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Show Me the Evidence: The Ethical Aspects of Pharmaceutical Marketing, Evidence-Based Medicine, and Rational Prescribing

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ABSTRACT

Pharmaceutical industry research and marketing methods and relationships with prescribing providers pose numerous ethical challenges. The authors review the impact pharmaceutical treatments and their costs play in the overall health care system. Several problematic prescribing practices are described along with a discussion of how the pharmaceutical industry has contributed to these practices. The Food and Drug Administration and the legislation that guides it bear much responsibility for how the pharmaceutical industry performs, but is significantly impaired in its ability to sufficiently monitor and regulate some pharmaceutical industry practices.

Although the pharmaceutical industry has made major contributions to the improvement of health through the introduction of newer and better therapeutic agents and through its support of physician education and patient access to some medications, it is nonetheless driven in part by its profit motivation, which may undermine some of its more noble goals. In particular the marketing methods utilized by the industry, including the use of pharmaceutical sales representatives, direct-to-consumer advertising, biased or misleading professional journal advertisements, and biased professional educational events, make it very difficult for prescribing providers to make rational and effective treatment decisions.

The authors review how conflicts of interest can be avoided and how evidence-based decision-making may be accomplished. Many useful and less biased resources on drugs and evidence-based prescribing are provided.

Key Words:

drug industry, marketing, ethics, evidence-based medicine

Introduction:

Several recent newspaper exposés have revealed previously unreported financial relationships between prominent physician researchers and various pharmaceutical companies. Such stories raise serious questions about the objectivity of such research and whether improved effectiveness and safety of pharmaceutical agents is as important as commercial profit to the pharmaceutical industry or the direct financial benefits researchers may derive from their scientific activities.[1, 2]

This paper is an attempt to sort out some of the knottier issues involving the relationship between health care providers and the pharmaceutical industry. We intend to identify and increase awareness of bias in pharmaceutical industry marketing practices. We describe methods for reducing that bias or, at least, to reduce the impact or influence of such bias. This involves encouraging practitioners to increase their understanding and use of evidence-based resources and helping them adopt strategies for managing their relationships with pharmaceutical representatives and interpreting the information the companies provide.

Health Care in the US is Expensive:

Although it is not the main thrust of this paper, it is nonetheless essential to acknowledge that the US spends enormous amounts of

money on health care and gets mixed results of questionable value for that investment. Health care costs have risen consistently at a much faster rate than the overall economy with a negative impact on affordability, access, and quality of care.[3] The US spends more than any other country on health care, but lags behind dozens of European and Asian countries in key population health indicators, such as life expectancy and childhood mortality.[4, 5] Annual family health insurance premium expenses in the US are projected to exceed average family household income within 15-20 years.[6]

Pharmaceutical Costs Drive Health Costs:

Pharmaceutical costs have historically been among the fastest growing components of the US health care system, and are a major contributor to insurance premium increases.[7] These pharmaceutical cost increases are due to multiple factors, but primarily to increased prescribing (more prescriptions per patient and more patients receiving medications) and increased cost per prescription (greater average prescription price).

Increased prescription drug utilization is driven by both demand and supply side forces. Pharmaceutical coverage in insurance benefit packages has increased, most notably with the passage and implementation of Medicare Part D, even though many of these policies have increased out-of-pocket share costs. With an aging population having higher rates of chronic illness and co-morbidity, more people live longer with more chronic health problems necessitating drug therapy. In addition, prescribing providers are more likely to turn to medications as the choice for treatment for more illnesses in all age groups. Some of these trends are appropriate and reflect the progress that scientific research has made in improving the quality of care.

However, the pharmaceutical industry has actively induced demand, sometimes in excess of what is necessary or appropriate, for their products through marketing to clinicians and directly to the public. At the same time, drug price increases have been significantly greater than the inflation rate and appear to have a greater impact on the overall increase in pharmaceutical spending.[8] Providers tend to prescribe newer (and more expensive) drugs in more circumstances. Many of these drugs compete with drugs that are as effective as their newer cousins. Marketing pressure may be part of the influence for earlier adoption of these drugs, as well as pressure for the Food and Drug Administration (FDA) to approve drugs earlier in the research and development process.

These trends imply further erosion of health care affordability, resulting in increased premiums, deductibles, and co-pays; deeper state and federal health budget deficits; and increasing numbers of uninsured and underinsured individuals and families. As public and private payers seek ways to lower costs and to obtain better value, pressure is building for major reforms in the US health care system. In addition to the overwhelming societal and political responsibility to create a more rational system that provides universal coverage, there are opportunities for providers to learn more about how they can contribute to improving quality and value in relation to prescribing practices and modifying their relationships with the pharmaceutical industry.

Problematic Prescribing Practices:

Three specific practice-related activities that require more attention are:

- Polypharmacy
- Off-label prescribing
- Over-medicalization and premature initiation of drug treatments.

Some practitioners have developed practice patterns that reflect these activities to a greater extent than others. Unfortunately, in addition to the genuine desire to bring more immediate relief to suffering patients, the activities of the pharmaceutical industry have contributed greatly to such behaviors.

Polypharmacy and off-label prescribing are much studied and reported concerns, so they will only be mentioned in passing. Polypharmacy is the use of two or more drugs from the same therapeutic class or multiple drugs from several classes to treat a particular condition when there is limited or no evidence that such multiple drug regimens are effective. Polypharmacy can actually undermine the benefits of certain treatments, can lead to unnecessary side effects or drug-drug interactions, and certainly is associated with increased pharmaceutical costs.[9]

Off-label prescribing is the practice of providing medications for conditions for which they were not approved by the FDA. In some cases, off-label uses are well-established and have some scientific evidence to support them, but in many cases they are the result of speculation, anecdotal experience, or misinformation.[10] Off-label prescribing, sometimes encouraged in indirect ways by drug company representatives and, because such marketing practices are illegal, has resulted in major litigation. One such case involved the mismarketing of Neurontin (gabapentin) as a treatment for bipolar disorder, and off-label pain conditions which led to the funding of this paper and associated educational activities through grants made possible by some of the proceeds from the settlement of the case.[11-12] More recently, Eli Lilly agreed to pay over $1.4 billion in penalties and payments to government agencies for off-label promotion of its antipsychotic drug, Zyprexa and Pfizer agreed to pay $2.3 billion for similar off-label promotions for a number of its products. [13-14]

Over-medicalization can sometimes be due to disease mongering, which is the promotion of sickness that widens the boundaries of illness and expands the markets for those who sell and deliver treatments. It is exemplified most explicitly by many pharmaceutical industry–funded disease-awareness campaigns—more often designed to sell drugs than to illuminate, inform or educate about the prevention of illness or the maintenance of health. Some examples of disease mongering include aspects of ordinary life, such as menopause, being medicalized; mild problems portrayed as serious illnesses, as has occurred in the drug-company-sponsored promotion of irritable bowel syndrome; and risk factors, such as high cholesterol and low bone mineral density being framed as diseases that must be treated with medications. Creating demand for pharmaceuticals has been suggested as the genesis for several new conditions such as premenstrual dysphoric disorder, or expansion of definitions of existing disorders such as pre-hypertension and pre-diabetes.[15]

Needless to say, direct-to-consumer advertising fans the flames of over-medicalization by inducing those who are exposed to such advertising to accept the implied or subtle suggestions that they may have conditions that are serious and necessarily treated with medications. This may contribute to the US having the world's highest per capita pharmaceutical spending. [16]

The Food and Drug Administration's Roles, Responsibilities, and Stresses:

Many would ask what the FDA's role is to prevent such unnecessary treatments or marketing irregularities. The FDA's primary pharmaceutical mission is to review and approve drugs by determining if proposed medications are effective and safe. The usual standard for effectiveness is whether the agent is statistically superior to placebo, which can be based on the results from as few as two randomized controlled clinical trials. There is not requirement that the difference be of clinical significance.

The safety determination is based on a relatively limited number of studies and may be restricted to data provided solely by the pharmaceutical manufacturer's funded researchers.[6] The FDA's safety review does not require sufficiently large trials that would have the statistical power to identify potentially rare but serious side effects. A typical newly approved drug may be tested in several thousand individuals during preapproval clinical research. This may be insufficient to detect adverse effects that occur with an incidence rate of less than 1%.[17] The FDA is also expected to review pharmaceutical advertising for accuracy, but is generally unable to meet this goal sufficiently because of resource limitations.

Unlike drug regulation in most European countries, the FDA's review of drugs does not take into consideration the absolute or relative cost of drugs or the relative effectiveness of the proposed drug to other drugs already approved for the proposed indication. Likewise, the FDA is unlikely to approve a drug for all the indications for which it may end up being used. However, pharmaceutical manufacturers have proposed additional indications for a particular drug for FDA approval, usually at a time towards the end of the drug's patent life. In some circumstances, this allows the drug to continue to be sold exclusively by the proprietary manufacturer at a higher price than if it were to go off patent and be available as a generic drug, but also expands the drug's potential market share by being approved for more indications and, therefore, more patients.

Much has been written elsewhere about the apparent excessive influence of the pharmaceutical industry over FDA operations in terms of pressure to obtain drug approval before sufficient evidence has been gathered; the tendency for data to be manipulated or obscured in ways that increase the probability that drugs will be approved in spite of potentially contradictory findings; the legal methods pharmaceutical companies have used to prevent drugs from becoming eligible for generic status; and the appearance of undue influence derived from federal rules that require pharmaceutical industry financial contributions to the FDA approval process.[18]

The Pharmaceutical Industry's Contributions to Health and Health Care:

It is important to point out the positive contributions of the pharmaceutical industry. The manufacturers provide substantial support, through grants to researchers as well as their own direct research activities, towards the development of new agents for the treatment of illnesses. Pharmaceutical companies provide funding and educational support for a wide range of academic, health care, and professional organizations. The provision of free medications through industry sponsored patient assistance programs provide many uninsured persons access to medicines that may be otherwise unaffordable. Although most of these practices are promoted as beneficial, e.g., good public policy and evidence of the industry's generosity and good will, none of them is without controversy. Numerous studies and media reports highlight the quid pro quo nature of the "generosity" as reflected in increased sales of the drugs which have been provided gratis, the increased appearance of drug company product placement and literature at industry funded events, and the previously mentioned appearance of bias associated with some industry funded research.[19]

In any case, it is abundantly clear that one of the primary goals and functions of pharmaceutical manufacturers, as corporate entities, is to make profits for their owners and shareholders. The individual companies and their industry umbrella organization spend enormous amount of money and time in efforts to influence all persons in key decision-making positions, including legislators, providers, patients, and the general public, to help them maintain or increase those profits. This truth is borne out by the fact that the pharmaceutical industry is among the most profitable of all business types (1999 average profit for 6 major companies was 16% of revenues.).[20] It is difficult to escape the conclusion that the industry's business interests seem to conflict with or confound its efforts to improve health and health care.

Pharmaceutical Industry Marketing Methods:

To fully understand the impact of pharmaceutical industry efforts to influence prescribing providers and patients, it is essential to review how much is spent on such efforts and the specific marketing strategies utilized. It should be no surprise to any resident of the US, especially those who watch commercial television, read newspapers or magazines, or surf the internet, that drug companies spend enormous sums to promote their products.

In 2005, US pharmaceutical marketing expenditures were $29 billion, differentially allocated to: visits to physician offices (22% of the marketing expense), which usually involves the provision of patient samples (62%), direct-to-consumer ads (14%), and professional journal ads (2%).[20] The importance of marketing in relation to research activities can be seen by the gap between the number of persons working in these two areas. In 1995 there were 12% more marketing positions in marketing than in research, but by 2000 that gap widened to 81%, with an absolute increase of 59% of marketing positions while the number of research positions remained relatively static.[21] The primary marketing strategies detail visits by sales representatives, direct-to-consumer advertising, and professional journal advertising, each of which merits separate analysis to understand the rationale and effectiveness for these approaches.

Pharmaceutical Representatives:

The use of sales representatives is the drug industry's main marketing activity and is used to influence providers to prescribe targeted drugs through the provision of selected journal articles and selectively presented data, often supplemented by the provision of gifts for physicians and staff and samples for patients. The number of representatives in the US in 2005 was over 100,000, 1 for every 6 practicing physicians. This sales force provides approximately 6 million office visits yearly, at a cost of over $12,000 per physician. Family practice and internists have been documented to meet with pharmaceutical representatives more frequently than other specialties suggesting a strategy aimed at increasing adoption to a broader range of patients.[22]

Studies consistently show that physicians do not believe that such promotion affects their prescribing habits, but other studies conclusively show that such marketing efforts lead to significantly increased rates of prescription of targeted drugs.[23-26] Reviews on the topic generally show that interaction with the pharmaceutical industry is associated with increased likelihood of formulary requests for targeted drugs; increased awareness, preference and rapid prescribing of new drugs; higher prescribing costs; less use of lower cost, but equally effective, generics; and less rational prescribing.[27]

Direct-to-Consumer Advertising:

Direct-to-consumer (DTC) advertising involves various forms of print, television, radio, and internet promotion of pharmaceutical products, as well as the indirect impact of product and company name placement in entertainment, sports, and recreation venues. In 1997 the FDA relaxed regulations on DTC advertising, eliminating the requirement for detailed lists of potential serious side effects, allowing the substitution of passing reference to informational toll-free phone numbers or websites. As of 2005, the US and New Zealand were the only industrialized countries to allow DTC ads.

DTC expenditures are enormous, totaling over $4.5 billion in 2005, an increase of almost 300% since 1997.[28] For example, Hoescht spent over half a million dollars on one 60-second ad for Allegra.[29] In one year Merck spent $161 million advertising a single drug, Vioxx, (which ultimately was taken off the market for safety reasons), an amount exceeding the entire annual advertising budget for companies like Dell, Pepsi, Budweiser, or Nike.[30]

But, DTC ads result in enormous revenue returns. In 1998-99 the 25 most advertised drugs experienced 43% sales growth, whereas all other drugs only averaged sales growth of 13.3%.[29] In the same period of time, Claritin, Allegra, and Zyrtec, which were heavily advertised, increased their sales by 32%, 50%, and 56% respectively.[29]

The DTC strategy effectively facilitates the practice of over-medicalization, described above. Being bombarded with ads for vaguely described conditions, such as erectile dysfunction, sleep disorders, or conditions that affect one's appearance, understandably leads many people to dread the risk of such conditions but also to overestimate the likelihood that their symptoms may mean that they need such drugs. In 2002 over 53 million persons in the US discussed DTC-advertised drugs with their physicians. Given the greater pressure physicians in the US are under to see more patients for shorter visits, it is not surprising that many of these patients have received the drugs that they discussed with their physicians.[31]

Journal Advertising and Biased Information:

Many professional medical journals depend on advertising support from the pharmaceutical industry in order to provide their publications to physicians free or at subscription rates that are well below their publication costs.[32] However, advertising which often dominates medical journals, has been found to not meet FDA adverstising standards, to be of little educational value, and generally misleading.[33] Much has been written about the unnecessarily close relationship between the pharmaceutical industry and such journals, but also individual physicians and clinics, academic health centers, and other professional organizations.[32, 34-37]

In a 2003 review of all ads in 10 major medical journals, approximately 500 unduplicated ads contained 74 unique graphs, of which 36% contained "numeric distortions" and 66% had "chart junk", leading to confusing and misleading conclusions supporting the advertiser's product without establishing significance of difference from competing medications.[37] In many cases the ads focused on short or intermediate outcomes rather than more meaningful longer-term outcomes that would be more correlated with true therapeutic effectiveness.

Prescribing Practice Profiling Databases:

The pharmaceutical industry has access to a vast prescribing database, that when paired with the American Medical Association (AMA) Physician Master file, allows them to track the prescribing patterns of most prescribing providers.[38-39] The AMA receives a considerable amount of its revenue from the sale of its physician data. The data is frequently used by individual companies to target specific providers for promotional messages or sales representative visits. Very few providers know of this database nor that they have the right to "opt out" of their own practice data from being used for such purposes.[40] The companies must honor the expressed wish to opt out of the program, but the individual provider must renew the opt out provision (www.ama-assn.org/go/prescribingdata) every three years.

What Can Clinicians Do?

The response to the question of what clinicians can do to reduce the influence of the pharmaceutical industry's tendency to promote distorted or biased information is a either denial or hopelessness, in the form of "my practice is not affected" or "what can I, a mere individual do in the face of this overwhelming pressure?"

Of the many strategies proposed in various papers and conference presentations, we have distilled a few:

- Reduce or eliminate contact with industry representatives ("Just say no").
- Identify/use unbiased and independent sources of prescribing information.
- Opt out of use of one's data in the AMA master profile.

Of particular concern is the seductive and influential impact of commercially sponsored continuing medical education (CME) . The ancillary non-educational perks associated with such activities, including free or subsidized tuition, travel support, meals, books, equipment, and other gifts bearing product or company identification are fairly well documented and are now becoming less common, partly because such practices are under serious scrutiny by watchdog groups and Congressional committees. However, the content of such educational offerings bears closer scrutiny as well.

It is important to recognize the extent of industry involvement in continuing medical education. In 2006, half of the $2 billion dollars spent on CME came from industry sponsorship.[41] Medical Education and Communication Companies (MECCs) are private companies that organize meetings, find speakers for grand rounds and symposia, and develop written materials. Approximately 76% of MECC income is derived from industry sources. In addition, many medical school faculty and departments depend on industry to provide support in the form of CME income. This faculty support is above and beyond that for researchers as mentioned in the articles referred to in the opening of this paper.

The question of whether drug company sponsored educational events have a disproportionate influence on prescribing behaviors is well established. In one study, attending drug company–sponsored CME presentations led to a 5-19% increase in rate of prescription of the sponsor's drug versus the competitor's drug. Similarly, Funding for travel or lodging to attend educational symposia increased formulary requests for the sponsor's drug, increased the rate of prescribing of sponsor's drug, and impacted hospital prescribing practices as much as 2 years later.[27]

It has also been clearly demonstrated that the source of funding can affect the content of CME events. Content analysis of two different CME courses sponsored by two different drug companies, in which each discussed 3 calcium channel blockers, showed that the drug company–sponsored CME preferentially highlighted the sponsor's drug(s) compared with other CME programs and that there was a 2.5-3 times greater likelihood of positive effects of sponsor's drug and negative or equivocal effects of competitor's being mentioned.[42]

What can clinicians do to eliminate or reduce their own actual or perceived conflicts of interest? Many are advocating to simply eliminate or dramatically limit any relationships with drug company detail or sales representatives.[18] Even though it may mean ending or significantly altering relationships that have been long-standing ("some of my best friends are…."), the risk of unconscious bias and the appearance to staff and patients that one is more interested in pharmaceutical perks than providing quality clinical care would seem to far outweigh any inconvenience or hurt feelings. To implement such policies for oneself or the organization within which one works may require addressing individual or collective tendencies to rationalize ("It's really an educational dinner", "who is hurt by my accepting this free clock?" or "my patients need samples") or to deny the potential negative impacts of these conflicts ("It doesn't affect my prescribing decisions" or "I take it with a grain of salt").[43]

Evidence-Based and Relatively Unbiased Sources of Information:

In addition to shedding the burden of various real or perceived conflicts of interest, it is incumbent upon clinicians to develop more consistent and evidence-based methods of treatment, including prescribing practices. This is not so easy in an age when all kinds of information is available, much more than anyone can possibly absorb and much of it questionable or ambiguous in terms of its validity and relevance to one's clinical practice. David Sackett, a pioneer of evidence-based medicine (EBM) defines evidence-based medicine as "the conscientious, explicit and judicious use of best current evidence in making decisions about the care of individual patients." By "conscientious", he means good faith efforts to use the best treatment for patients, in ways that are "explicit" or in which one's treatment plan and recommendations are logical and transparent, and with judiciousness, i.e., allowing clinical judgment to remain important to interpret and apply results within individual, cultural and other relevant contexts.[44] It is important to keep in mind that EBM is not:

- The same old thing we've always done
- Something that can only be done from ivory towers
- A "cookbook" method of practice
- A method for administrators to save costs
- Restricted to randomized trials

There is too much variation in clinical behavior among clinicians. There are many examples of clinical teams that have improved outcomes by explicitly using EBM principles, sometimes facilitated by the use of internet resources or other decision supports. EBM may actually be a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient values/choice. EBM makes use of the BEST evidence available, whatever that is. EBM should identify and apply the most efficacious interventions to improve quality and quantity of life for patients, irrespective of its direct costs. Presumably, providing better quality of care over time to a greater portion of the population will lead to decreased burden of disease and reduced overall utilization of health care services.

It has also been said that "evidence based medicine requires the integration of the best research evidence with our clinical expertise and our patient's unique values and circumstances." But how do we do this with so little time and so much information to absorb in order to make an intelligent and rational prescribing decision?

One simple mantra to follow is a restatement of the Hippocratic Oath: [45]

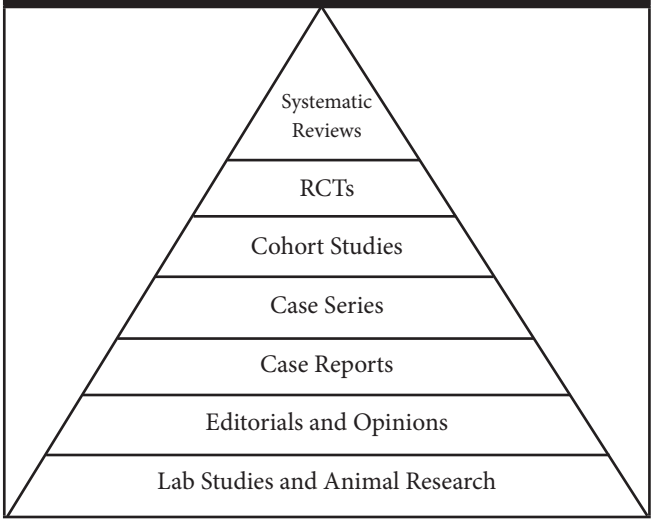
- When there is evidence of benefit and value, do it.

- When there is evidence of no benefit, harm or poor value, don't do it.
- When there is insufficient evidence to know for sure, be conservative.
- When considering the treatment of individual patients, we should also consider the potential help/harm to the patient's family and overall community in this equation.[46]

Such an evidence-based approach involves sorting through the marketing, opinions, and theory to get an accurate assessment of the proven and comparative benefits and risks of various treatments. It supports policies that reduce variations in practice, especially expensive or inappropriate prescribing. It provides incentives to conduct research on more meaningful questions, especially comparative studies.

It is essential to understand the various levels of evidentiary confidence as exemplified by the following illustration. The higher the available data for a particular condition or treatment is on this theoretical hierarchy, the more reliable it generally would be considered to be.

FIGURE 1: LEVELS OF EVIDENTIARY CONFIDENCE



In order to be most successful in understanding and using research findings, it is recommended that the clinician should seek information from sources that are derived from the higher levels of this conceptual pyramid. In reviewing specific studies, one needs to become familiar and conversant with terms associated with research findings, such as generalizability/applicability/relevance, number needed to treat, confounding variables, and target outcomes. It is also important to recognize signs of publication bias when they appear or when the lack of mention of certain key factors is apparent.

However, it is generally difficult, if not impossible for most practicing clinicians to absorb the key research studies in medicine, even those restricted to the clinician's narrower area of clinical focus. Therefore, it is essential that, whenever possible, clinicians seek out and use systematic or comparative reviews rather than single studies. Too often drug company representatives will gladly hand out reprints of single studies that tend to favor their particular product. Objectively conducted systematic and comparative reviews are becoming a much more important area of research.

Systematic reviews are now becoming quite consistent in their methodological approaches and, because of the power of pooling data from numerous studies, can be used to develop more cogent and meaningful recommendations about the effectiveness and applicability of certain treatments, including more reliable treatment guidelines.

Sources of Relatively Unbiased Information:

How can a clinician get connected with reliable, succinct, and user-friendly resources to assist them in their decision-making? There are numerous publications and internet web sites that have emerged to address the wide array of clinical concerns mentioned in this paper. We list a selection of current and relevant resources by type.

Relatively Unbiased Sources on Drugs and Drug Studies:

- Agency for Health Care Research and Quality's Effective Healthcare Program: http://effectivehealthcare.ahrq.gov, conducts comparative effectiveness reviews of many high priority conditions through the network of evidence-based practice centers and other research institutions throughout the US and Canada.
- National Institute for Clinical Excellence: www.nice.org.uk, an independent British organization responsible for providing guidance on the promotion of good health and the prevention and treatment of ill health.
- Cochrane Collaboration: www.cochrane.org, an international collaborative initiative, also based in the UK, whose intention is to improve healthcare decision-making globally, through systematic reviews of the effects of healthcare interventions.
- Drugs @ FDA: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/, the FDA's public access site to search for official information about approved brand name and generic drugs and therapeutic biological products, including available generics, therapeutic equivalent drugs, consumer information, and drug approval history related documents.
- Canadian Common Drug Review: www.cadth.ca/index.php/en/cdr, provides objective, rigorous reviews of clinical and cost effectiveness of drugs, and provides formulary listing recommendations relevant to publicly funded drug plans in Canada.
- Drug Effectiveness Review Program: www.ohsu.edu/drugeffectiveness, aka DERP, funded by and overseen by

public payers from over 15 states and Canada, does systematic and comparative effectiveness reviews on over 25 classes of drugs. Reviews are updated on a regular basis.

- Pub Med: http://www.ncbi.nlm.nih.gov/pubmed/, creates summaries of many of the DERP reports and will have links to them in relation to individual drugs about which users may be inquiring.

- Consumer Union: http://www.consumerreports.org/health/prescription-drugs/index.htm, provides well organized information on most pharmaceutical agents, derived from effectiveness reviews, and translated into less technical language that is more accessible to consumers.

- Clinical Trials Database: http://clinicaltrials.gov/, obtains all registered clinical trials that hope to be published; began including outcomes in 2009.

- Carlat Report: http://www.thecarlatreport.com/, a monthly newsletter (in both print and online form) that provides clinically relevant, unbiased information on psychiatric practice.

- Therapeutics Initiative: http://ti.ubc.ca/, from the University of British Columbia, provides evidence-based reviews of drug prescribing for physicians and pharmacists

- Oregon Health Policy & Research: www.OregonRx.gov, contracts with the Oregon Evidence-based Practice Center to conduct evidence-based reviews of all literature available on specific drug classes; creates one-page summaries for consumers which synthesize the reports focusing on which drugs are most safe and effective.

- Oregon Drug Use Review Board Newsletter:

- http://pharmacy.oregonstate.edu/drug_policy/index.php?nav=newsletter. This is a periodic newsletter published by the Oregon State University College of Pharmacy on behalf of the state's Drug Utilization Review Board. Provides drug utilization reviews, drug and therapeutic guideline reviews, and cost-effective prescribing recommendations.

- Oregon DHS Pocket Drug Guide: http://pharmacy.oregonstate.edu/drug_policy/prescriber_tools/POCKETFinal.pdf, a convenient printable pocket guide of cost comparison data of the more commonly prescribed drugs.

- OregonRx: www.OregonRx.gov, provides information concerning prescription drugs to consumers and health professionals with a goal to provide current, reliable, evidence-based medicine information so as to empower consumers, prescribers, and medical professionals to utilize the information for their needs and practices.

Sources of Information on Industry Practices, Drug Comparisons, Formularies:

- No Free Lunch: www.nofreelunch.org/, a comprehensive collection of primary material and links to other sites, produced in conjunction with the American Medical Student Association, to encourage health care providers to practice medicine on the basis of scientific evidence rather than on the basis of pharmaceutical promotion.

- Pharmed Out: http://www.pharmedout.org/, an independent project (funded by the same grant program that supported the creation of this paper) that empowers physicians to identify and counter inappropriate pharmaceutical promotion practices. PharmedOut promotes evidence-based medicine by providing news, resources, and links to PhRMA-free CME courses.

- Oregon's Attorney Generals Prescriber and Consumer Education Grant website; http://pharmacy.oregonstate.edu/drug_policy/index.php?nav=aggrant, provides a curriculum to educate healthcare professionals (CME accredited) to critically view pharmaceutical marketing strategies and to access unbiased evidence-based drug comparisons to encourage quality and cost–effective prescribing, including the PowerPoint presentation from which this paper is derived.

Conclusion:

In this paper we have attempted to cover a great deal of territory regarding:

- the connections between health care costs and outcomes, with specific reference to the development of and process of treatment with pharmaceutical agents, highlighting some problematic prescribing practices;

- the roles and relationships between the government oversight entity, the FDA, and the pharmaceutical companies that develop and market therapeutic medications;

- the specific marketing methods utilized by the pharmaceutical industry and how those methods appear to be more devoted to maximizing profit than health;

- ethical and practical guidance for clinicians to develop or maintain more distinct and less conflicted relationships with pharmaceutical companies, their representatives, and their proprietary products and profit-motivated interests;

- the relevance of effectiveness research findings and the methods for translating such research into evidence-based recommendations or guidelines; and

- several examples of relatively unbiased sources of information related to medications, formularies, evidence-based systematic and comparative effectiveness reviews.

This is an exhaustive topic about which several excellent books have been written.[47-49] There are undoubtedly areas we didn't discuss that could have been stressed and areas that we did discuss that could have been more comprehensively developed. However, our overarching goal was to present, in a relatively short paper, a broader gestalt view of the issues as they relate to clinicians and

their roles and attitudes vis a vis the pharmaceutical industry and rational clinical practice. If we achieve that level of understanding, provoke sufficient consciousness about the interrelatedness of the topics we covered, and stimulate sober assessments of individual and organizational ethical behavior, we will have succeeded.

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