	Eli Lilly	$800	$515
2009	Pfizer	$1,000	$1,300
2010	AstraZeneca	$520	
2010	Ortho McNeil, Ortho McNeil Janssen	$73	$6.1
2010	Novartis	$72.5	
2010	Forest Labs	$149	$164
2010	Allergan	$225	$375
2010	Novartis	$238	$185
2010	Kos	$38	$3.7
2010	Elan/Eisei	$103	$101
TOTAL		**$4,943,000,000**	**$3,080,000,000**

Kesselheim Amer J Law Med 2011

Rationales for limits on off-label promotion

- Real risk that industry bury physicians in avalanche of unbalanced and potentially inaccurate information about the product being sold
- Encourage manufacturers aware of effective off-label use to submit evidence to FDA for expert, neutral review
- Potential for patient harm from ineffective or dangerous treatments
- Increases to health care costs at time when can't afford to do that, without evidence of patient benefits
- Other solutions, such as disclaimers, are unlikely to work

Summary: two different worlds

	Academic Detailing	Industry Promotion
Communication agent	Professional/peer	Sales agent
Developer of information	Academic content expert	Company who makes drug
Role of funding source	State, or private payors, interested in promoting effective & cost-effective care; do not control content	Salary of sales agents directly related to increased sales of product
Perspective	Global	Product-focused
Goal	Education	Sell product

Conclusions

- 1. Increased funding for CER will lead to huge growth in data and knowledge about different uses of drugs, devices, etc.
  - Will be important to disseminate accurate info widely
- 2. Who does the communicating matters
  - Academic detailers and industry sales representatives have different training, perspective, goals
- 3. Restrictions on industry communication to physicians are rational and supported by substantial evidence emerging from prior behavior
  - Same concerns do not apply to education materials supplied by academic detailers

Conclusions, Part 2

- 4. Some falsely claim that the government or health systems that support academic detailing use it to push cheap drugs even when not appropriate, but there's no evidence that this has ever occurred or is occurring
  - If some unscrupulous insurance company sought to do that, it would be a problem to deal with on a case-by-case basis

Learn more about academic detailing

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

Aaron Kesselheim
akesselheim@partners.org

Thank you!