BUSINESS REPORT

MONTANA HOUSE OF REPRESENTATIVES
61st LEGISLATURE - REGULAR SESSION

HOUSE HUMAN SERVICES COMMITTEE

Date: Monday, February 9, 2009 **Time:** 3:00 pm
Place: Capitol **Room:** 472

BILLS and RESOLUTIONS HEARD:
Prefix (HB, HR, HJR, SB, SR, or SJR) and number. Add Postponed (PP) when appropriate:

HB 394
SB 53

EXECUTIVE ACTION TAKEN:
Prefix (HB, HR, HJR, SB, SR, or SJR) and number. Enter P(pass) F(failed) DPAA (do pass as amended) BC(be concurred in) BCAA (be concurred in as amended):

HB 365 P
HB 367 DPAA
HB 267 TABled
SB 53 BC

COMMENTS:

Arlene Becker
REP. Arlene Becker, Chairman

HOUSE OF REPRESENTATIVES
Roll Call
HUMAN SERVICES COMMITTEE

DATE: 2/9/09

NAME	PRESENT	ABSENT/ EXCUSED
Rep. Mary Caferro	\	
Rep. Pat Ingraham	\	
Rep. Bill Beck	\	
Rep. Julie French	\	
Rep. Timothy Furey	\	
Rep. David Howard	\	
Rep. Chuck Hunter	\	
Rep. Dave McAlpin	\	
Rep. Michael More	\	
Rep. Pat Noonan	\	
Rep. Ken Peterson	\	
Rep. Diane Sands	\	
Rep. Cary Smith	\	
Rep. Ron Stoker	\	
Rep. Jeffery Welborn	\	
Rep. Arlene Becker	\	

HOUSE STANDING COMMITTEE REPORT

Mr. Speaker:

We, your committee on **Human Services** recommend that **House Bill 367** (first reading copy – white) **do pass as amended.**

Signed: Arlene Becker
Representative Arlene Becker, Chair

And, that such amendments read:

1. Page 1, line 10.
Strike: "mother"
Insert: "parent"
Strike: "women"
Insert: "parents"

2. Page 1, line 12.
Strike: "women"
Insert: "parents"

3. Page 1, line 13.
Strike: "women who are"
Insert: "parents"

4. Page 1, line 14.
Strike: "woman"
Insert: "parent"

5. Page 1, line 15.
Following: "give"
Strike: "her"
Insert: "the parent"
Following: "assist"
Strike: "her"
Insert: "the parent"

Committee Vote:
Yes 16, No 0
Fiscal Note Required __

HB0367001SC.hjd

HOUSE STANDING COMMITTEE REPORT

Mr. Speaker:

We, your committee on **Human Services** recommend that **Senate Bill 53** (third reading copy – blue) **be concurred in**.

Signed: Arlene Becker
Representative Arlene Becker, Chair

To be carried by Representative Ken Peterson

- END -

Committee Vote:
Yes 16, No 0
Fiscal Note Required __

SB0053001SC05152.hjd

HOUSE STANDING COMMITTEE REPORT

Mr. Speaker:

We, your committee on **Human Services** recommend that **House Bill 365** (first reading copy – white) **do pass.**

Signed: Arlene Becker
Representative Arlene Becker, Chair

- END -

Committee Vote:
Yes 16, No 0
Fiscal Note Required __

HB0365001SC.hjd

All Notices are to be printed, none will be EMailed

COMMITTEE FILE COPY

TABLED BILL

The **HOUSE HUMAN SERVICES COMMITTEE** TABLED **HB 267**, by motion, on **Monday, February 9, 2009**.

(For the Committee)

(Chief Clerk of the House)

_____, 2/11
(Time) (Date)

February 11, 2009 Santella Baglivo, Secretary Phone: 4457

Rm 173

HOUSE OF REPRESENTATIVES
Roll Call Vote
HUMAN SERVICES COMMITTEE

DATE 2-9-09 BILL NO HB 267 MOTION NO. _____
MOTION: _____

~~Do Pass as~~ Amendment #026702.asd

NAME	AYE	NO	If Proxy Vote, check here & include signed Proxy Form with minutes
Rep. Mary Caferro	\		
Rep. Pat Ingraham	\		
Rep. Bill Beck		\	
Rep. Julie French	\		
Rep. Timothy Furey	\		
Rep. David Howard		\	
Rep. Chuck Hunter	\		
Rep. Dave McAlpin	\		
Rep. Michael More		\	
Rep. Pat Noonan	\		
Rep. Ken Peterson		\	
Rep. Cary Smith		\	
Rep. Diane Sands	\		
Rep. Ron Stoker		\	
Rep. Jeffery Welborn	\		
Rep. Arlene Becker	\		

HOUSE OF REPRESENTATIVES
Roll Call Vote
HUMAN SERVICES COMMITTEE

DATE 2/9/09 BILL NO HB267 MOTION NO. _____
MOTION: _____

Do Pass as Twice Amended.

NAME	AYE	NO	If Proxy Vote, check here & include signed Proxy Form with minutes
Rep. Mary Caferro		\	
Rep. Pat Ingraham		\	
Rep. Bill Beck		\	
Rep. Julie French		\	
Rep. Timothy Furey		\	
Rep. David Howard		\	
Rep. Chuck Hunter	\		
Rep. Dave McAlpin	\		
Rep. Michael More		\	
Rep. Pat Noonan		\	
Rep. Ken Peterson		\	
Rep. Cary Smith		\	
Rep. Diane Sands		\	
Rep. Ron Stoker		\	
Rep. Jeffery Welborn		\	
Rep. Arlene Becker		\	

AUTHORIZED
COMMITTEE PROXY

I request to be excused from the Human Services

Committee because of other commitments. I desire to leave my proxy vote with:

Rep French

Indicate Bill number and your vote Aye or No. If there are amendments, list them by name and number under the bill and indicate a separate vote for each amendment.

BILL/AMENDMENT	AYE	NO
SB 53	X	
HB 365	X	

BILL/AMENDMENT	AYE	NO

Rep. Mary M. Cafferata
(Signature)

Date

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AUTHORIZED
COMMITTEE PROXY

I request to be excused from the Human Services

Committee because of other commitments. I desire to leave my proxy vote with:

Rep. French

Indicate Bill number and your vote Aye or No. If there are amendments, list them by name and number under the bill and indicate a separate vote for each amendment.

BILL/AMENDMENT	AYE	NO
SB 57	X	
~~HB 365~~	~~X~~	

BILL/AMENDMENT	AYE	NO

Rep. Chuck Hunter
(Signature)

Date

S:\Word Processing\Forms\Proxy.wpd

Montana House of Representatives
Visitors Register

HUMAN SERVICES COMMITTEE **Date** 2/9/09

Bill No. HB 394 **Sponsor(s)** Rep

PLEASE PRINT **PLEASE PRINT** **PLEASE PRINT**

Name and Address	Representing	Support	Oppose	Inf.
Bruce Spencer	MEDCO		X	
Cindy Laubacher	Medco		X	
Pat Melby	Mt Med Assn	✓		
Meredith Jacob	Prescription Proj	✓		
[illegible]	BioTech Fnd org		X	
Chris Lepore	Johnson & Johnson		X	
Kristi Black	Johnson & Johnson		X	
Kathleen Traylor MD	Amgen		X	
Jon Bennion	MT chamber		X	
Ronald Klein	Brd of Pharmacy			✓

Please leave prepared testimony with Secretary. Witness Statement forms are available if you care to submit written testimony.

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Montana House of Representatives
Visitors Register

HUMAN SERVICES COMMITTEE **Date** 2/9/09

Bill No. SB 53 **Sponsor(s)** Sen Lewis

PLEASE PRINT **PLEASE PRINT** **PLEASE PRINT**

Name and Address	Representing	Support	Oppose	Inf.

Please leave prepared testimony with Secretary. Witness Statement forms are available if you care to submit written testimony.

C:\Documents and Settings\cl3192\Desktop\Forms HUH\CommVisitorRegSample2009.wpd

Additional Document

Wolters Kluwer Health

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Phoenix, Arizona 85016
USA

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McLean, VA 22102
202.997.8123 direct
703.734.0819 fax

Cathy Betz
Vice President,
Government Affairs

Wolters Kluwer Health
Written Testimony for the Hearing Record

In opposition to
House Bill 394
An Act prohibiting the use of individually identified (prescriber or patient) prescribing information for marketing purposes

House Human Services Committee
Monday, February 09, 2009

House Bill 394 would prohibit the commercial use of patient and prescriber-identifiable information in the state of Montana. Wolters Kluwer Health is concerned that, as written, this bill will decrease the flow of important health information in Montana and beyond. This bill will eliminate many beneficial uses of physician prescribing information and will have unintended consequences that will ultimately hurt patients in the state. We strongly believe that more information, not less, is appropriate public policy. Wolters Kluwer Health respectfully requests that the Committee reject HB 394 and oppose restrictions on the sale and use of prescriber-identifiable information.

SUMMARY: Wolters Kluwer is a leading multinational publishing and information services company active in many markets, including the sale of health care products. One division, Wolters Kluwer Health, Inc., a wholly-owned subsidiary of Wolters Kluwer U.S. Corporation, is a primary supplier of information to professionals and students in the fields of medicine, nursing, allied health, and pharmacy, as well as to entities in the pharmaceutical industry. It produces textbooks, reference products, journals, and other informational materials that professionals employ in the knowledge-intensive, rapidly changing practice of medicine.

Wolters Kluwer Health, through its wholly-owned subsidiary, Source Healthcare Analytics, Inc., sells a variety of information products that use "prescriber-identified prescription data," i.e., records that match individual prescriptions to the prescribing professional. Health information organizations (HIOs) like Wolters Kluwer Health provide prescriber-identifiable data to biotechnology firms, pharmaceutical manufacturers and distributors, government agencies, health care groups, researchers, consulting organizations, the financial community, manufacturers of generic drugs, pharmacy benefit managers, and others.

Some of these entities use, license, sell, or transfer the information to identify physicians who may be interested in learning more about their respective products, while others, like academic and medical research, humanitarian organizations, and law enforcement authorities, use the information for noncommercial purposes such as tracking patterns of disease and treatment, conducting research and clinical trials, implementing best practices, and engaging in economic analyses.

Wolters Kluwer Health unequivocally opposes legislative measures that restrict the dissemination and use of prescriber-identifiable information. There are numerous uses for this data that serve the public's interest, further the government's mandate for greater transparency in medicine, and support value-based purchasing initiatives intended to improve the efficacy, quality, and cost of health care. Importantly, all of this is possible due to the legitimate commercial use of these data.

The legislative measure before you today will have a chilling effect on the movement toward transparency in health care and the development of a national health information network. There is broad consensus among lawmakers in the U.S. Congress, the White House, and in the policy community that in order to improve our nation's health care delivery system we must cultivate a rich, data-driven infrastructure. On that basis, sound policy decisions can be made. Such data-driven decision making will not only benefit patient outcomes but will also provide a foundation for adequate evidence-based and outcome-based reimbursement.

Over the past several years, legislation like HB 394 has been introduced in more than two dozen states and virtually all states have rejected them - only New Hampshire, Vermont and Maine have adopted these types of restrictions and those laws are all subject to constitutional challenges in federal court. Based on these constitutional arguments as well as on numerous public policy grounds, Wolters Kluwer Health respectfully requests that the Committee reject HB 394 in its current form.

Use of Prescriber Data

Approximately 1.4 million licensed health care providers are authorized to write prescriptions in the United States for approximately 8,000 different pharmaceutical products in various forms, strengths and doses. These prescriptions are filled by approximately 54,000 retail pharmacies and other licensed medical facilities throughout the United States.

Wolters Kluwer Health sells a variety of information products that use prescriber-identified data that match prescriptions to the prescribing professional. To create these information products, Wolters Kluwer Health purchases prescriber-identified data from a pharmacy or other originating entity, then aggregates, analyzes, and packages it for client use. Wolters Kluwer Health is one of three major health information organizations in the United States.

Wolters Kluwer Health's clients have used the data in a broad range of activities. For example, pharmaceutical manufacturers have used it to identify doctors who may be interested in their products and who may have patients who would be suitable participants in clinical trials of promising new drugs. Similarly, a number of governmental agencies, including the FDA, have used the data in discharging their regulatory and law enforcement responsibilities. Products like Wolters Kluwer Health's can help governmental agencies direct drug safety alert letters toward doctors whose prescribing practices make them relevant, and enforce civil and criminal laws against abusive prescribing practices. In addition, a variety of individuals and organizations use the data in research concerning drug usage, interactions, effectiveness, and costs.

Healthcare information organizations like Wolters Kluwer Health are important sources of data for researchers and policy analysts worldwide. Below are some examples of recent studies that used data provided by Wolters Kluwer Health:

- The American College of Cardiology (ACC) and the American Heart Association (AHA) used prescriber-identifiable data from Wolters Kluwer Health to examine compliance of beta-blocker utilization in post-discharge myocardial infarction (MI) and cardiac arrest patients relative to ACC and AHA guidelines. Concern was expressed that patients

were not complying with recommended beta blocker therapy over time after being discharged from the hospital. Analysis revealed that only 40 percent of patients are compliant at 360 days after discharge.

- Using prescriber level data from Wolters Kluwer Health, health policy researchers at Cornell University and Arizona State University sought to discover whether the Medicare Part D prescription drug program is meeting its intended goals, i.e., Medicare savings would accrue from reduced hospitalizations as a result of drug coverage. Specifically, the study tested the extent to which Medicare Part D has increased the use of medications linked to reduction in hospital use among seniors. In addition, the study was designed to quantify the extent to which disparities in access to prescription drugs have changed due to Medicare Part D prescription drug coverage.

- Massachusetts Institution of Technology (MIT) used data supplied by Wolters Kluwer Health to detail the impact that the Medicare Modernization Act's government sponsored prescription drug coverage program has had on patient behavior and the overall implications the Medicare Part D benefit has had on the pharmaceutical sector. Analysis revealed that 32 percent or 4.2 million Medicare Part D eligibles entered the "donut hole" i.e., a $3,000 gap in coverage under the program, by the end of 2006. Generic drug utilization increased at that time and brand drug utilization decreased; patients did not restart taking brand medications once

Prescribing information is used not only by pharmaceutical, biotechnology and medical device companies, but also, providers, government agencies (U.S. Food & Drug Administration, the Department of Defense, the Drug Enforcement Administration, the Centers for Disease Control and Prevention), academia and researchers to monitor and manage the safety of medications, implement drug recalls, rapidly communicate information to doctors about innovative new treatments and conduct public health studies.

Health Care Cost Implications

There is no systemic evidence that the use of prescriber-identifiable data by pharmaceutical companies in their marketing endeavors increases drug costs. Prescriber-identifiable data are used in pharmaceutical marketing as a means of *lowering* the costs of promotion. Focused marketing directs goods and services towards those who are most likely to be interested in them, such as prescribers who prefer pharmaceutical therapies for conditions they frequently treat. These data are used to develop messaging and determine the appropriate frequency of contacts. Samples are provided to those physicians who most need to evaluate the drug in practice and whose patients most benefit. And perhaps most importantly, prescriber-identifiable data are used to efficiently disseminate new information about drugs to physicians (e.g., results of recent clinical trials).

It is unlikely that banning the commercial use of prescriber-identifiable data would decrease marketing by sales representatives. In the absence of this information, pharmaceutical firms will either *increase* the number of sales representatives to adequately deliver product messages to a larger number of physicians or market to physicians who may not have cause to prescribe particular drugs, or both, resulting in increased cost. Marketing would be less efficient, more scattered and less focused thus increasing the cost of these marketing efforts.

Available Alternatives to Restrictive Legislation

In response to physicians' concerns of inappropriate use of prescribing data by some pharmaceutical sales representatives, the American Medical Association developed the Physician Data Restriction Program (PDRP), a private sector solution by which physicians can

indicate whether they would like to keep their prescribing information from pharmaceutical representatives.

Because physician's choice is so important, Wolters Kluwer Health has helped fund the AMA's PDRP Physician Awareness Campaign. We have made space available in the over 300 medical journals we publish to ensure all physicians are informed of this option. As of February 6, 2009, 21,181 doctors were enrolled in the PDRP, 59 from the state of Montana.

There are a number of other options available to the State in advancing any legitimate state interests that are more narrowly tailored than the prohibition of prescriber-identifiable data use and thereby do not improperly infringe upon speech protected by the First Amendment. As enumerated by New Hampshire District Court Judge Paul Barbadoro in his April, 2007 decision, legislators could limit inducements to physicians by pharmaceutical companies; prepare and distribute "best practices" guidelines to educate providers on the implications of their prescribing decisions; develop counter-detailing programs; and require participation in continuing medical education programs. Wolters Kluwer Health urges members of this Committee to seriously consider alternatives along these lines.

Business Impact of Prescriber-Identifiable Data Restrictions

The prohibition of commercial use of prescriber-identifiable data threatens the existence of critical databases maintained by health information organizations such as Wolters Kluwer Health. The public uses of these data would not be possible if it were not for the commercial aspects that drive the rigors required to maintain a comprehensive, robust and near real-time database that also offers governmental agencies, academia, medical researchers, and businesses a wide range of health care studies. Certain public health benefits, such as drug safety studies, are possible using data that is produced and paid for by companies that purchase the data for commercial purposes.

Conclusion

Wolters Kluwer Health and other health information organizations have been advancing public health for decades. We have done so by responsibly and legally collecting, analyzing and sharing information with a variety of healthcare stakeholders. The use of this information extends well beyond pharmaceutical marketing into such areas as drug safety, public health monitoring, and patient treatment variability-all benefiting the public interest, all necessary to improving overall healthcare.

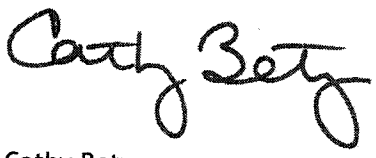
We oppose HB 394 because it deprives the healthcare system of critical information that is vital to ensuring patient safety and improving healthcare quality. These measures will do nothing to improve the well being of the citizens of Montana, but will have far-reaching, unintended consequences by limiting sources of information for research and other public health purposes. Commercial databases developed by healthcare information companies like Wolters Kluwer Health offer the only comprehensive sources of prescribing information that can be used for a variety of applications that benefit the healthcare system.

In the public and private sectors, demand for evidence-based medicine, accountability, and transparency has never been greater. At a time when greater transparency and free flow of information is being advanced at the national level to improve the quality of health care and patient safety, any restriction that will impede this initiative is not only misguided but may have serious constitutional implications.

In conclusion, we firmly believe that the public good and that of the state of Montana is best served by evidence-based medicine, improved transparency in the health care system, and continued responsible use of and access to prescriber-identifiable information. We appreciate

the opportunity to submit our comments for your review and consideration. We hope the information contained herein is helpful in the Committee's consideration of HB 394, and that you will agree to reject this measure outright. If you have any questions or require further information, please do not hesitate to contact me. Thank you again for your consideration.

Respectfully submitted,



Cathy Betz
Vice President, Government Affairs
Pharma Solutions Business Unit
Wolters Kluwer Health

Additional Documents

THE PRESCRIPTION PROJECT

AUGUST 29, 2007

Rx Fact Check

Data Mining: Myths and Rebuttals

The Prescription Project promotes evidence-based prescribing and works to eliminate conflicts of interest in medicine due to pharmaceutical marketing to physicians.

It is promoting policy change by working with

- *State and Federal Policymakers*
- *Academic Medical Centers*
- *Professional Medical Societies*
- *Private Payers*

Created with The Pew Charitable Trusts, the Project is led by Community Catalyst in partnership with the Institute on Medicine as a Profession.

Do data mining laws prohibit legitimate uses of prescriber-identifiable data?

- No.
- The existing statutes in Maine, Vermont and New Hampshire prohibit only marketing uses of prescriber-identifiable prescription data.
- Prescriber-identifiable data in these states is permitted for other purposes including, but not limited to: health care research; formulary compliance and utilization reviews by providers, insurers and pharmacy benefit managers; and law enforcement.

Do health researchers rely on IMS and other health information organizations for this data?

- No.
- Researchers cite numerous alternative sources for useful medication use data, including Medicaid and Medicare; HMOs; Veterans Affairs medical programs; pharmacy benefit managers. According to Jerry Avorn, an internationally recognized health researcher, "These other sources are far more useful for research because they contain more detailed data about patients' diagnoses and use of clinical services."[1]
- Data sets sold by health information organizations are cost prohibitive for researchers and there has been very limited use of them for non-marketing purposes.
- IMS Health, the world's largest aggregator of prescription data, clarifies, "Sales to the pharmaceutical industry accounted for

[1] Avorn, J., Kesselheim, A. *Testimony in support of LD 838:An Act Protecting the Confidentiality of Prescription Information.* Maine Legislature Joint Standing Committee on Health & Human Services. March 28, 2007.

substantially all our revenue in 2006, 2005 and 2004."[2] 2006 revenue was $1.96 billion.

Do restrictions on data mining compromise patient safety?

- No.
- The sale of prescriber-identifiable data does not have a role in an effective drug safety alert system.
- The FDA Center for Drug Evaluation and Research distributes drug safety notices widely and physicians can subscribe to their email alert service.
- It is ineffective for drug manufacturers to use prescriber-identifiable data to target alerts on safety issues because:

  1. Prescriber-identifiable information purchased from companies like IMS Health is incomplete and does not identify all prescribers of a certain medication.[3]

  2. Each physician is a potential prescriber of every drug and should be made aware of *all* alerts.

- Pharmacies have the most comprehensive information on which patients are taking which medications and are the most appropriate party contact people regarding safety concerns.
- Controlled Substances: the Drug Enforcement Agency (DEA) is responsible for monitoring the prescribing and use of controlled substances.

  1. Drug companies should not be relied upon to monitor the prescribing and use of controlled substances.

  2. In federal court Purdue Pharma was found to have intentionally misled doctors about the safety of the powerful narcotic Oxycontin, all the while in possession of physicians' prescribing data.[4]

Does the American Medical Association's Prescription Data Restriction Program (PDRP) solve the problem?

- No.
- The PDRP is a weak program. Physicians can enroll if they do not want their prescribing information to be used for marketing

[2] IMS Health. *2006 Annual Report.*2007. Available at: http://ir.imshealth.com/phoenix.zhtml?c=67124&p=irol-reportsAnnual Accessed August 25, 2007.

[3] Steinbrook, R. For Sale: Physicians' Prescribing Data. *New England Journal of Medicine.* 2006: 2745-2747.

[4] .Meier, B. Narcotic maker guilty of deceit over marketing. *New York Times*. May 10, 2007.

purposes by pharmaceutical companies.

- However, even after physicians enroll in the PDRP, the AMA continues to provide their information to data mining companies.
- The PDRP relies on pharmaceutical companies to check an updated "opt-out" list quarterly and voluntarily halt the release of enrolled physicians' prescribing info to their sales representatives.[5] However, marketing executives may still use the information to create individual prescriber profiles to develop marketing strategies or reward sales representatives.
- While only "about one in three doctors are AMA members, roughly 244,500 of the estimated 850,000 physicians practicing in the USA," the AMA Masterfile lists all MDs and over 93% of doctors of osteopathic medicine in the United States.[6, 7]
- The PDRP does not offer any increased privacy to non-physician prescribers, including physicians assistants, nurse practitioners or pharmacists. The profiles of these prescribers are not included in the Physician Masterfile and pharmaceutical companies can simply obtain their information elsewhere. This is indicative of a greater problem: even if the AMA discontinues the sale of its Physician Masterfile, prescriber profiles can be legally obtained elsewhere.
- The PDRP has been poorly publicized and underutilized; less than 25% of physicians are even aware of the program.[8] About two-thirds of physicians indicated in an AMA Gallup poll that they are opposed to their prescribing records being used for drug industry marketing,[9]yet less than 2% of all physicians have opted out using the AMA's internet-based system.
- It is not reasonable to expect the AMA to voluntarily establish and maintain an effective physician opt-out system if it makes their Masterfile a less useful tool for pharmaceutical marketing purposes. The AMA received 16% of its 2005 revenue, $44.5 million, from

[5] American Medical Association. PDRP: The choice is yours. 2007. Available at: http://www.ama-assn.org/ama1/pub/upload/mm/432/pdrp_brochure.pdf

[6] Boddiger,D. AMA Hopes streamlined agenda will boost membership. *The Lancet.* 2005; 366: 971-972.

[7] American Medical Association. Description of AMA Physician Masterfile Data Elements. 2004. Available at: https://profiles.ama-assn.org/amaprofiles/info/pdf/mfile_elements.pdf Accessed: August 25, 2007.

[8] Greene, J.A. Pharmaceutical marketing research and the prescribing physician. *Annals of Internal Medicine.* 2007; 146:742:748.

[9] Grande, D. Prescriber Profiling: Time to call it quits. *Annals of Internal Medicine.* 2007;146:751-752.

sales of its Masterfile to health information organizations.[10]

For more information and the complete tool kit, visit the Prescription Project website: www.PrescriptionProject.org

[10] ibid.

THE PRESCRIPTION PROJECT

November 19, 2008

Fact Sheet

Prescription Data Mining

The Prescription Project promotes evidence-based prescribing and works to eliminate conflicts of interest in medicine due to pharmaceutical marketing to physicians.

It is promoting policy change by working with

- *State and Federal Policymakers*
- *Academic Medical Centers*
- *Professional Medical Societies*
- *Private Payers*

Created with The Pew Charitable Trusts, the Project is led by Community Catalyst in partnership with the Institute on Medicine as a Profession.

The Problem

Pharmaceutical companies buy doctors' prescribing records from pharmacies and use the information to target their marketing to physicians. This practice negatively affects:

- **Public Health**: Marketing based on prescriber data often involves biased and inaccurate information about health risks, and encourages the prescription of new drugs that might be riskier to patients than already established treatments.
- **Cost**: Marketing based on prescriber data is a key factor in the skyrocketing costs of prescription drugs and the increased usage of expensive brand-name medicines.
- **Privacy**: Sales of prescriber data take place without the consent, and generally without the knowledge, of physicians. Patient records may also be inadequately protected, particularly in small communities with few physicians or few patients with particular diagnoses.

The pharmaceutical industry spent $29 billion on promoting and marketing prescription drugs in 2005, with $7.2 billion spent on marketing directly to physicians.[i] ($29 billion includes detailing, advertisements in medical journals, direct-to-consumer advertising and drug samples.) The industry employs over 90,000 drug representatives and spends up to about $8,800 per doctor, per year marketing its products directly to physicians.[ii]

New and expensive drugs are often promoted over less expensive drugs that are equally or more effective. According to the data mining industry itself, "research has shown that winning just one more prescription per week from each prescriber yields an annual gain of $52 million in sales."[3]

How Does Data Mining Work?

When a patient fills a prescription at a major pharmacy, a record of that prescription (minus patient name) is sold to companies – so-called *health information organizations* – that pool information from multiple pharmacies. The bundled information is combined with individual physician identities purchased from the American Medical Association to create prescriber profiles (name, specialty, practice site, which and how many prescriptions written, etc.) that are sold to the drug companies.

Drug companies then give the information to their salespeople, who use it to tailor marketing strategies, messages, gifts and other inducements for individual physicians.[iii] As a result, many patients are prescribed expensive medicines that are no better, and may be worse, than other available medicines or non-pharmacological therapies.[iv]

For example, Dendrite International touts its data mining product as follows: "[N]ow, pharmaceutical manufacturers who partner with Dendrite can gain a level of insight that allows them to predict and influence physician prescribing behavior like never before."[v]

Addressing the Problem

Physician organizations, patient advocacy groups, and legislators have highlighted problems associated with data mining and have taken steps to minimize its use for commercial marketing purposes in the following states:

New Hampshire: The Prescription Privacy Law (2006) prevents patient and prescriber identifying data from being sold or used for advertising, marketing, promotion or any activity intended to influence sales or market share of a pharmaceutical product (http://www.gencourt.state.nh.us/rsa/html/XXX/318/318-47-f.htm). The law was passed as a consumer protection and public health measure, and seeks to ensure privacy in prescribing.

Vermont: As part of a comprehensive package to control the costs of prescription drugs and regulate inappropriate marketing tactics, Vermont recently passed legislation that provides strong privacy protections by limiting the use of personally identifiable prescription information for marketing purposes unless doctors and other health care providers explicitly agree to waive the protections. The law includes a physician *opt-in* provision at the time of licensure or renewal.

This provision, managed by the state's professional licensing board, allows a prescriber to choose to have his or her identifying information used for marketing and promotion of prescription drugs. The Vermont Medical Society supports the measure.[vi]

Maine: Maine also passed legislation requiring its Board of Licensure to include confidentiality protection of prescribing data as part of its licensure and license

renewal process.[vii] The Board must inform applicants that their prescription drug information is used for marketing purposes and how the prescribers may "opt out," a weaker alternative to the prescribing data protection systems in Vermont and New Hampshire.

Other states, including Hawaii, Maryland, Massachusetts, Nevada, New York, Washington, and the District of Columbia, have introduced legislation to limit data-mining.

All existing or proposed legislation restricts only the sale and use of patient or prescriber data specifically for marketing or commercial purposes. They do not restrict the sale and use of such identifiable data for other purposes, including for insurance reimbursement, dispensing prescriptions, utilization review, public health research, law enforcement purposes, controlled substances monitoring, adverse effects reporting, or compliance with Medicaid or private insurance formularies and rules.

The AMA's inadequate response

The response of the American Medical Association (AMA) to concerns about data-mining has been weak. The AMA plays a key role in enabling the data-mining industry by selling its physician database to data-mining companies. The AMA "Physician Masterfile" contains the name, identity, practice location, training site, licensure and disciplinary history for nearly every U.S. physician[viii] – even the two-thirds of doctors who are not AMA members. Sale of Masterfile data brought the AMA $44.5 million in 2005. Although the AMA initiated an option in 2006 to allow physicians to "opt out" of this program, the process is cumbersome and few physicians are aware of the option. Moreover, even when a doctor "opts out," the AMA continues to sell that doctor's personally identifiable prescribing information. Pharmaceutical companies may still use the information to target their marketing efforts, as long as they pledge not to provide that individual prescriber's data directly to salespeople. Furthermore, the collection of prescribing data and identities through pharmacies is not affected by the AMA policies.

Industry Challenges

The data mining industry has challenged the New Hampshire, Maine, and Vermont statutes. The Federal District Court of New Hampshire overturned the law on constitutional free speech grounds. The State of New Hampshire appealed the decision, asserting that the state has a substantial interest in protecting the confidentiality of prescriber data from use for drug marketing purposes. On November 19, 2008, the Court of Appeals for the First Circuit overturned the ruling of the district court, and unanimously upheld the New Hampshire law. The Court found that the law regulates conduct, rather than protected speech, and that it is further justified by the state's substantial interest in promoting containment of prescription drugs costs.

"There is a second basis for our decision. Even if the Prescription Information Law amounts to a regulation of protected speech — a proposition with which we disagree

— it passes constitutional muster. In combating this novel threat to the cost-effective delivery of health care, New Hampshire has acted with as much forethought and precision as the circumstances permit and the Constitution demands."[ix]

The challenge in Maine is covered by the First Circuit's ruling and it is therefore very likely that the Maine law will be upheld. The Vermont lawsuit is governed by the law of the Second Circuit Court of Appeals, which has not yet ruled on this issue. That lawsuit will continue, although it is likely to be affected by the forceful reasoning of the First Circuit panel in the New Hampshire case.

The data mining and pharmaceutical industries have also opposed these initiatives in state legislatures. They argue that allowing companies like IMS and Verispan to profit from collecting and analyzing individual prescriber data for marketing purposes serves a public interest because it is then available (at a price) for research and to track drug safety problems.[x] However, all state legislation passed or proposed explicitly allows for the collection of this data for non-marketing purposes, and the data are available for such purposes through other sources, such as pharmacies, Medicare and Medicaid.

Other materials on data mining, including a legal analysis, model policy, policy brief, and a myths and rebuttals piece are available on the Prescription Project website and http://www.reducedrugprices.org/advertising.asp

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May 4, 2006

Doctors Object to Gathering of Drug Data

By STEPHANIE SAUL

Although virtually unknown to consumers, the information has long been considered the most potent weapon in pharmaceutical sales — computerized dossiers showing which physicians are prescribing what drugs. Armed with such data, a drug sales representative can pressure a doctor to write more prescriptions for a name-brand medicine or fewer orders for a competitor's drug.

But now a rebellion is under way by some doctors, who consider the data-gathering an intrusion that feeds overzealous sales practices among the nation's estimated 90,000 drug company representatives. Public officials are also weighing in. A vote on a state bill to clamp down on the practice is scheduled for today in New Hampshire, and similar bills have been introduced in other states, including Arizona and West Virginia.

To appease the doctors and try to stave off the state restrictions, the American Medical Association will soon give individual physicians the choice of declaring their prescription records off limits to drug sales representatives. The new measure is viewed as a self-policing move that the drug industry and the A.M.A., which has lucrative contracts with data-mining companies, hope will keep states from banning sales of prescription data altogether.

If the A.M.A effort succeeds, "legislators will turn their attention elsewhere, and the industry can hang on to one of its most valuable data sources," according to an article this week in the industry trade magazine Pharmaceutical Executive, which was co-written by an A.M.A. official and an executive with the leading vendor of prescription data. Even many critics concede that patients' privacy is apparently not an issue, because the tracking systems identify only the prescribing doctors, not patients. But many doctors find the use of the data by sales representatives an intrusion into the way they practice medicine.

"These doctors were outraged that people came into their office and talked to them about how many times they prescribed a particular drug," said Dr. John C. Lewin, the chief executive of the state medical association in California, one of the states where complaints about the current system arose.

The California group is beginning its own program under which doctors who do not opt out under the A.M.A. system will get comparisons of their prescribing patterns in 17 classes of drugs from the data companies, said Dr. Lewin, who added that the program was being started as a pilot effort that he hoped would be extended statewide.

Among the doctors who raised an early complaint about the system was Dr. Brad Drexler, an obstetrician in Healdsburg, Calif., who said he was surprised four years ago when pharmaceutical representatives began thanking him for writing prescriptions — the first time he realized that the drug representatives had information he assumed was private.

"I think it adds to the potential that physicians could be targeted one way or another for perks," said Dr. Drexler, alluding to the practice by drug companies of deciding which doctors to reward with the gifts, meals and other

perks that sales representatives have dangled over the years, or to gauge which physicians might be worthy of signing up as paid speakers or consultants.

"It's the most powerful tool a drug rep has, for sure," said Jamie Reidy, a former drug salesman who was fired last year by Eli Lilly & Company after writing "Hard Sell," a humorous exposé of the pharmaceutical industry. Mr. Reidy said the pharmaceutical representatives received updated prescription data every two weeks. The information also sometimes characterizes each physician's prescribing patterns, Mr. Reidy said.

For example, "early prescribers" — also known among drug representatives as "cowboys," according to Mr. Reidy — are those doctors who start prescribing a drug as soon as it comes to market. If you are a drug sales representative, "you go to see that doctor in the first week," Mr. Reidy said.

Although the drug representatives are told not to share the prescribing details with doctors, some nonetheless have confronted doctors with the data. A representative might become frustrated, for example, if after providing numerous lunches to a doctor's staff, the data show that the doctor is not writing prescriptions for the company's drug.

"It just creates a weird atmosphere," Mr. Reidy said.

State Representative Cindy Rosenwald of New Hampshire, lead sponsor of her state's bill, said she was motivated partly by high Medicaid drug costs, which she said she believed had been driven up by the pharmaceutical industry's success in coaxing doctors to prescribe expensive brand-name drugs.

"To me this is a money issue," Ms. Rosenwald said. "When I look at our state's budget, the fastest-growing part of the Medicaid program here in New Hampshire is for prescription drugs. It's an enormous cost for a small state like New Hampshire."

Ms. Rosenwald's legislation has been adopted by the New Hampshire House and is tentatively set for a Senate vote this afternoon.

She said she did not believe the A.M.A.'s self-policing measure would provide enough protection, partly because even if doctors specify that their prescription records not be available to drug sales representatives, the information would still be sold to drug companies for other marketing and research purposes. The drug companies, she said, would be on their honor not to share the data with their sales staffs. A Gallup Poll commissioned by the A.M.A. in 2004 found that two-thirds of doctors surveyed were opposed to the release of such data to pharmaceutical representatives, and that 77 percent felt that an opt-out program would alleviate concerns about the release of data. Nearly a quarter of the doctors were not even aware that the pharmaceutical industry had access to such information.

That same year, the American College of Physicians requested that the A.M.A. prohibit the release or sale of doctors' prescribing information. The college represents internists and related medical subspecialties, while the A.M.A. is a broader trade group whose members include all doctors, including surgeons.

Dr. Dean Abramson, an Iowa physician, is among the doctors who plan to opt out under the new A.M.A. process, which will involve a sign-up registry that goes into use on July 1. His opposition began nearly a decade ago, he recalled, when a representative from TAP Pharmaceutical Products let slip during a sales call that Dr. Abramson

wrote more prescriptions for Prevacid, a treatment for acid reflux, than any other doctor in the state.

"I was pretty surprised that they kept that data, and I was not happy at all," Dr. Abramson said. "I said, 'Why is that data even kept?' She didn't really give me an answer."

Since then, Dr. Abramson has become something of an activist against the lunches and gifts that the pharmaceutical industry dispenses to doctors. His gastroenterology group in Cedar Rapids, Iowa, accepts neither, he said.

The leading compiler and vendor of prescription data is IMS Health, a publicly traded company based in Fairfield, Conn., that had revenue last year of $1.75 billion. IMS and its competitors gather the data through contracts with retail pharmacy chains and companies that manage drug plans for insurers, then sell it to pharmaceutical companies.

IMS and its competitors — the main ones are Verispan, Dendrite International and a Dutch company, Wolters Kluwer — also pay the A.M.A. for access to its repository of information on approximately one million doctors who are graduates of American medical schools, as well as foreign medical school graduates licensed in the United States.

The A.M.A., which calls this repository Masterfile, begins collecting the information when a doctor enters medical school. Over doctors' careers, additional material includes information on their board certifications, types of practice and disciplinary records. The Masterfile information is among data that companies like IMS use in developing physician profiles.

In an interview, IMS officials said they believed that state efforts to curtail their activities were misguided. "Limiting the access to our data will not stop pharmaceutical marketing," said Robert J. Hunkler, whose job with the company includes serving as a liaison with the medical profession. Mr. Hunkler also says that the data his company collects is valuable for medical research and is sometimes shared free with researchers.

Mr. Hunkler was a co-author of the Pharmaceutical Executive article describing the new A.M.A. program. The other writer was Robert A. Musacchio, the A.M.A.'s senior vice president for publishing and business services. While Mr. Musacchio declined to disclose the exact value of its Masterfile contracts with the four main data companies, he said that the organization made $40 million a year selling information, which also includes mailing lists and a service through which hospitals can check the credentials of doctors. Mr. Musacchio said that doctors had always been able to put a "no contact" status on their Masterfile record, meaning their name would not be licensed for marketing by mail, telephone or fax.

The A.M.A.'s new registry, administered partly through a Web site, will enable doctors listed in its Masterfile to indicate that they do not want their prescribing data shared with pharmaceutical sales representatives. The decision will remain in force for three years.

And yet, even those doctors' prescription information will still be collected and transmitted to drug companies, whose other uses of the data include tallying bonuses paid to pharmaceutical representatives, which are based on sales. "What we've always stressed is that physicians have rights and they can always tell pharmaceutical representatives that they don't want to be called upon," said Mr. Musacchio. But he said the organization had

always made clear to the pharmaceutical industry that its representatives should never "badger or embarrass or harass" physicians.

"They sometimes try to get their point across a little too strongly," he said.

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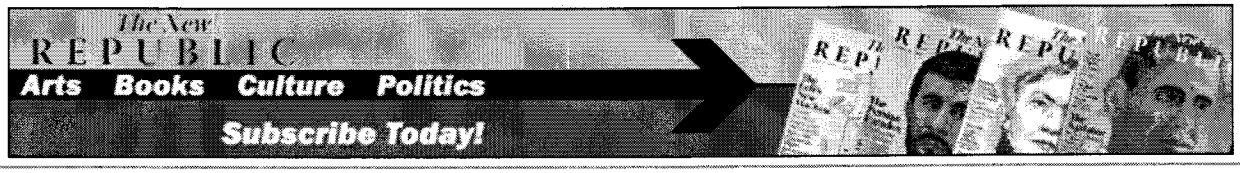

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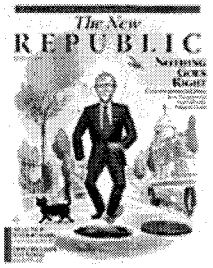

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HOW DRUG REPS KNOW WHICH DOCTORS TO TARGET.

Big (Brother) Pharma

by Jake Whitney
Only at **TNR Online** | Post date 08.29.06

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For years Dr. Peter Klementowicz suspected that pharmaceutical sales representatives knew more about the prescriptions he was writing than they let on. Klementowicz, a cardiologist in Nashua, New Hampshire, would occasionally hear curious statements from drug reps, such as, "you're one of my targets." His suspicion peaked when a friend told him she overheard a group of reps at a local Panera Bread discussing ways to induce Klementowicz to prescribe their drugs. How did they know he wasn't *already* prescribing their drugs? It wasn't until last year, after Klementowicz's wife stumbled upon a two-year-old newspaper article, that he learned what more and more doctors are also just discovering: Drug companies know almost everything about which physicians prescribe which drugs and how often.

Klementowicz's case is unusual: His wife, Cindy Rosenwald, is a New Hampshire state representative. The revelation that drug reps knew about his prescribing habits prompted her bill--signed into law by Governor John Lynch this summer--that bans the sale for commercial use of prescription data throughout the state. Rosenwald's bill was the first of its kind to become law, but several other states are considering regulating what they increasingly see as an onerous practice. And it's not hard to see why.

For more than a decade, drug companies have been tracking physicians' prescription records. It helps their bottom line immensely by allowing their sales reps to hound and ply physicians who, they believe, are underprescribing their drugs. But the practice is only just starting to receive widespread attention. In fact, a 2004 survey sponsored by the American Medical Association (AMA) found that about 25 percent of doctors were still unaware of the practice. And they're not all happy about it, either. Some doctors see it as disruptive of their professional prerogatives. Others resent the violation of their privacy. But the real effects may be far worse than the physician outcry suggests. The real problem is financial: skyrocketing drug prices. Buying and selling prescription records is a lucrative business, and, perhaps as no other factor, it inflates the cost of drugs.

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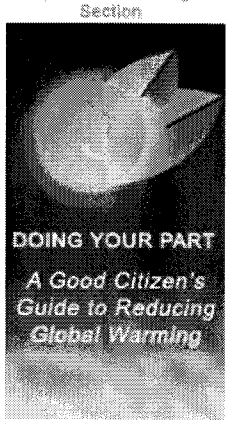
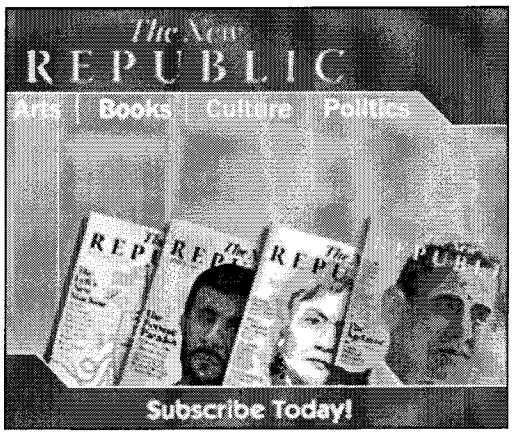


companies get prescription data in a few different ways. One is by buying the information from companies like IMS Health, which purchases and sorts records from pharmacies, hospitals, nursing homes, and insurance companies. This, itself, is a profitable business. Last year, IMS Health earned $1.75 billion in revenue--$848 million from "Sales Force Effectiveness" offerings. To help them understand pharmacies' records, drug companies must also access an AMA database called the "Physician Masterfile." This file is a detailed professional history of every physician in the United States, and it contains such unique identifiers as license and Drug Enforcement Agency numbers--which drug companies use to match doctors to prescription records, since not all records contain the doctor's name (patient names are always excluded).



Proponents of the practice--including the AMA, the pharmaceutical industry, and data-mining companies--say prescription data is crucial for research purposes. (In an e-mailed statement, Ken Johnson, senior vice president of PhRMA, the pharmaceutical lobby, said that the data has been used in a study by the Centers for Disease Control and Prevention to "reduce unnecessary prescribing" of antibiotics.) The real explanation is that it's quite good for the bottom line: It creates a cottage industry for middlemen like IMS Health and nets extra revenue at little cost for the AMA. (The organization wouldn't say how much it made from the lease of its Masterfile, but, according to its annual report, the group earned $44.5 million in 2005 from the sale of "Database Products.") But the real benefit is for drug companies, which collect the data because it allows them to target their marketing efforts on specific physicians with pinpoint accuracy (instead of only advertising in broad-penetration venues like medical journals and conferences).

A drug company's marketers can tell from the data not only how much of its drugs Dr. X is prescribing, but also whether Dr. X is a "high prescriber" in that drug class--which tells them if it should target Dr. X at all. Kathleen Slattery-Moschkau, a former rep who worked for Johnson & Johnson and Bristol-Myers Squibb, told me that the data was "sliced and diced" into various reports, such as the "Heavy Hitter List," which included the top physicians she should seek to "convert." "When I took Dr. Smith to dinner at that fancy restaurant," she says, "I could look at the following week's numbers to see if it had an impact. If not, I could try a different approach."

Jamie Reidy, a former Pfizer and Eli Lilly rep who skewered his erstwhile profession last year in *Hard Sell*, says prescription data "was our greatest tool in planning our approach to manipulating doctors." Reidy used prescriber reports to hone his sales tactics, which included befriending top physicians and wooing their office staffs. If the data showed that a particular doctor was a target physician, Reidy might treat the nursing staff to cocktails, where he'd make it clear that, if the doctor

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prescribed his drug over the competitors', "they'll be having regular happy hours." Slattery-Moschkau says that top prescribers are not only "targeted, wined, and dined," but also called upon repeatedly by different reps about the same drug. The idea is that each rep can bond with the doctor in a different way. "One might be a female who's kind of a looker, one might be a sports person who would bring [the doctor] to the game, one might be more analytical."

But tactics like these are expensive, and, while they may spike sales, the marketing expenditures also spike costs. The "extras" that reps give their top prescribers include expensive lunches and dinners, gift certificates, and fees for speaking at ostensibly educational events--all of this on top of the ubiquitous promotional trinkets that virtually all physicians receive, such as pens, notepads, mouse pads, tote bags, umbrellas, and stuffed animals. Faced with incentives like these, doctors often prescribe brand-name drugs where cheaper generics might have worked--and that is driving up insurance premiums and co-pays.

Skyrocketing prescription costs were a driving force behind Rosenwald's bill, and California, Arizona, Hawaii, and West Virginia have also considered restricting drug companies' access to the data. According to a spokesman for West Virginia's Office of the Pharmaceutical Advocate, although no legislation has yet been proposed, the state is "taking a look" at regulating the use of prescription data as a means for controlling drug costs. And, in California, negotiations over a bill like Rosenwald's have resulted in a unique program that will allow physicians to "opt out" of having their physician-specific data released to salespeople. But companies like IMS Health hope to discourage doctors from the opt-out with enticements of their own, such as educational newsletters, patient compliance reports, and data packages containing the prescribing information of physicians in their region and specialty.

The AMA has responded in two ways. First, it defends the practice as not only crucial to research, but also as a way for drug companies to actually *reduce* marketing costs. In a recent article for *Pharmaceutical Executive* magazine, the AMA's Robert Musacchio and IMS Health's Robert Hunkler argued that access to prescription data reduces drug costs by allowing "pharmaceutical promotion to be relevant and specific, making the whole process more cost-effective." While, on the surface, this argument seems to have merit, it fails to take into account the cost of the data itself on drug prices. And its implication that only certain physicians are targeted (while others are not) is false. Certainly--as reps like Reidy and Slattery-Moschkau explained--top prescribers are "targeted" more than lower-prescribing physicians. But this doesn't mean the latter are ignored by drug companies.

Second, the AMA has responded with its own "opt-out" program, known as the Prescribing Data Restriction Program (PDRP). Since July 1, the AMA has given physicians across the country the right to request that their physician-specific data be withheld from drug representatives. But critics of the AMA's opt-out, such as Rosenwald, say it is insufficient and fraught with holes--and, in light of the AMA's financial interest in the practice, it's just a self-policing measure intended to avoid more legislation. The authors of the *Pharmaceutical Executive* article even admit that avoiding more legislation is a goal: "If [the rules of the program] succeed, legislators will turn their attention elsewhere, and the

industry can hang onto one of its most valuable data sources."

And there are other worries about the PDRP. For one, prescription data will continue to be made available to drug companies, including their marketing departments--just not reps and their direct supervisors--so drug firms will be on the honor system to keep the data from salespeople. This could give rise, as Rosenwald points out, to executives "winking" at reps or giving other tacit signals to go after targeted physicians. Another problem is that compliance will be measured strictly by physician complaints. This means, conceivably, that companies could continue to provide reps with the data; they would just need to better hide it from doctors. Finally, and most significantly, the PDRP does not offer any potential reduction in drug costs. Whether or not pharmaceutical companies adhere to PDRP rules, they will still spend millions on the records and the Masterfile, which, as always, will be reflected in higher drug prices. Clearly the PDRP is not the answer.

While prescription data can be beneficial for research purposes--like locating appropriate physicians for clinical trials--patients do not benefit from drug companies' access to the data. As Slattery-Moschkau told me, "prescriber reports are a perfect example that the industry's direct-to-physician advertising has little or nothing to do with what is in the best interest of the patient. It's all about market share and grabbing market share from our competitors." Since the industry can't be trusted to police itself, only bills like Rosenwald's can make drug companies focus on research and development rather than conspiratorial Panera Bread bull sessions. And that's just fine by Peter Klementowicz.

JAKE WHITNEY is a freelance writer in New York.

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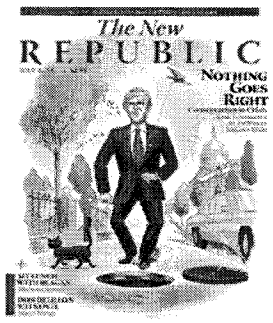

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Doctors, Legislators Resist Drugmakers' Prying Eyes

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By Christopher Lee
Washington Post Staff Writer
Tuesday, May 22, 2007; A01

Seattle pediatrician Rupin Thakkar's first inkling that the pharmaceutical industry was peering over his shoulder and into his prescription pad came in a letter from a drug representative about the generic drops Thakkar prescribes to treat infectious pinkeye.

In the letter, the salesperson wrote that Thakkar was causing his patients to miss more days of school than they would if he put them on Vigamox, a more expensive brand-name medicine made by Alcon Laboratories.

"My initial thought was 'How does she know what I'm prescribing?' " Thakkar said. "It feels intrusive. . . . I just feel strongly that medical encounters need to be private."

He is not alone. Many doctors object to drugmakers' common practice of contracting with data-mining companies to track exactly which medicines physicians prescribe and in what quantities -- information marketers and salespeople use to fine-tune their efforts. The industry defends the practice as a way of better educating physicians about new drugs.

Now the issue is bubbling up in the political arena. Last year, New Hampshire became the first state to try to curtail the practice, but a federal district judge three weeks ago ruled the law unconstitutional.

This year, more than a dozen states have considered similar legislation, according to the National Conference of State Legislatures. They include Arizona, Illinois, Kansas, Maine, Massachusetts, New York, Nevada, Rhode Island, Texas, Vermont and Washington, although the results so far have been limited. Bills are stalled in some states, and in others, such as Maryland and West Virginia, they did not pass at the committee level.

The concerns are not merely about privacy. Proponents say using such detailed data for drug marketing serves mainly to influence physicians to prescribe more expensive medicines, not necessarily to provide the best treatment.

"We don't like the practice, and we want it to stop," said Jean Silver-Isenstadt, executive director of the National Physicians Alliance, a two-year-old group with 10,000 members, most of them young doctors in training. (Thakkar is on the group's board of directors.) "We think it's a contaminant to the doctor-patient relationship, and it's driving up costs."

The American Medical Association, a larger and far more established group, makes millions of dollars each year by helping data-mining companies link prescribing data to individual physicians. It does so by licensing access to the AMA Physician Masterfile, a database containing names, birth dates, educational background, specialties and addresses for more than 800,000 doctors.

After complaints from some members, the AMA last year began allowing doctors to "opt out" and shield their individual prescribing information from salespeople, although drug companies can still get it.

So far, 7,476 doctors have opted out, AMA officials said.

"That gives the physician the choice," said Jeremy A. Lazarus, a Denver psychiatrist and high-ranking AMA official.

Some critics, however, contend that the AMA's opt-out is not well publicized or tough enough, noting that doctors must renew it every three years.

The New Hampshire court's ruling has raised new doubts about how effective legislative efforts to curb the use of prescribing data will be, but the state attorney general has promised to appeal. And state Rep. Cindy Rosenwald (D), the law's chief sponsor, vowed not to give up the fight.

"In this case, commercial interests took precedence over the interests of the private citizens of New Hampshire," Rosenwald said. "This is like letting a drug rep into an exam room and having them eavesdrop on a private conversation between a physician and a patient."

The April 30 ruling by U.S. District Judge Paul Barbadoro, nominated to the federal bench in 1992 by President George H. W. Bush, called the state's pioneering law an unconstitutional restriction on commercial speech.

Since at least the early 1990s, drug companies have used the data to identify doctors who write the most prescriptions and go after them the way publishers court people who subscribe to lots of magazines. They zero in on physicians who prescribe a competitors' drug and target them with campaigns touting their own products. Salespeople chart the changes in a doctor's prescribing patterns to see whether their visits and offers of free meals and gifts are having the desired effect.

"It's a key weapon in determining how we want to tailor our sales pitch," said Shahram Ahari, a former drug detailer for Eli Lilly who is now a researcher at the University of California at San Francisco's School of Pharmacy. "The programs give them [doctors] a score of 1 to 10 based on how much they write. Once we have that, we know who our primary targets are. We focus our time on the big [prescription] writers -- the 10s, the 9s, and then less so on the 8s and 7s. . . . We're dealing with individual physicians who might give us the biggest dividend for our investment."

Ahari said he used the data to tout the virtues of Eli Lilly's antidepressant Prozac to doctors who favored the rival drug Effexor -- noting, for example, that its longer half-life meant that if patients missed a dose over a weekend, they would experience less severe agitation and other withdrawal symptoms that might prompt them to call their doctor. He did not mention the rival drug by name or disclose that he knew the physician's prescribing habits, he said.

Data-mining companies and the pharmaceutical industry argue that the practice has value far beyond the corporate bottom line. The information helps companies, federal health agencies and others educate physicians about drugs, track whether prescribing habits change in response to continuing medical education programs, and promote higher-quality care, they say. They stress that patient names are encrypted early in the process and cannot be accessed, even by the data-mining companies.

A drug company might use the database to help determine whether physicians prescribing a particular high-risk drug have undergone required training about the medicine, said Marjorie E. Powell, senior assistant general counsel for the Pharmaceutical Research and Manufacturers of America, a trade association.

"If you don't have that information, then you are in a very difficult situation," Powell said. "There is no way you can implement the risk-management plan that the FDA [Food and Drug Administration] is requiring you to implement in order to allow the drug to be on the market."

The prescribing data also let "the company do more targeted marketing, which lowers the total costs of

its marketing," she said.

Randolph Frankel, a vice president at IMS Health Inc., the Connecticut-based health-data-mining company that challenged the New Hampshire law, said the more a drug representative knows about a physician, the easier it is to provide information that meets the needs of the doctor's practice.

"We are about more information and more education, and not less," said Frankel, whose company had operating revenue of $1.75 billion in 2005, not all of it from sales to drugmakers. "The vast majority of physicians welcome these people as part of the overall educational process about drugs and their use. And any doctor in the country can close the door to these sales reps. It doesn't require legislation to do that."

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Drugmakers, Doctors Get Cozier

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Gifts Continue, Contacts Increase Despite Guidelines

By Christopher Lee
Washington Post Staff Writer
Sunday, April 29, 2007; A03

Despite efforts to curb drug companies' avid courting of doctors, the industry is working harder than ever to influence what medicines they prescribe, sending out sales representatives with greater frequency and plying physicians with gifts, meals and consulting fees, according to several new papers.

One study published in the New England Journal of Medicine last week found that 94 percent of doctors have some type of relationship with the drug industry -- most commonly accepting free food or drug samples, which about 80 percent of physicians did. More than one-third of the 1,662 physicians who responded to a survey conducted from November 2003 to June 2004 reported being reimbursed by the drug industry for costs of going to professional meetings or continuing medical education, and 28 percent said they had been paid for consulting, giving lectures or signing up patients for clinical trials.

Two other papers examined in detail the strategies that pharmaceutical representatives, or "detailers," use and how effective the industry is at influencing doctors.

"We now know that virtually every doctor in the United States has some form of relationship with the pharmaceutical industry," said Eric G. Campbell, lead researcher of the New England Journal of Medicine study and an assistant professor of medicine at Harvard Medical School. "They are common. A quarter receive honoraria or some form of payment for their services, and that was much higher than we expected."

Contacts between doctors and drug salespeople have jumped from the average of 4.4 per month reported in 2000, Campbell and other researchers found. In the survey period, drug representatives met with family practitioners an average of 16 times a month, with cardiologists and internists nine or 10 times a month, with pediatricians eight times a month and with surgeons four times a month. Only anesthesiologists, who saw the representatives twice a month, appear to be meeting with the industry less often than before, the study found.

As those numbers suggest, the companies shower more attention on certain doctors, the researchers said. Cardiologists -- whose prescribing patterns tend to influence primary care doctors -- were more likely to be paid for consulting and other services than were family practitioners, pediatricians, anesthesiologists and surgeons, the study found.

"When I send somebody to a cardiologist, if he puts somebody on a medicine, I'm not going to change it," said co-author David Blumenthal, a general internist and the director of the Institute for Health Policy at Massachusetts General Hospital in Boston. "If they use a particular agent, I'm more likely personally to prescribe that agent because I figure the guy is an expert and he has got some reason for picking that brand as opposed to some other brand."

The ties between doctors and drug companies are deepening despite voluntary guidelines to curb excesses, adopted in 2002 by the American Medical Association, the American College of Physicians, the Accreditation Council for Continuing Medical Education and the Pharmaceutical Research and Manufacturers of America. The inspector general of the Department of Health and Human Services issued similar guidance in 2003.

Under the industry code, gifts must be worth less than $100 and should primarily benefit patients -- items such as stethoscopes or medical dictionaries. Meals should be "modest" in cost, and a physician's spouse should not be included. Gifts of cash or tickets to sporting events are inappropriate. Consulting arrangements must be for real services, and doctors should not be paid for listening to marketing pitches.

"Clearly, adequate safeguards are already in place," Ken Johnson, senior vice president of the drug industry association, said in a statement. "The goal is to make sure the focus of conversations between company representatives and physicians remains providing accurate information about medicines."

A former industry insider, however, painted a different picture in an article last week in PLoS Medicine, a journal published by the Public Library of Science. Shahram Ahari, a former drug company representative, and physician Adriane Fugh-Berman wrote that the estimated 100,000 representatives who visit doctors' offices look for details such as family photos or hobbies that they can use to forge a relationship. They use food, gifts and money to make often-overworked doctors feel more appreciated -- and more loyal to the company's drugs. If a physician will not meet with them, the representatives often woo the office staff with flattery and meals.

"Pharmaceutical gifting . . . involves carefully calibrated generosity," Ahari and Fugh-Berman wrote. "Many prescribers receive pens, notepads, and coffee mugs, all items kept close at hand, ensuring that a targeted drug's name stays uppermost in a physician's subconscious mind. High prescribers receive higher-end presents, for example, silk ties or golf bags."

Drug companies also purchase prescription records from pharmacies and, with the help of an American Medical Association database, identify individual physicians' prescribing patterns and rank doctors based on how many prescriptions they write, the authors wrote.

The tactics work. Another study in PLoS Medicine last week found that visits by detailers prompted nearly half of 97 physicians to increase prescriptions of gabapentin, a drug approved to treat seizures. In many cases, the drug representatives were pushing non-approved, or "off-label," uses of the drug, the study found.

A study in the Journal of General Internal Medicine in February found that physicians in focus groups said that they understand the potential conflicts of interest but that they still view their meetings with drug detailers as informative and appropriate. Such findings suggest that voluntary guidelines are inadequate, researchers wrote.

In an interview, one District-based physician, orthopedic surgeon Peter E. Lavine, said that drug representatives used to visit his office daily but have cut back in recent years to stopping by about twice a week. The conduct guidelines have eliminated most excesses, Lavine said, and many doctors view the sessions as a way to learn about side effects and how drugs compare.

"The vast majority of physicians appreciate the information but find them [detailers] as a nuisance," said Lavine, chairman of the Medical Society of the District of Columbia.

"They always tend to come in the middle of the day when you are busy seeing patients, and it's very difficult to break away and talk to them. And if they've bought lunch for the staff, then you are sort of obligated to give them a little bit of your time. I think they certainly have a valuable educational benefit. I don't think that physicians are going to change their prescribing patterns for free samples."

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AMA faces storm on data sales

Doctor groups ask: Is prescription info used to improve safety or to boost sales?

By Bruce Japsen
Tribune staff reporter

Advertisement

June 24, 2007

How do pharmaceutical companies know which doctors prescribe the latest and most expensive brand name drugs?

They have inside information on the prescribing habits of virtually every doctor in the United States. Pharmaceutical and device manufacturers buy this information from the American Medical Association and from companies that match the AMA's data with pharmacy records.

While such practices have gone on for years, the issue is expected to be a hot topic at this week's annual meeting of the AMA in Chicago, with some groups planning to protest during the gathering at the Hilton Chicago.

"Doctors are not aware that companies are out there that know every prescription a doctor prescribes," said Dr. John Santa, an internist at the Portland Veterans Affairs Medical Center and consultant to the Prescription Project, which is part of a coalition trying to curb drug companies' access to doctor prescribing information.

"Consumers should care because here's this very effective information and data system that is not being used to improve quality or safety of their care but to increase the sales of specific drugs, many of which are no more effective than much-cheaper alternatives," Santa said. "If these data-mining companies use this information in a systematic way to improve safety or quality, that would be different. But they don't. They use it for sales, and most doctors don't even know it's there."

The controversy also has triggered bills in more than a dozen state legislatures, including Illinois, as lawmakers see a worrisome connection between the release of such data to the drug and device manufacturers and consumers' rising health-care costs.

In its defense, the AMA says such information has been available for years and has helped get public health and education to the right doctors when new products or devices have come on the market. The AMA also says its contracts with data-mining companies allow doctors who do not want certain information shared to "opt out" of what

is sold to commercial interests.

Patient information is not included in the AMA records, but its Masterfile includes profiles of more than 900,000 physicians, two-thirds of whom are not members of the AMA. Revenue generated from the Masterfile is an undisclosed part of the more than $44 million the association reaped in 2005 from sales of data licensing and credentialing services.

More current information is not yet available.

Opposition to the data sales comes from a coalition of doctor groups, including the Prescription Project, the American Medical Student Association and the National Physicians Alliance. The group plans to stage protests as well as handing out fliers advocating an end to the AMA's practices.

"The average doctor has no idea that this is going on," said Dr. Michael Mendoza, clinical assistant professor in the department of family medicine at the University of Chicago's Pritzker School of Medicine who is involved in the Prescription Project.

"If doctors are unaware it happens, they aren't in a position to choose," Mendoza said. "It's a practice that flies under the radar of most docs. At least two-thirds of doctors do not know that this goes on because they are not members of the AMA."

Under pressure from member doctors about its role in selling its database to companies that do business with the drug industry, the AMA last year began allowing doctors to opt out of having their information sold, through the creation of a "physician data restriction program."

More than 8,000 doctors have opted out, and the AMA said it has launched a campaign to let physicians know they can hide their prescribing information from pharmaceutical sales reps. The physician data restriction program is prominently displayed at the AMA's Web site.

The AMA said it is also stepping up a campaign, using ads in specialty medical journals, to let doctors outside of its membership know they can opt out.

The AMA considers its data to be licensed rather than sold. So it says it can pull the plug on any licensing if it feels the information is used inappropriately.

"I think the pharmaceutical industry is on notice about physicians' concerns about this," said Dr. Jeremy Lazarus, a Denver psychiatrist and member of the AMA board.

"We are giving physicians a choice. Our main approach has been [the physician data restriction program] and this allows docs to opt out. If we were not in it, physicians would have less control in how that data is used."

The AMA's Web site also says there are other beneficial uses from selling physician prescribing data, such as "evidence-based medical research, structuring clinical trials, efficient drug recalls, aiding the Food and Drug Administration's ongoing post-approval assessment of drug benefits versus risks, and many other uses."

The AMA also said its database helped rebuild patient records lost in the floods and devastation in New Orleans and nearby Gulf Coast areas.

The AMA also pointed out that legislative initiatives to curb the use of prescribing information by commercial interests have not been all that successful.

In New Hampshire, for example, a federal judge two months ago ruled unconstitutional a "prescription information law" pushed by the state's attorney general to curb the collection and use of data identifying

doctor prescribing practices. The ruling was in favor of IMS Health Inc. and Verispan LLC, which purchased prescription data, removed information that identified patients, and combined it with data from other sources.

The information was then sold largely to the pharmaceutical industry.

But Vermont two weeks ago passed a law that allows doctors to consent to whether identifying information can be used to market or promote drugs. Maine, too, is close to enacting a law that would allow doctors to hide certain prescribing information from commercial interests, a move akin to the federal "Do Not Call" lists used to curtail telemarketing.

Companies who buy AMA data see such laws as restricting free speech.

"This new [Vermont] law incorporates the bulk of the provisions of the New Hampshire law limiting the commercial use of prescribing information that was recently struck down by a federal court," data-mining firms IMS and Verispan said in a joint statement this month. "Improvements in health-care quality, cost management and patient safety hinge on access to more health-care information, not less. These is no evidence that these kinds of restrictions on the flow of health-care information serve to lower medical costs."

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THE NEXT GREAT SCI FI EPIC

January 28, 2006

Drug Maker's Efforts to Compete in Lucrative Insulin Market Are Under Scrutiny

By GARDINER HARRIS and ROBERT PEAR

WASHINGTON — For years, Novo Nordisk, a Danish company and one of the earliest makers of insulin, has raced behind Eli Lilly to capture the lucrative insulin market in the United States.

When in 1996 Lilly started selling Humalog, a synthetic insulin with speedier blood-sugar control, Novo needed four more years to get approval to market a similar product.

When Lilly's huge sales force put Novo at a disadvantage, Novo fought back. The company hired hundreds of sales representatives. When Lilly struck a marketing deal with the Eckerd pharmacy chain, Novo responded with a partnership with Rite Aid.

But in its race, several former Novo sales representatives say, Novo may have crossed the line. Sales representatives paid at least one Rite Aid pharmacist to encourage switches from Lilly products or Novo's own lower-priced versions to higher-priced ones, according to documents and former and present company officials. Novo also paid doctors' assistants when prescriptions were switched, according to two former sales representatives.

Several former sales representatives said they were told by pharmacists and doctors' assistants that some patients first became aware of the switches when they picked up the new medicines at a pharmacy.

Officials from Novo and Rite Aid said that their activities were intended primarily to educate patients or improve care and that similar programs were common in the industry.

Karen A. Rugen, a spokeswoman for Rite Aid, said, "Our alliance with Novo Nordisk is standard industry practice." Ms. Rugen said, however, that Novo had paid one of Rite Aid's pharmacists directly, although she said that top Rite Aid executives had been unaware of the practice.

Susan Jackson, a spokeswoman for Novo Nordisk, said that the overall agreement between Novo Nordisk and Rite Aid "has benefited many people with diabetes."

Ms. Jackson would not address questions about payments made to doctors' assistants or a Rite Aid pharmacist, nor would she say how much Novo paid Rite Aid. But she said the partnership "is not unlike other agreements common in the industry that provide 'preferred status' for branded drugs."

But prosecutors are now investigating possible criminal violations. On Dec. 20, Novo said it had received a subpoena from the United States attorney for the Eastern District of New York for documents relating to its marketing practices.

The company said that it "believes that the investigation is limited to its insulin products." The subpoena indicated that "the documents are necessary for the investigation of potential criminal offenses," the company said.

Drug companies may pay for consulting or educational services, but federal anti-kickback statutes prohibit them from offering financial incentives to doctors or pharmacists to encourage or reward the prescribing of particular drugs, according to a 2003 guidance from the Department of Health and Human Services.

"In short, practices that may be common or longstanding in other businesses are not necessarily acceptable or lawful" in health care, the guidance states.

A Marketing Battle

The rivalry between Novo and Lilly illustrates the efforts companies will undertake to become No. 1 in a drug market, especially for chronic diseases like diabetes, which in the United States is a $3.3 billion market annually, according to IMS Health, a pharmaceutical information and consulting company.

From a business perspective, Novo's efforts were a great success. From December 2001 through November 2005, Novo's insulin sales rose 364 percent to $963 million while Lilly's insulin sales rose only 13 percent to $1.43 billion, according to figures provided by IMS Health.

The marketing programs were detailed in dozens of internal Novo and Rite Aid documents obtained by The New York Times. Three former Novo sales representatives described the programs. These people, some of whom spoke to The Times separately from one another, do not wish their names to be used because all still work in the industry and fear retribution. Parts of the programs were also confirmed by company officials and another sales representative who allowed their names to be used. The former sales representatives would not comment on whether they had filed whistle-blower lawsuits against Novo.

In its marketing battle with Lilly, Novo's sales representatives undertook a variety of efforts to persuade doctors to prescribe Novo's insulin products, one of which was known as the "anchor in the office" program.

Under this program, Novo sales representatives established contacts in some medical offices that served many diabetics, three former sales representatives said. The contacts were generally nurses or medical assistants responsible for monitoring diabetic patients. Officially, Novo paid these "anchors" to educate patients about Novo's products.

But two of the three former sales representatives who participated in the program said that Novo paid anchors as much as $25 for each prescription they helped switch to higher-priced insulin products.

Vikki Tolbert, a Novo district sales manager, said in an interview that "people are up in arms for no reason."

"Novo, like other companies, used to have a program to reimburse nurses and medical assistants," Ms. Tolbert said. "The purpose was not to switch patients, but to educate them and train them on insulin and insulin devices."

The formal program and the payments ended several years ago, Ms. Tolbert said, but some sales representatives still wanted to have trainers, or "anchors in the office."

"We would never tell a sales rep to pay anyone," Ms. Tolbert said. "That's crazy. But some reps do things of their own volition. They are out in the field by themselves every day. Managers are not with them. A pharmaceutical company cannot know what each individual sales rep is doing."

Deals Becoming Routine

A number of drug companies are running afoul of the anti-kickback law. In October, Serono Laboratories pleaded guilty to two counts of conspiracy and agreed to pay $704 million to settle criminal charges that it engaged in an elaborate kickback scheme to encourage sales of its AIDS drug, Serostim. In 2004, prosecutors accused Pfizer of paying doctors to prescribe its epilepsy drug Neurontin, and the company pleaded guilty to two criminal charges and paid $430 million.

State and federal prosecutors are investigating scores of other criminal and civil cases of marketing abuse, all of which are under seal. The possible health consequences for patients are rarely emphasized, however. For instance, physicians say aggressive marketing of insulin products can hurt patients.

Dr. David M. Nathan, director of the diabetes center at Massachusetts General Hospital and professor at Harvard Medical School, said that switching insulin prescriptions without providing thorough counseling to patients can be dangerous.

Newer, more expensive rapid-acting insulins begin working within five minutes. Older, cheaper insulins take 30 to 40 minutes to lower blood-sugar levels. Patients who are switched from older to newer insulins without their knowledge may wait too long to eat, Dr. Nathan said.

"If their blood-sugar levels drop too low, they can become confused, lose coordination, lose consciousness and have seizures," Dr. Nathan said. "This can result in accidents and even death."

Drug makers routinely provide financial incentives to managed-care firms for greater sales, but providing similar incentives to pharmacy chains can raise legal and ethical questions in part because pharmacists' advice to patients, like that of doctors', is supposed to be based on the best interests of patients, not pharmacists.

Still, deals between drug makers and pharmacy chains are now routine. As part of these deals, drug companies pay pharmacy chains for drug promotions that can range from simple refill reminders to efforts to switch patients to higher-priced drugs. If sales then rise, payments can increase, said Jeffrey Krinsk, a lawyer in San Diego who specializes in suing over the deals.

The companies say that these arrangements benefit patients, but some pharmacy regulators disagree, saying the partnerships may result in prescriptions being switched inappropriately, hurting patients.

David R. Work, executive director of the North Carolina Board of Pharmacy, said that his board had tried unsuccessfully to restrict such deals, one of the few boards to make such an effort. The practice of pharmacy, like that of medicine, is regulated by state boards.

"These switches have nothing to do with patient interest, they're all about money," Mr. Work said.

Novo's marketing campaigns also highlight the conflicting loyalties of many health care professionals. Doctors and their staff often consult for or receive gifts from drug makers, which may affect prescribing decisions. Pharmacists sometimes suggest one drug over another to patients for financial, not medical, reasons, pharmacy regulators say.

In April 2004, Novo Nordisk sent information to its field managers and sales representatives about marketing guidelines issued by the federal government and by a trade association for the pharmaceutical industry.

After reviewing the guidelines, a Novo sales representative sent an e-mail message to Ms. Tolbert, the Novo district manager, asking, "Are we allowed to do the anchors in the office then?" Ms. Tolbert replied, "As far as I know, and in discussing it with other managers, we are allowed to compensate for patient education."

In March 2004, Ms. Tolbert sent an e-mail message to sales representatives describing the purpose of Novo's marketing efforts.

"Our goal is 50 or more scripts per week for each territory," Ms. Tolbert wrote, according to a copy of the message provided to The Times. "If you are not achieving this goal, ask yourself if those doctors that you have such great relationships with are being fair to you. Hold them accountable for all of the time, samples, lunches, dinners, programs and past preceptorships that you have provided or paid for and get the business!! You can do it!!""

Preceptorships are consulting arrangements with doctors.

After Novo announced its partnership with Rite Aid in March 2002, Ms. Jackson, the Novo spokeswoman, was quoted in Diabetes Health magazine explaining that Rite Aid pharmacists "will actively intervene to introduce Novo Nordisk products."

Novo Nordisk produces a variety of insulin products, including preloaded syringes and synthetic versions. These products are often more convenient to use but are also more expensive than standard insulin. Since diabetes is a difficult disease to manage, convenience is important. But some doctors question whether the convenience of the new products is worth the premium prices.

One Pharmacist's Role

Lawrence M. Schultz, a Rite Aid pharmacist in Maryland, was paid by Novo to identify diabetics from databases in Rite Aid pharmacies, according to the three former Novo sales representatives.

Mr. Schultz or a pharmacy technician then contacted doctors to persuade them to switch their patients to higher-priced insulin products, according to the three former sales representatives. It is not known why doctors agreed to the changes, but the sales representatives say that they may have assumed the switch was required under the patient's insurance policy.

Two former sales representatives who contracted with Mr. Schultz and hired "anchors" say that Mr. Schultz, doctors' assistants and others told them that patients often only became aware that their prescriptions had been switched to a different insulin when they arrived at the pharmacy to pick up their medicines. The sales representatives said they knew of no patients who were directly harmed by these surprise switches.

Ms. Rugen of Rite Aid acknowledged that Rite Aid has a partnership with Novo but says that "no official at Rite Aid knew that Larry Schultz," the Rite Aid pharmacist, "was being paid by Novo Nordisk."

Mr. Schultz confirmed that he had "pushed Novo Nordisk" products. He refused to give details, but said: "Everything I did was done completely ethically. The one thing I would never do is put my job, or Rite Aid, in jeopardy."

Three Novo sales representatives who described Mr. Schultz's efforts on their behalf said they knew of no other Rite Aid pharmacist who received payments directly from Novo. But internal documents from Rite Aid provided to The Times show that Rite Aid executives urged pharmacists throughout the chain to dispense Novo products.

Rite Aid encouraged pharmacists to run computerized "drug utilization reports" to identify patients who could be switched, documents show.

Rite Aid had powerful financial incentives, documents show. In a letter to Rite Aid pharmacists in February 2005, top Rite Aid executives said, "Each Novo Nordisk product we dispense brings us 20 to 40 percent better profit margin." Moreover, they said, such sales add millions of dollars to Rite Aid's "bottom line."

Ms. Jackson, the Novo spokeswoman, said the company was "pursuing this matter with great urgency" and intended "to take remedial action in the event we find violations of our policies."

Carmen Catizone, executive director of the National Association of Boards of Pharmacy, said marketing deals between drug companies and pharmacy chains had often misled doctors and hurt patients. .

"We are opposed to plans where the financial interest of the manufacturer takes precedence over the patient's health," Mr. Catizone said. "To call a physician and say that we're changing a patient's medication and make it seem as if it's on behalf of the patient when it's actually part of

this marketing deal is not right."

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June 3, 2007

After Sanctions, Doctors Get Drug Company Pay

By GARDINER HARRIS and JANET ROBERTS

A decade ago the Minnesota Board of Medical Practice accused Dr. Faruk Abuzzahab of a "reckless, if not willful, disregard" for the welfare of 46 patients, 5 of whom died in his care or shortly afterward. The board suspended his license for seven months and restricted it for two years after that.

But Dr. Abuzzahab, a Minneapolis psychiatrist, is still overseeing the testing of drugs on patients and is being paid by pharmaceutical companies for the work. At least a dozen have paid him for research or marketing since he was disciplined.

Medical ethicists have long argued that doctors who give experimental medicines should be chosen with care. Indeed, the drug industry's own guidelines for clinical trials state, "Investigators are selected based on qualifications, training, research or clinical expertise in relevant fields." Yet Dr. Abuzzahab is far from the only doctor to have been disciplined or criticized by a medical board but later paid by drug makers.

An analysis of state records by The New York Times found more than 100 such doctors in Minnesota, at least two with criminal fraud convictions. While Minnesota is the only state to make its records publicly available, the problem, experts say, is national.

One of Dr. Abuzzahab's patients was David Olson, whom the psychiatrist tried repeatedly to recruit for clinical trials. Drug makers paid Dr. Abuzzahab thousands of dollars for every patient he recruited. In July 1997, when Mr. Olson again refused to be a test subject, Dr. Abuzzahab discharged him from the hospital even though he was suicidal, records show. Mr. Olson committed suicide two weeks later.

In its disciplinary action against Dr. Abuzzahab, the state medical board referred to Mr. Olson as Patient No. 46.

"Dr. Abuzzahab failed to appreciate the risks of taking Patient No. 46 off Clozaril, failed to respond appropriately to the patient's rapid deterioration and virtually ignored this patient's suicidality," the board found.

In an interview, Dr. Abuzzahab dismissed the findings as "without heft" and said drug makers were aware of his record. He said he had helped study many of the most popular drugs in psychiatry, including Paxil, Prozac, Risperdal, Seroquel, Zoloft and Zyprexa.

The Times's examination of Minnesota's trove of records on drug company payments to doctors found that from 1997 to 2005, at least 103 doctors who had been disciplined or criticized by the state medical board received a total of $1.7 million from drug makers. The median payment over that period was $1,250; the largest was $479,000.

The sanctions by the board ranged from reprimands to demands for retraining to suspension of licenses. Of those

103 doctors, 39 had been penalized for inappropriate prescribing practices, 21 for substance abuse, 12 for substandard care and 3 for mismanagement of drug studies. A few cases received national news media coverage, but drug makers hired the doctors anyway.

The Times included in its analysis any doctor who received drug company payments within 10 years of being under medical board sanction. At least 38 doctors received a combined $140,000 while they were still under sanction. Dr. Abuzzahab received more than $55,000 from 1997 to 2005.

Drug makers refused to comment, said they relied on doctors to report disciplinary or criminal cases, or said they were considering changing their hiring systems.

Asked about the Minnesota analysis, the deputy commissioner and chief medical officer of the Food and Drug Administration, Dr. Janet Woodcock, said the federal government needed to overhaul regulations governing clinical trials and the doctors who oversaw them.

"We recognize that we need to modernize the F.D.A. approach in keeping people safe in clinical trials," Dr. Woodcock said.

Drug makers are not required to inform the agency when they discover that investigators are falsifying data, and indeed some have failed to do so in the past. The F.D.A. plans to require such disclosures, Dr. Woodcock said. The agency inspects at most 1 percent of all clinical trials, she said.

Karl Uhlendorf, a spokesman for the Pharmaceutical Research and Manufacturers of America, said the trade group would not comment on The Times's findings.

The records most likely understate the extent of the problem because they are incomplete. And the Minnesota Board of Medical Practice disciplines a smaller share of the state's doctors than almost any other medical board in the country, according to rankings by Public Citizen, an advocacy group based in Washington.

Dr. David Rothman, president of the Institute on Medicine as a Profession at Columbia University, said the Times analysis revealed a national problem. "There's no reason to think Minnesota is unique," Dr. Rothman said.

"Clinical trial investigators must be culled from only the finest physicians in the country," he said, "since they work on the frontiers of new knowledge. That drug makers are scraping the bottom of the medical barrel is an outrage."

Payments by drug companies to doctors, whether or not the doctors have been disciplined, are a matter of much debate. Drug makers and doctors say the money finances vital research and helps educate doctors about helpful medicines. But others in the medical profession say the payments are thinly disguised incentives for doctors to prescribe more, and more expensive, drugs.

Among the other doctors who were disciplined or criticized by the board and paid by pharmaceutical companies:

¶Dr. Barry Garfinkel, a child psychiatrist from Minneapolis who was convicted in federal court in 1993 of fraud involving a study for Ciba-Geigy. His criminal case made headlines across the state. From 2002 to 2004, Eli Lilly paid him more than $5,500 in honoraria, according to state records.

Dr. Garfinkel said in an interview that he had wondered why drug makers would hire him as a speaker considering his statewide notoriety. He decided that "they're hiring me to influence my prescribing habits," so he quit giving sponsored talks and taking money from drug makers, he said.

¶Dr. John Simon, a Minneapolis psychiatrist who for years shared an office with Dr. Abuzzahab and was told by the state medical board in 1994 to complete a clinical training program after it concluded in a report that he "frequently makes abrupt and drastic changes in type and dosage of medication which seem erratic, not well considered and poorly integrated with nonmedication strategies." He prescribed addictive drugs to addicts and failed to stop giving medicines to patients suffering severe drug side effects, the board concluded.

Dr. Simon earned more than $350,000 from five drug makers from 1998 to 2005 for consulting and giving drug marketing talks. Of this, Eli Lilly paid more than $314,000. Dr. Simon said in an interview that the board's action was a learning experience, and that drug makers continued to hire him to speak because "I am respected by my peers."

Asked about Drs. Garfinkel and Simon, Phil Belt, a spokesman for Eli Lilly, said that both doctors were licensed to practice medicine and that the company relied on doctors to report disciplinary actions or criminal convictions against them.

¶Dr. Ronald Hardrict, a psychiatrist from Minneapolis who pleaded guilty in 2003 to Medicaid fraud. In 2004 and 2005, he collected more than $63,000 in marketing payments from seven drug makers. In an interview, Dr. Hardrict said it was "insulting" and "ridiculous" to suggest that income from drug makers might influence doctors' prescribing habits.

"I bought the Mercedes because it has air bags, and I use Risperdal because it works," Dr. Hardrict said, referring to an antipsychotic medicine for schizophrenia. Johnson & Johnson, the maker of Risperdal, paid Dr. Hardrict more than $30,000 in 2003 and 2004.

Srikant Ramaswami, a spokesman for Johnson & Johnson, said the company removed Dr. Hardrict as a speaker in 2004 when, as a result of his conviction, his name appeared in a government database.

Asked why other drug makers continue to hire him despite a fraud conviction, Dr. Hardrict responded with an e-mail message stating only, "I will pray for you daily."

In cases involving Dr. Abuzzahab over 15 years in the 1980s and '90s, the medical board found that he repeatedly prescribed narcotics and other controlled substances to addicts, renewing one patient's prescriptions six weeks after the patient was jailed and telling another that his addictive pills should be thought of as "Hamburger Helper." He prescribed narcotics to pregnant patients, one of whom prematurely delivered a baby who soon died.

In explaining his abrupt discharge of the suicidal Mr. Olson, Dr. Abuzzahab told the medical board that "if a patient is determined to kill himself, he can't be prevented from doing it and hospitalization postpones the event," records show.

Mr. Olson's sister, Susie Olson, said Dr. Abuzzahab "had no time for my brother unless David agreed to get into a drug study. He said, 'You're wasting my time and the hospital's.' It was all about money."

Separately, the F.D.A. in 1979 and 1984 concluded that Dr. Abuzzahab had violated the protocols of every study he led that they audited, and reported inaccurate data to drug makers. He routinely oversaw four to eight drug trials simultaneously, often moved patients from one study to another, sometimes gave experimental medicines to patients at their first consultation, and once hospitalized a patient for the sole purpose of enrolling him in a study, the F.D.A. found.

Dr. Abuzzahab, 74, was president of the Minnesota Psychiatric Society and two decades ago was chairman of its continuing education and ethics committees. He would not discuss the specifics of his disciplinary record, saying he did not have the time. But in 1998 he signed an agreement with the board saying that his conduct "constitutes a reasonable basis in law and fact to justify the disciplinary action."

A simple Google search reveals Dr. Abuzzahab's 1998 medical board disciplinary file, which was reported at the time by a local newspaper and a TV station. In 1998, The Boston Globe featured Dr. Abuzzahab in a front-page article questioning the safety of psychiatric drug experiments. And in 1999, the NBC program "Dateline" did a segment about a woman who committed suicide while in a drug experiment he supervised.

In June 2006, the medical board criticized Dr. Abuzzahab, this time for writing narcotics prescriptions for patients he knew were using false names, a violation of federal narcotics laws.

Despite all this, drug makers continued to hire him. Dr. Abuzzahab's résumé lists 11 publications or research presentations since 2000, when the medical board lifted its restrictions on his license.

Takeda, a Japanese drug maker, confirmed that Dr. Abuzzahab was doing a study financed by the company on its sleep medicine, Rozerem. Eisai, another Japanese drug maker, said that although Dr. Abuzzahab had signed a clinical trial agreement with the company to study its Alzheimer's drug, Aricept, it told him two days after a reporter asked for comment on the case that he was not qualified to be an investigator. And at AstraZeneca, for which Dr. Abuzzahab said he had performed clinical trials and still gave drug marketing lectures, a spokesman said the company was "concerned" about Dr. Abuzzahab's disciplinary record.

"We have our own internal processes for dealing with these matters, which are under way," said Jim Minnick, an AstraZeneca spokesman.

The Minnesota records often fail to distinguish between drug company payments to doctors for research and for marketing, so it is sometimes impossible to determine why doctors were paid. Some doctors, like Dr. Abuzzahab, clearly performed both research and marketing.

Gene Carbona, who left Merck on good terms in 2001 as a regional sales manager after 12 years in drug sales, said the only thing the company considered when hiring doctors to give marketing lectures was "the volume or potential volume of prescribing that doctor could do."

A Merck spokesman declined to comment.

Mr. Carbona, now executive director of sales for The Medical Letter, which reviews drugs, said that had he known that a doctor had a disciplinary record for excessive prescribing, "I would have been more inclined to use them as a speaker."

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Psychiatrists, Children and Drug Industry's Role

By GARDINER HARRIS, BENEDICT CAREY and JANET ROBERTS

When Anya Bailey developed an eating disorder after her 12th birthday, her mother took her to a psychiatrist at the University of Minnesota who prescribed a powerful antipsychotic drug called Risperdal.

Created for schizophrenia, Risperdal is not approved to treat eating disorders, but increased appetite is a common side effect and doctors may prescribe drugs as they see fit. Anya gained weight but within two years developed a crippling knot in her back. She now receives regular injections of Botox to unclench her back muscles. She often awakens crying in pain.

Isabella Bailey, Anya's mother, said she had no idea that children might be especially susceptible to Risperdal's side effects. Nor did she know that Risperdal and similar medicines were not approved at the time to treat children, or that medical trials often cited to justify the use of such drugs had as few as eight children taking the drug by the end.

Just as surprising, Ms. Bailey said, was learning that the university psychiatrist who supervised Anya's care received more than $7,000 from 2003 to 2004 from Johnson & Johnson, Risperdal's maker, in return for lectures about one of the company's drugs.

Doctors, including Anya Bailey's, maintain that payments from drug companies do not influence what they prescribe for patients.

But the intersection of money and medicine, and its effect on the well-being of patients, has become one of the most contentious issues in health care. Nowhere is that more true than in psychiatry, where increasing payments to doctors have coincided with the growing use in children of a relatively new class of drugs known as atypical antipsychotics.

These best-selling drugs, including Risperdal, Seroquel, Zyprexa, Abilify and Geodon, are now being prescribed to more than half a million children in the United States to help parents deal with behavior problems despite profound risks and almost no approved uses for minors.

A New York Times analysis of records in Minnesota, the only state that requires public reports of all drug company marketing payments to doctors, provides rare documentation of how financial relationships between doctors and drug makers correspond to the growing use of atypicals in children.

From 2000 to 2005, drug maker payments to Minnesota psychiatrists rose more than sixfold, to $1.6 million. During those same years, prescriptions of antipsychotics for children in Minnesota's Medicaid

program rose more than ninefold.

Those who took the most money from makers of atypicals tended to prescribe the drugs to children the most often, the data suggest. On average, Minnesota psychiatrists who received at least $5,000 from atypical makers from 2000 to 2005 appear to have written three times as many atypical prescriptions for children as psychiatrists who received less or no money.

The Times analysis focused on prescriptions written for about one-third of Minnesota's Medicaid population, almost all of whom are disabled. Some doctors were misidentified by pharmacists, but the information provides a rough guide to prescribing patterns in the state.

Drug makers underwrite decision makers at every level of care. They pay doctors who prescribe and recommend drugs, teach about the underlying diseases, perform studies and write guidelines that other doctors often feel bound to follow.

But studies present strong evidence that financial interests can affect decisions, often without people knowing it.

In Minnesota, psychiatrists collected more money from drug makers from 2000 to 2005 than doctors in any other specialty. Total payments to individual psychiatrists ranged from $51 to more than $689,000, with a median of $1,750. Since the records are incomplete, these figures probably underestimate doctors' actual incomes.

Such payments could encourage psychiatrists to use drugs in ways that endanger patients' physical health, said Dr. Steven E. Hyman, the provost of Harvard University and former director of the National Institute of Mental Health. The growing use of atypicals in children is the most troubling example of this, Dr. Hyman said.

"There's an irony that psychiatrists ask patients to have insights into themselves, but we don't connect the wires in our own lives about how money is affecting our profession and putting our patients at risk," he said.

The Prescription

Anya Bailey is a 15-year-old high school freshman from East Grand Forks, Minn., with pictures of the actor Chad Michael Murray on her bedroom wall. She has constant discomfort in her neck that leads her to twist it in a birdlike fashion. Last year, a boy mimicked her in the lunch room.

"The first time, I laughed it off," Anya said. "I said: 'That's so funny. I think I'll laugh with you.' Then it got annoying, and I decided to hide it. I don't want to be made fun of."

Now she slumps when seated at school to pressure her clenched muscles, she said.

It all began in 2003 when Anya became dangerously thin. "Nothing tasted good to her," Ms. Bailey said.

Psychiatrists at the University of Minnesota, overseen by Dr. George M. Realmuto, settled on Risperdal, not for its calming effects but for its normally unwelcome side effect of increasing appetite and weight gain, Ms. Bailey said. Anya had other issues that may have recommended Risperdal to doctors, including occasional angry outbursts and having twice heard voices over the previous five years, Ms. Bailey said.

Dr. Realmuto said he did not remember Anya's case, but speaking generally he defended his unapproved use of Risperdal to counter an eating disorder despite the drug's risks. "When things are dangerous, you use extraordinary measures," he said.

Ten years ago, Dr. Realmuto helped conduct a study of Concerta, an attention deficit hyperactivity disorder drug marketed by Johnson & Johnson, which also makes Risperdal. When Concerta was approved, the company hired him to lecture about it.

He said he gives marketing lectures for several reasons.

"To the extent that a drug is useful, I want to be seen as a leader in my specialty and that I was involved in a scientific study," he said.

The money is nice, too, he said. Dr. Realmuto's university salary is $196,310.

"Academics don't get paid very much," he said. "If I was an entertainer, I think I would certainly do a lot better."

In 2003, the year Anya came to his clinic, Dr. Realmuto earned $5,000 from Johnson & Johnson for giving three talks about Concerta. Dr. Realmuto said he could understand someone's worrying that his Concerta lecture fees would influence him to prescribe Concerta but not a different drug from the same company, like Risperdal.

In general, he conceded, his relationship with a drug company might prompt him to try a drug. Whether he continued to use it, though, would depend entirely on the results.

As the interview continued, Dr. Realmuto said that upon reflection his payments from drug companies had probably opened his door to useless visits from a drug salesman, and he said he would stop giving sponsored lectures in the future.

Kara Russell, a Johnson & Johnson spokeswoman, said that the company selects speakers who have used the drug in patients and have either undertaken research or are aware of the studies. "Dr. Realmuto met these criteria," Ms. Russell said.

When asked whether these payments may influence doctors' prescribing habits, Ms. Russell said that the talks "provide an educational opportunity for physicians."

No one has proved that psychiatrists prescribe atypicals to children because of drug company payments. Indeed, some who frequently prescribe the drugs to children earn no drug industry money. And nearly all

psychiatrists who accept payments say they remain independent. Some say they prescribed and extolled the benefits of such drugs before ever receiving payments to speak to other doctors about them.

"If someone takes the point of view that your doctor can be bought, why would you go to an E. R. with your injured child and say, 'Can you help me?' " said Dr. Suzanne A. Albrecht, a psychiatrist from Edina, Minn., who earned more than $188,000 from 2002 to 2005 giving drug marketing talks.

The Industry Campaign

It is illegal for drug makers to pay doctors directly to prescribe specific products. Federal rules also bar manufacturers from promoting unapproved, or off-label, uses for drugs.

But doctors are free to prescribe as they see fit, and drug companies can sidestep marketing prohibitions by paying doctors to give lectures in which, if asked, they may discuss unapproved uses.

The drug industry and many doctors say that these promotional lectures provide the field with invaluable education. Critics say the payments and lectures, often at expensive restaurants, are disguised kickbacks that encourage potentially dangerous drug uses. The issue is particularly important in psychiatry, because mental problems are not well understood, treatment often involves trial and error, and off-label prescribing is common.

The analysis of Minnesota records shows that from 1997 through 2005, more than a third of Minnesota's licensed psychiatrists took money from drug makers, including the last eight presidents of the Minnesota Psychiatric Society.

The psychiatrist receiving the most from drug companies was Dr. Annette M. Smick, who lives outside Rochester, Minn., and was paid more than $689,000 by drug makers from 1998 to 2004. At one point Dr. Smick was doing so many sponsored talks that "it was hard for me to find time to see patients in my clinical practice," she said.

"I was providing an educational benefit, and I like teaching," Dr. Smick said.

Dr. Steven S. Sharfstein, immediate past president of the American Psychiatric Association, said psychiatrists have become too cozy with drug makers. One example of this, he said, involves Lexapro, made by Forest Laboratories, which is now the most widely used antidepressant in the country even though there are cheaper alternatives, including generic versions of Prozac.

"Prozac is just as good if not better, and yet we are migrating to the expensive drug instead of the generics," Dr. Sharfstein said. "I think it's the marketing."

Atypicals have become popular because they can settle almost any extreme behavior, often in minutes, and doctors have few other answers for desperate families.

Their growing use in children is closely tied to the increasingly common and controversial diagnosis of

pediatric bipolar disorder, a mood problem marked by aggravation, euphoria, depression and, in some cases, violent outbursts. The drugs, sometimes called major tranquilizers, act by numbing brain cells to surges of dopamine, a chemical that has been linked to euphoria and psychotic delusions.

Suzette Scheele of Burnsville, Minn., said her 17-year-old son, Matt, was given a diagnosis of bipolar disorder four years ago because of intense mood swings, and now takes Seroquel and Abilify, which have caused substantial weight gain.

"But I don't have to worry about his rages; he's appropriate; he's pleasant to be around," Ms. Scheele said.

The sudden popularity of pediatric bipolar diagnosis has coincided with a shift from antidepressants like Prozac to far more expensive atypicals. In 2000, Minnesota spent more than $521,000 buying antipsychotic drugs, most of it on atypicals, for children on Medicaid. In 2005, the cost was more than $7.1 million, a 14-fold increase.

The drugs, which can cost $1,000 to $8,000 for a year's supply, are huge sellers worldwide. In 2006, Zyprexa, made by Eli Lilly, had $4.36 billion in sales, Risperdal $4.18 billion and Seroquel, made by AstraZeneca, $3.42 billion.

Many Minnesota doctors, including the president of the Minnesota Psychiatric Society, said drug makers and their intermediaries are now paying them almost exclusively to talk about bipolar disorder.

The Diagnoses

Yet childhood bipolar disorder is an increasingly controversial diagnosis. Even doctors who believe it is common disagree about its telltale symptoms. Others suspect it is a fad. And the scientific evidence that atypicals improve these children's lives is scarce.

One of the first and perhaps most influential studies was financed by AstraZeneca and performed by Dr. Melissa DelBello, a child and adult psychiatrist at the University of Cincinnati.

Dr. DelBello led a research team that tracked for six weeks the moods of 30 adolescents who had received diagnoses of bipolar disorder. Half of the teenagers took Depakote, an antiseizure drug used to treat epilepsy and bipolar disorder in adults. The other half took Seroquel and Depakote.

The two groups did about equally well until the last few days of the study, when those in the Seroquel group scored lower on a standard measure of mania. By then, almost half of the teenagers getting Seroquel had dropped out because they missed appointments or the drugs did not work. Just eight of them completed the trial.

In an interview, Dr. DelBello acknowledged that the study was not conclusive. In the 2002 published paper, however, she and her co-authors reported that Seroquel in combination with Depakote "is more effective for the treatment of adolescent bipolar mania" than Depakote alone.

In 2005, a committee of prominent experts from across the country examined all of the studies of treatment for pediatric bipolar disorder and decided that Dr. DelBello's was the only study involving atypicals in bipolar children that deserved its highest rating for scientific rigor. The panel concluded that doctors should consider atypicals as a first-line treatment for some children. The guidelines were published in The Journal of the American Academy of Child and Adolescent Psychiatry.

Three of the four doctors on the panel served as speakers or consultants to makers of atypicals, according to disclosures in the guidelines. In an interview, Dr. Robert A. Kowatch, a psychiatrist at Cincinnati Children's Hospital and the lead author of the guidelines, said the drug makers' support had no influence on the conclusions.

AstraZeneca hired Dr. DelBello and Dr. Kowatch to give sponsored talks. They later undertook another study comparing Seroquel and Depakote in bipolar children and found no difference. Dr. DelBello, who earns $183,500 annually from the University of Cincinnati, would not discuss how much she is paid by AstraZeneca.

"Trust me, I don't make much," she said. Drug company payments did not affect her study or her talks, she said. In a recent disclosure, Dr. DelBello said that she received marketing or consulting income from eight drug companies, including all five makers of atypicals.

Dr. Realmuto has heard Dr. DelBello speak several times, and her talks persuaded him to use combinations of Depakote and atypicals in bipolar children, he said. "She's the leader in terms of doing studies on bipolar," Dr. Realmuto said.

Some psychiatrists who advocate use of atypicals in children acknowledge that the evidence supporting this use is thin. But they say children should not go untreated simply because scientists have failed to confirm what clinicians already know.

"We don't have time to wait for them to prove us right," said Dr. Kent G. Brockmann, a psychiatrist from the Twin Cities who made more than $16,000 from 2003 to 2005 doing drug talks and one-on-one sales meetings, and last year was a leading prescriber of atypicals to Medicaid children.

The Reaction

For Anya Bailey, treatment with an atypical helped her regain her appetite and put on weight, but also heavily sedated her, her mother said. She developed the disabling knot in her back, the result of a nerve condition called dystonia, in 2005.

The reaction was rare but not unknown. Atypicals have side effects that are not easy to predict in any one patient. These include rapid weight gain and blood sugar problems, both risk factors for diabetes; disfiguring tics, dystonia and in rare cases heart attacks and sudden death in the elderly.

In 2006, the Food and Drug Administration received reports of at least 29 children dying and at least 165

more suffering serious side effects in which an antipsychotic was listed as the "primary suspect." That was a substantial jump from 2000, when there were at least 10 deaths and 85 serious side effects among children linked to the drugs. Since reporting of bad drug effects is mostly voluntary, these numbers likely represent a fraction of the toll.

Jim Minnick, a spokesman for AstraZeneca, said that the company carefully monitors reported problems with Seroquel. "AstraZeneca believes that Seroquel is safe," Mr. Minnick said.

Other psychiatrists renewed Anya's prescriptions for Risperdal until Ms. Bailey took Anya last year to the Mayo Clinic, where a doctor insisted that Ms. Bailey stop the drug. Unlike most universities and hospitals, the Mayo Clinic restricts doctors from giving drug marketing lectures.

Ms. Bailey said she wished she had waited to see whether counseling would help Anya before trying drugs. Anya's weight is now normal without the help of drugs, and her counseling ended in March. An experimental drug, her mother said, has recently helped the pain in her back.

This article is by Gardiner Harris, Benedict Carey and Janet Roberts.

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THE DRUG PUSHERS

As America turns its health-care system over to the market, pharmaceutical reps are wielding more and more influence—and the line between them and doctors is beginning to blur

BY CARL ELLIOTT

Illustrations by Marcellus Hall

Back in the old days, long before drug companies started making headlines in the business pages, doctors were routinely called upon by company representatives known as "detail men." To "detail" a doctor is to give that doctor information about a company's new drugs, with the aim of persuading the doctor to prescribe them. When I was growing up, in South Carolina in the 1970s, I would occasionally see detail men sitting patiently in the waiting room outside the office of my father, a family doctor. They were pretty easy to spot. Detail men were usually sober, conservatively dressed gentlemen who would not have looked out of place at the Presbyterian church across the street. Instead of Bibles or hymn books, though, they carried detail bags, which were filled with journal articles, drug samples, and branded knickknacks for the office.

Today detail men are officially known as "pharmaceutical sales representatives," but everyone I know calls them "drug reps." Drug reps are still easy to spot in a clinic or hospital, but for slightly different reasons. The most obvious is their appearance. It is probably fair to say that doctors, pharmacists, and medical-school professors are not generally admired for their good looks and fashion sense. Against this backdrop, the average drug rep looks like a supermodel, or maybe an A-list movie star. Drug reps today are often young, well groomed, and strikingly good-looking. Many are women. They are usually affable and sometimes very smart. Many give off a kind of glow, as if they had just emerged from a spa or salon. And they are always, hands down, the best-dressed people in the hospital.

Drug reps have been calling on doctors since the mid-nineteenth century, but during the past decade or so their numbers have increased dramatically. From 1996 to 2001 the pharmaceutical sales force in America doubled, to a total of 90,000 reps. One reason is simple: good reps move product. Detailing is expensive, but almost all practicing doctors see reps at least occasionally, and many doctors say they find reps useful. One study found that for drugs introduced after 1997 with revenues exceeding $200 million a year, the average return for each dollar spent on detailing was $10.29. That is an impressive figure. It is almost twice the return on investment in medical-journal advertising, and more than seven times the return on direct-to-consumer advertising.

But the relationship between doctors and drug reps has never been uncomplicated, for reasons that should be obvious. The first duty of doctors, at least in theory, is to their patients. Doctors must make prescribing decisions based on medical evidence and their own clinical judgment. Drug reps, in contrast, are salespeople. They swear no oaths, take care of no patients, and profess no high-minded ethical duties. Their job is to persuade doctors to prescribe their drugs. If reps are lucky, their drugs are good, the studies are clear, and their job is easy. But sometimes reps must persuade doctors to prescribe drugs that are marginally effective, exorbitantly expensive, difficult to administer, or even dangerously toxic. Reps that succeed are rewarded with bonuses or commissions. Reps that fail may find themselves unemployed.

Most people who work in health care, if they give drug reps any thought at all, regard them with mixed feelings. A handful avoid reps as if they were vampires, backing out of the room when they see one approaching. In their view, the best that can be said about reps is that they are a necessary by-product of a market economy. They view reps much as NBA players used to view Michael Jordan: as an awesome, powerful force that you can never really stop, only hope to control.

Yet many reps are so friendly, so easygoing, so much fun to flirt with that it is virtually impossible to demonize them. How can you demonize someone who brings you lunch and touches your arm and remembers your birthday and knows the names of all your children? After awhile even the most steel-willed doctors may look forward to visits by a rep, if only in the self-interested way that they look forward to the UPS truck pulling up in their driveway. A rep at the door means a delivery has arrived: take-out for the staff, trinkets for the kids, and, most indispensably, drug samples on the house. Although samples are the single

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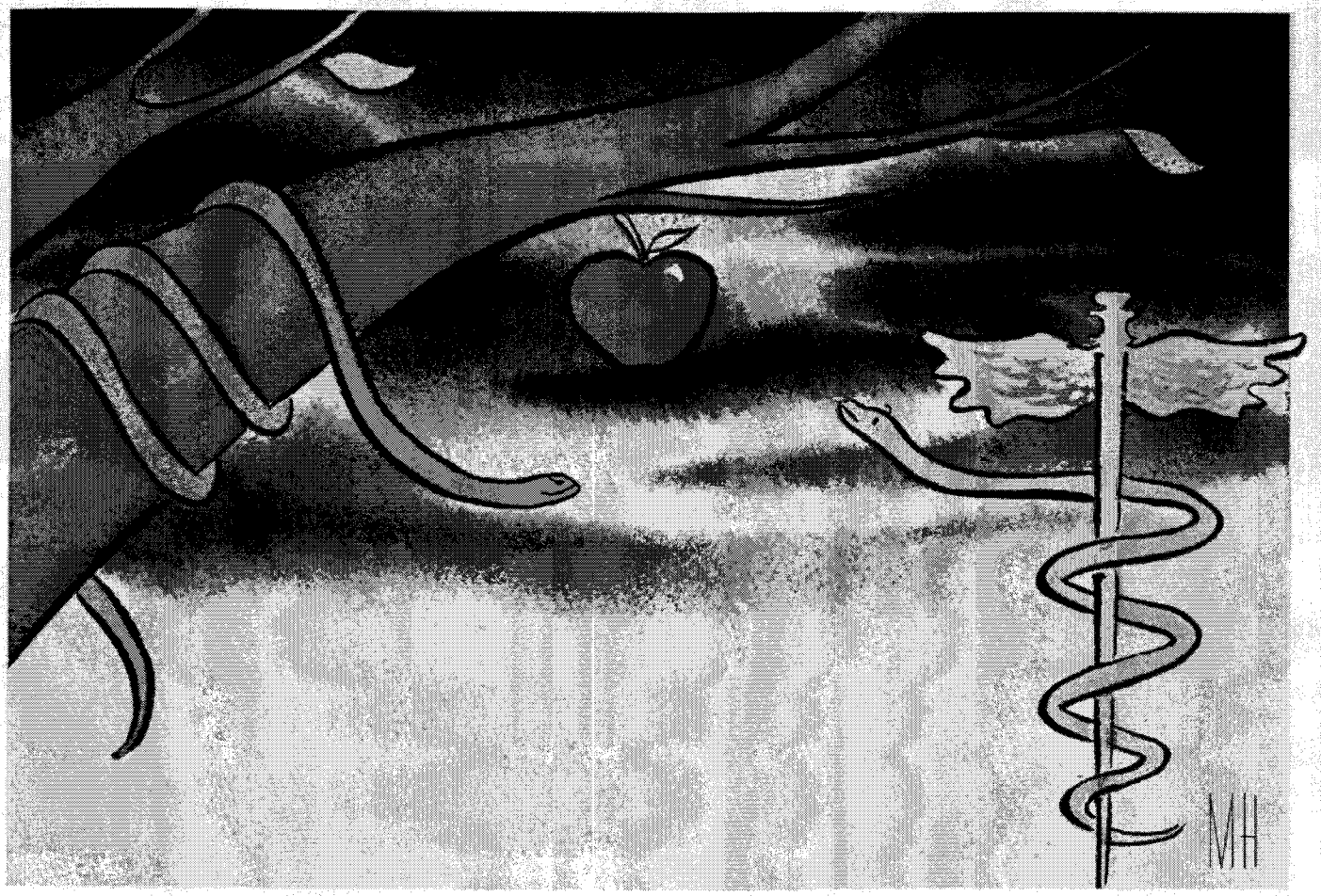

largest marketing expense for the drug industry, they pay handsome dividends: doctors who accept samples of a drug are far more likely to prescribe that drug later on.

Drug reps may well have more influence on prescriptions than anyone in America other than doctors themselves, but to most people outside the drug industry their jobs are mysterious. What exactly do they do every day? Where do they get their information? What do they say about doctors when the doctors are not around? Reps can be found in hospitals, waiting rooms, and conference halls all over the country, yet they barely register on the collective medical consciousness. Many doctors notice them only in the casual, utilitarian way that one might notice a waitress or a bartender. Some doctors look down on them on ethical grounds. "Little Willy Lomans," they say, "only in it for the money." When I asked my friends and colleagues in medicine to suggest some reps I could talk to about detailing, most could not come up with a single name.

These doctors may be right about reps. It is true that selling pharmaceuticals can be a highly lucrative job. But in a market-based medical system, are reps really so different from doctors? Most doctors in the United States now work, directly or indirectly, for large corporations. Like reps, many doctors must answer to managers and bureaucrats. They are overwhelmed by paperwork and red tape. Unlike my father, who would have sooner walked to Charleston barefoot than take out an ad for his practice, many doctors now tout their services on roadside billboards. My medical-school alumni magazine recently featured the Class of 1988 valedictorian, who has written a diet book, started her own consulting firm, and become the national spokesperson for a restaurant chain. For better or worse, America has turned its health-care system over to the same market forces that transformed the village hardware store into Home Depot and the corner pharmacy into a strip-mall CVS. Its doctors are moving to the same medical suburb where drug reps have lived for the past 150 years. If they want to know what life is like there, perhaps they should talk to their neighbors.

The King of Happy Hour

Gene Carbona was almost a criminal. I know this because, thirty minutes into our first telephone conversation, he told me, "Carl, I was almost a criminal." I have heard ex–drug reps speak bluntly about their former jobs, but never quite so cheerfully and openly. These days Carbona works for *The Medical Letter*, a highly respected nonprofit publication (Carbona stresses that he is speaking only for himself), but he was telling me about his twelve years working for Merck and then Astra Merck, a firm initially set up to market the Sweden-based Astra's drugs in the United States. Carbona began training as a rep in 1988, when he was only eleven days out of college. He detailed two drugs for Astra Merck. One was a calcium-channel blocker he calls "a dog." The other was the heartburn medication Prilosec, which at the time was available by prescription only.

Prilosec is the kind of drug most reps can only dream about. The industry usually considers a drug to be a blockbuster if it reaches a billion dollars a year in sales. In 1998 Prilosec became the first drug in America to reach $5 billion a year. In 2000 it made $6 billion. Prilosec's success was not the result of a massive heartburn epidemic. It was based on the same principle that drove the success of many other 1990s blockbusters, from Vioxx to Viagra: the restoration of an ordinary biological function that time and circumstance had eroded. In the case of Prilosec, the function was digestion. Many people discovered that the drug allowed them to eat the burritos and curries that their gastrointestinal systems had placed off-limits. So what if Prilosec was $4 a pill, compared with a quarter or so for a Tagamet? Patients still begged for it. Prilosec was their savior. Astra Merck marketed Prilosec as the "purple pill," but, according to Carbona, many patients called it "purple Jesus."

How did Astra Merck do it? Prilosec was the first proton pump inhibitor (a drug that inhibits the production of stomach acid) approved by the Food and Drug Administration, and thus the first drug available in its class. By definition this gave it a considerable head start on the competition. In the late 1990s Astra Merck mounted a huge direct-to-consumer campaign; ads for the purple pill were ubiquitous. But consumer advertising can do only so much for a drug, because doctors, not patients, write the prescriptions. This is where reps become indispensable.

Drug reps are easy to spot in a hospital or clinic. They are often young and strikingly good-looking. They are usually affable and sometimes very smart. And they are always, hands down, the best-dressed people in the hospital.

Many reps can tell stories about occasions when, in order to move their product, they pushed the envelope of what is ethically permissible. I have heard reps talk about scoring sports tickets for their favorite doctors, buying televisions for waiting rooms, and arranging junkets to tropical resorts. One rep told me he set up a putting green in a hospital and gave a putter to any doctor who made a hole-in-one. A former rep told me about a colleague who somehow managed to persuade a pharmacist to let him secretly write the prescribing protocol for antibiotic use at a local hospital.

But Carbona was in a class of his own. He had access to so much money for doctors that he had trouble spending it all. He took residents out to bars. He distributed "unrestricted educational grants." He arranged to buy lunch for the staff of certain private practices every day for a year. Often he would invite a group of doctors and their guests to a high-end restaurant, buy them drinks and a lavish meal, open up the club in back, and party until 4:00 a.m. "The more money I spent," Carbona says, "the more money I made." If he came back to the restaurant later that week with his wife, everything would be on the house. "My money was no good at restaurants," he told me, "because I was the King of Happy Hour."

My favorite Carbona story, the one that left me shaking my head in admiration, took place in Tallahassee. One of the more important clinics Carbona called on was a practice there consisting of about fifty doctors. Although the practice had plenty of patients, it was struggling. This problem was not uncommon. When the movement toward corporate-style medicine got under way, in the 1980s and 1990s, many doctors found themselves ill-equipped to run a business; they didn't know much about how to actually make money. ("That's why doctors are such great targets for Ponzi schemes and real-estate scams," Carbona helpfully points out.) Carbona was detailing this practice twice a week and had gotten to know some of the clinicians pretty well. At one point a group of them asked him for help. "Gene, you work for a successful business," Carbona recalls them saying. "Is there any advice you could give us to help us turn the practice around?" At this point he knew he had stumbled upon an extraordinary opportunity.

Carbona decided that the clinic needed a "practice-management consultant." And he and his colleagues at Astra Merck knew just the man: a financial planner and accountant with whom they were very friendly. They wrote up a contract. They agreed to pay the consultant a flat fee of about $50,000 to advise the clinic. But they also gave him another incentive. Carbona says, "We told him that if he was successful there would be more business for him in the future, and by 'successful,' we meant a rise in prescriptions for our drugs."

The consultant did an extremely thorough job. He spent eleven or twelve hours a day at the clinic for months. He talked to every employee, from the secretaries to the nurses to the doctors. He thought carefully about every aspect of the practice, from the most mundane administrative details to big-picture matters such as bill collection and financial strategy. He turned the practice into a profitable, smoothly running financial machine. And prescriptions for Astra Merck drugs soared.

When I asked Carbona how the consultant had increased Astra Merck's market share within the clinic so dramatically, he said that the consultant never pressed the doctors directly. Instead, he talked up Carbona. "Gene has put his neck on the line for you guys," he would tell them. "If this thing doesn't work, he might get fired." The consultant emphasized what a remarkable service the practice was getting, how valuable the financial advice was, how everything was going to turn around for them—all courtesy of Carbona. The strategy worked. "Those guys went

berserk for me," Carbona says. Doctors at the newly vitalized practice prescribed so many Astra Merck drugs that he got a $140,000 bonus. The scheme was so successful that Carbona and his colleagues at Astra Merck decided to duplicate it in other practices.

I got in touch with Carbona after I learned that he was giving talks on the American Medical Student Association lecture circuit about his experiences as a rep. At that point I had read a fair bit of pharmaceutical sales literature, and most of it had struck me as remarkably hokey and stilted. Merck's official training materials, for example, instruct reps to say things like, "Doctor, based on the information we discussed today, will you prescribe Vioxx for your patients who need once-daily power to prevent pain due to osteoarthritis?" So I was unprepared for a man with Carbona's charisma and forthright humor. I could see why he had been such an excellent rep: he came off as a cross between a genial con artist and a comedic character actor. After two hours on the phone with him I probably would have bought anything he was selling.

Most media accounts of the pharmaceutical industry miss this side of drug reps. By focusing on scandals—the kickbacks and the fraud and the lavish gifts—they lose sight of the fact that many reps are genuinely likeable people. The better ones have little use for the canned scripts they are taught in training. For them, effective selling is all about developing a relationship with a doctor. If a doctor likes a rep, that doctor is going to feel bad about refusing to see the rep, or about taking his lunches and samples but never prescribing his drugs. As Jordan Katz, a rep for Schering-Plough until two years ago, says, "A lot of doctors just write for who they like."

A variation on this idea emerges in *Side Effects*, Kathleen Slattery-Moschkau's 2005 film about a fictional fledgling drug rep. Slattery-Moschkau, who worked for nine years as a rep for Bristol-Myers Squibb and Johnson & Johnson, says the carefully rehearsed messages in the corporate training courses really got to her. "I hated the crap I had to say to doctors," she told me. The heroine of *Side Effects* eventually decides to ditch the canned messages and stop spinning her product. Instead, she is brutally honest. "Bottom line?" she says to one doctor. "Your patients won't shit for a week." To her amazement, she finds that the blunter she is, the higher her market share rises. Soon she is winning sales awards and driving a company BMW.

For most reps, market share is the yardstick of success. The more scripts their doctors write for their drugs, the more the reps make. Slattery-Moschkau says that most of her fellow reps made $50,000 to $90,000 a year in salary and another $30,000 to $50,000 in bonuses, depending on how much they sold. Reps are pressured to "make quota," or meet yearly sales targets, which often increase from year to year. Reps who fail to make quota must endure the indignity of having their district manager frequently accompany them on sales calls. Those who meet quota are rewarded handsomely. The most successful reps achieve minor celebrity within the company.

One perennial problem for reps is the doctor who simply refuses to see them at all. Reps call these doctors "No Sees." Cracking a No See is a genuine achievement, the pharmaceutical equivalent of a home run or a windmill dunk. Gene Carbona says that when he came across a No See, or any other doctor who was hard to influence, he used "Northeast-Southwest" tactics. If you can't get to a doctor, he explains, you go after the people surrounding that doctor, showering them with gifts. Carbona might help support a Little League baseball team or a bowling league. After awhile, the doctor would think, *Gene is doing such nice things for all these people, the least I can do is give him ten minutes of my time.* At that point, Carbona says, the sale was as good as made. "If you could get ten minutes with a doctor, your market share would go through the roof."

For decades the medical community has debated whether gifts and perks from reps have any real effect. Doctors insist that they do not. Studies in the medical literature indicate just the opposite. Doctors who take gifts from a company, studies show, are more likely to prescribe that company's drugs or ask that they be added to their hospital's formulary. The pharmaceutical industry has managed this debate skillfully, pouring vast resources into gifts for doctors while simultaneously reassuring them that their integrity prevents them from being influenced. For example, in a recent editorial in the journal *Health Affairs*, Bert Spilker, a vice president for PhRMA, the pharmaceutical trade group, defended the practice of gift-giving against critics who, he scornfully wrote, "fear that physicians are so weak and lacking in integrity that they would 'sell their souls' for a pack of M&M candies and a few sandwiches and doughnuts."

Doctors' belief in their own incorruptibility appears to be honestly held. It is rare to hear a doctor—even in private, off-the-record conversation—admit that industry gifts have made a difference in his or her prescribing. In fact, according to one small study of medical residents in the *Canadian Medical Association Journal*, one way to convince doctors that they cannot be influenced by gifts may be to give them one; the more gifts a doctor takes, the more likely that doctor is to believe that the gifts have had no effect. This helps explain why it makes sense for reps to give away even small gifts. A particular gift may have no influence, but it might make a doctor more apt to think that he or she would not be influenced by larger gifts in the future. A pizza and a penlight are like inoculations, tiny injections of self-confidence that make a doctor think, *I will never be corrupted by money.*

Gifts from the drug industry are nothing new, of course. William Helfand, who worked in marketing for Merck for thirty-three years, told me that company representatives were giving doctors books and pamphlets as early as the late nineteenth century. "There is nothing new under the sun," Helfand says. "There is just more of it." The question is: Why is there so much more of it just now? And what changed during the past decade to bring about such a dramatic increase in reps bearing gifts?

AN ETHIC OF SALESMANSHIP

One morning last year I had breakfast at the Bryant-Lake Bowl, a diner in Minneapolis, with a former Pfizer rep named Michael Oldani. Oldani grew up in a working-class family in Kenosha, Wisconsin. Although he studied biochemistry in college, he knew nothing about pharmaceutical sales until he was recruited for Pfizer by the husband of a woman with whom he worked. Pfizer gave him a good salary, a company car, free gas, and an expense account. "It was kind of like the Mafia," Oldani told me. "They made me an offer I couldn't refuse." At the time, he was still in college and living with his parents. "I knew a good ticket out of Kenosha when I saw one," he says. He carried the bag for Pfizer for nine years, until 1998.

Today Oldani is a Princeton-trained medical anthropologist teaching at the University of Wisconsin at Whitewater. He wrote his doctoral dissertation on the anthropology of pharmaceutical sales, drawing not just on ethnographic fieldwork he did in Manitoba as a Fulbright scholar but also on his own experience as a rep. This dual perspective—the view of both a detached outsider and a street-savvy insider—gives his work authority and a critical edge. I had invited Oldani to lecture at our medical school, the University of Minnesota, after reading his work in anthropology journals. Although his writing is scholarly, his manner is modest and self-effacing, more Kenosha than Princeton. This is a man who knows his way around a diner.

Like Carbona, Oldani worked as a rep in the late 1980s and the 1990s, a period when the drug industry was undergoing key transformations. Its ethos was changing from that of the country-club establishment to the aggressive, new-money entrepreneur. Impressed by the success of AIDS activists in pushing for faster drug approvals, the drug industry increased pressure on the FDA to let companies bring drugs to the market more quickly. As a result, in 1992 Congress passed the Prescription Drug User Fee Act, under which drug companies pay a variety of fees to the FDA, with the aim of speeding up drug approval (thereby making the drug industry a major funder of the agency set up to regulate it). In 1997 the FDA dropped most restrictions on direct-to-consumer advertising of prescription drugs, opening the gate for the eventual Levitra ads on Super Bowl Sunday and Zoloft cartoons during daytime television shows. The drug industry also became a big political player in Washington: by 2005, according to the Center for Public Integrity, its lobbying organization had become the largest in the country.

Many companies started hitting for the fences, concentrating on potential blockbuster drugs for chronic illnesses in huge populations: Claritin for allergies, Viagra for impotence, Vioxx for arthritis, Prozac for depression. Successful drugs were followed by a flurry of competing me-too drugs. For most of the 1990s and the early part of this decade, the pharmaceutical industry was easily the most profitable business sector in America. In 2002, according to Public Citizen, a nonprofit watchdog group, the combined profits of the top ten pharmaceutical companies in the Fortune 500 exceeded the combined profits of the other 490 companies.

During this period reps began to feel the influence of a new generation of executives intent on bringing market values to an industry that had been slow to embrace them. Anthony Wild, who was hired to lead Parke-Davis in the mid-1990s, told the journalist Greg Critser, the author of *Generation Rx*, that one of his first moves upon his appointment was to increase the incentive pay given to successful reps. Wild saw no reason to cap reps' incentives. As he said to the company's older executives, "Why not let them get rich?" Wild told the reps about the change at a meeting in San Francisco. "We announced that we were taking off the caps," he told Critser, "and the sales force went nuts!"

In the 1990s, new technology made it easy for any rep to track any doctor's prescriptions. The result was an arms race of pharmaceutical gift-giving. If GSK flew doctors to Palm Springs for a conference, you flew them to Paris.

It was not just the industry's ethos that was changing; the technology was changing, too. According to Oldani, one of the most critical changes came in the way that information was gathered. In the days before computers, reps had to do a lot of legwork to figure out whom they could influence. They had to schmooze with the receptionists, make friends with the nurses, and chat up the pharmacists in order to learn which drugs the local doctors were prescribing, using the right incentives to coax what they needed from these informants. "Pharmacists are like pigeons," Jamie Reidy, a former rep for Pfizer and Eli Lilly, told me. "Only instead of bread crumbs, you toss them pizzas and sticky notes."

But in the 1990s, new information technology made it much simpler to track prescriptions. Market-research firms began collecting script-related data from pharmacies and hospitals and selling it to pharmaceutical companies. The American Medical Association collaborated by licensing them information about doctors (including doctors who do not belong to the AMA), which it collects in its "Physician Masterfile." Soon reps could find out exactly how many prescriptions any doctor was writing and exactly which drugs those prescriptions were for. All they had to do was turn on their laptops and download the data.

What they discovered was revelatory. For one thing, they found that a lot of doctors were lying to them. Doctors might tell a rep that they were writing prescriptions for, say, Lipitor, when they weren't. They were just being polite, or saying whatever they thought would get the rep off their backs. Now reps could detect the deception immediately. (Even today many doctors do not realize that reps have access to script-tracking reports.)

More important, script-tracking helped reps figure out which doctors to target. They no longer had to waste time and money on doctors with conservative prescribing habits; they could head straight to the "high prescribers," or "high writers." And they could get direct feedback on which tactics were working. If a gift or a dinner presentation did not result in more scripts, they knew to try another approach.

But there was a rub: the data was available to every rep from every company. The result was an arms race of pharmaceutical gift-giving, in which reps were forced to devise ever-new ways to exert influence. If the Eli Lilly rep was bringing sandwiches to the office staff, you brought Thai food. If GSK flew doctors to Palm Springs for a conference, you flew them to Paris. Oldani used to take residents to Major League Baseball games. "We did beer bongs, shots, and really partied," he told me. "Some of the guys were incredibly drunk on numerous occasions. I used to buy half barrels for their parties, almost on a retainer-like basis. I never talked product once to any of these residents, and they took care of me in their day-to-day practice. I never missed quota at their hospital."

Oldani says that script-tracking data also changed the way that reps thought about prescriptions. The old system of monitoring prescriptions was very inexact, and the relationship between a particular doctor's prescriptions and the work of a given rep was relatively hard to measure. But with precise script-tracking reports, reps started to feel a sense of ownership about prescriptions. If their doctors started writing more prescriptions for their drugs, the credit clearly belonged to them. However, more precise monitoring also invited micromanagement by the reps' bosses. They began pressuring reps to concentrate on high prescribers, fill out more paperwork, and report more frequently back to management.

"Script-tracking, to me at least, made everyone a potentially successful rep," Oldani says. Reps didn't need to be nearly as resourceful and street savvy as in the past; they just needed the script-tracking reports. The industry began hiring more and more reps, many with backgrounds in sales (rather than, say, pharmacy, nursing, or biology). Some older reps say that during this period the industry replaced the serious detail man with "Pharma Barbie" and "Pharma Ken," whose medical knowledge was exceeded by their looks and catering skills. A newer, regimented style of selling began to replace the improvisational, more personal style of the old-school reps. Whatever was left of an ethic of service gave way to an ethic of salesmanship.

Doctors were caught in a bind. Many found themselves being called on several times a week by different reps from the same company. Most continued to see reps, some because they felt obligated to get up to speed with new drugs, some because they wanted to keep the pipeline of free samples open. But seeing reps has a cost, of course: the more reps a doctor sees, the longer the patients sit in the waiting room. Many doctors began to feel as though they deserved whatever gifts and perks they could get because reps were such an irritation. At one time a few practices even charged reps a fee for visiting.

Professional organizations made some efforts to place limits on the gifts doctors were allowed to accept. But these efforts were halfhearted, and they met with opposition from indignant doctors ridiculing the idea that their judgment could be bought. One doctor, in a letter to the *American Medical News*, confessed, "Every time a discussion comes up on guidelines for pharmaceutical company gifts to physicians, I feel as if I need to take a blood pressure medicine to keep from having a stroke." In 2001 the AMA launched a campaign to educate doctors about the ethical perils of pharmaceutical

gifts, but it undercut its message by funding the campaign with money from the pharmaceutical industry.

Of course, most doctors are never offered free trips to Monaco or even a weekend at a spa; for them an industry gift means a Cialis pen or a Lexapro notepad. Yet it is a rare rep who cannot tell a story or two about the extravagant gifts doctors have requested. Oldani told me that one doctor asked him to build a music room in his house. Phyllis Adams, a former rep in Canada, was told by a doctor that he would not prescribe her product unless her company made him a consultant. (Both said no.) Carbona arranged a $35,000 "unrestricted educational grant" for a doctor who wanted a swimming pool in his back yard. "It was the Wild West," says Jamie Reidy, whose frank memoir about his activities while working for Pfizer in the 1990s, *Hard Sell: The Evolution of a Viagra Salesman*, recently got him fired from Eli Lilly. "They cashed the check, and that was it. And hopefully they remembered you every time they turned on the TV, or bought a drink on the cruise, or dived into the pool."

Doctors insist that gifts and perks from reps have no real effect. Studies in the medical literature indicate just the opposite. Doctors who take gifts from a company are more likely to prescribe that company's drugs.

The trick is to give doctors gifts without making them feel that they are being bought. "Bribes that aren't considered bribes," Oldani says. "This, my friend, is the essence of pharmaceutical gifting." According to Oldani, the way to make a gift feel different from a bribe is to make it personal. "Ideally, a rep finds a way to get into a scriptwriter's psyche," he says. "You need to have talked enough with a scriptwriter—or done enough recon with gatekeepers—that you know what to give." When Oldani found a pharmacist who liked to play the market, he gave him stock options. When he wanted to see a resistant oncologist, he talked to the doctor's nurse and then gave the oncologist a $100 bottle of his favorite cognac. Reidy put the point nicely when he told me, "You are absolutely buying love."

Such gifts do not come with an explicit quid pro quo, of course. Whatever obligation doctors feel to write scripts for a rep's products usually comes from the general sense of reciprocity implied by the ritual of gift-giving. But it is impossible to avoid the hard reality informing these ritualized exchanges: reps would not give doctors free stuff if they did not expect more scripts.

My brother Hal, a psychiatrist currently on the faculty of Wake Forest University, told me about an encounter he had with a drug rep from Eli Lilly some years back, when he was in private practice. This rep was not one of his favorites; she was too aggressive. That day she had insisted on bringing lunch to his office staff, even though Hal asked her not to. As he tried to make polite conversation with her in the hall, she reached over his shoulder into his drug closet and picked up a couple of sample packages of Zoloft and Celexa. Waving them in the air, she asked, "Tell me, Doctor, do the Pfizer and Forest reps bring lunch to your office staff?" A stony silence followed. Hal quietly ordered the rep out of the office and told her to never come back. She left in tears.

It's not hard to understand why Hal got so angry. The rep had broken the rules. Like an abrasive tourist who has not caught on to the code of manners in a foreign country, she had said outright the one thing that, by custom and common agreement, should never be said: that the lunches she brought were intended as a bribe. What's more, they were a bribe that Hal had never agreed to accept. He likened the situation to having somebody drop off a bag of money in your garage without your consent and then ask, "So what about our little agreement?"

When an encounter between a doctor and a rep goes well, it is a delicate ritual of pretense and self-deception. Drug reps pretend that they are giving doctors impartial information. Doctors pretend that they take it seriously. Drug reps must try their best to influence doctors, while doctors must tell themselves that they are not being influenced. Drug reps must act as if they are not salespeople, while doctors must act as if they are not customers. And if, by accident, the real purpose of the exchange is revealed, the result is like an elaborate theatrical dance in which the masks and costumes suddenly drop off and the actors come face to face with one another as they really are. Nobody wants to see that happen.

THE NEW DRUG REPS?

Last spring a small group of first-year medical students at the University of Minnesota spoke to me about a lecture on erectile dysfunction that had just been given by a member of the urology department. The doctor's PowerPoint slides had a large, watermarked logo in the corner. At one point during the lecture a student raised his hand and, somewhat disingenuously, asked the urologist to explain the logo. The urologist, caught off guard, stumbled for a moment and then said that it was the logo for Cialis, a drug for erectile dysfunction that is manufactured by Eli Lilly. Another student asked if he had a special relationship with Eli Lilly. The urologist replied that yes, he was on the advisory board for the company, which had supplied the slides. But he quickly added that nobody needed to worry about the objectivity of his lecture, because he was also on the advisory boards of the makers of the competing drugs Viagra and Levitra. The second student told me, "A lot of people agreed that it was a pharm lecture and that we should have gotten a free breakfast."

This episode is not as unusual as it might appear. Drug company–sponsored consultancies, advisory-board memberships, and speaking engagements have become so common, especially among medical-school faculty, that the urologist probably never imagined that he would be challenged for lecturing to medical students with materials produced by Eli Lilly. According to a recent study in *The Journal of the American Medical Association*, nine out of ten medical students have been asked or required by an attending physician to go to a lunch sponsored by a drug company. As of 2003, according to the Accreditation Council for Continuing Medical Education, pharmaceutical companies were providing 90 percent of the $1 billion spent annually on continuing medical education events, which doctors must attend in order to maintain their licensure.

Over the past year or two pharmaceutical profits have started to level off, and a backlash against reps has been felt; some companies have actually reduced their sales forces. But the industry as a whole is hiring more and more doctors as speakers. In 2004, it sponsored nearly twice as many educational events led by doctors as by reps. Not long before, the numbers had been roughly equal. This raises the question, Are doctors becoming the new drug reps?

Doctors are often the best people to market a drug to other doctors. Merck discovered this when it was developing a campaign for Vioxx, before the drug was taken off the market because of its association with heart attacks and strokes. According to an internal study by Merck, reported in *The Wall Street Journal*, doctors who attended a lecture by another doctor subsequently wrote nearly four times more prescriptions for Vioxx than doctors who attended an event led by a rep. The return on investment for doctor-led events was nearly twice that of rep-led events, even after subtracting the generous fees Merck paid to the doctors who spoke.

These speaking invitations work much like gifts. While reps hope, of course, that a doctor who is speaking on behalf of their company will give their drugs good PR, they also know that such a doctor is more likely to write prescriptions for their drugs. "If he didn't write, he wouldn't speak," a rep who has worked for four pharmaceutical companies told me. The semi-official industry term for these speakers and consultants is "thought leaders," or "key opinion leaders." Some thought leaders do not stay loyal to one company but rather generate a tidy supplemental income by speaking and consulting for a number of different companies. Reps refer to these doctors as "drug whores."

The seduction, whether by one company or several, is often quite gradual. My brother Hal explained to me how he wound up on the speakers' bureau of a major pharmaceutical company. It started when a company rep asked him if he'd be interested in giving a talk about clinical depression to a community group. The honorarium was $1,000. Hal thought, *Why not?* It seemed almost a public service. The next time, the company asked him to talk not to the public but to practitioners at a community hospital. Soon company reps were making suggestions about content. "Why don't you mention the side-effect profiles of the different antidepressants?" they asked. Uneasy, Hal tried to ignore these suggestions. Still, the more talks he gave, the more the reps became focused on antidepressants rather than depression. The company began giving him PowerPoint slides to use, which he also ignored. The reps started telling him, "You know, we have you on the local circuit giving these talks, but you're medical-school faculty; we could get you on the national circuit. That's where the real money is." The mention of big money made him even more uneasy. Eventually the reps asked him to lecture about a new version of their antidepressant drug. Soon after that, Hal told them, "I can't do this anymore."

Looking back on this trajectory, Hal said, "It's kind of like you're a woman at a party, and your boss says to you, 'Look, do me a favor: be nice to this guy over there.' And you see the guy is not bad-looking, and you're unattached, so you say, 'Why not? I can be nice.'" The problem is that it never ends with that party. "Soon you find yourself on the way to a Bangkok brothel in the cargo hold of an unmarked plane. And you say, 'Whoa, this is not what I agreed to.' But then you have to ask yourself, 'When did the prostitution actually start? Wasn't it at that party?'"

Thought leaders serve an indispensable function when it comes to a potentially very lucrative marketing niche: off-label promotion, or promoting a drug for uses other than those for which it was approved by the FDA—something reps are strictly forbidden to do. The case of Neurontin is

especially instructive. In 1996 a whistle-blower named David Franklin, a medical-science liaison with Parke-Davis (now a division of Pfizer), filed suit against the company over its off-label promotion of this drug. Neurontin was approved for the treatment of epilepsy, but according to the lawsuit, Parke-Davis was promoting it for other conditions—including bipolar disorder, migraines, and restless legs syndrome—for which there was little or no scientific evidence that it worked. To do so the company employed a variety of schemes, most involving a combination of rep ingenuity and payments to doctors. Some doctors signed ghostwritten journal articles.

Some drug companies have cut their sales forces, but the industry is hiring more and more doctors as speakers: they are often the best people to market a drug to other doctors. This raises the question: Are doctors becoming the new reps?

One received more than $300,000 to speak about Neurontin at conferences. Others were paid just to listen. Simply having some of your thought leaders in attendance at a meeting is valuable, Kathleen Slattery-Moschkau explains, because they will often bring up off-label uses of a drug without having to be prompted. "You can't get a better selling situation than that," she says. In such circumstances all she had to do was pour the wine and make sure everyone was happy.

The litigation over Neurontin cost Pfizer $430 million in criminal fines and civil damages for the period 1994 to 2002. It was well worth it. The drug's popularity and profitability soared. In spite of the adverse publicity, Neurontin generated more than $2.7 billion in revenues in 2003, more than 90 percent of which came from off-label prescriptions.

Of course, sometimes speakers discover that the drug they have been paid to lecture about is dangerous. One of the most notorious examples is Fen-Phen, the diet-drug combination that has been linked to primary pulmonary hypertension and valvular heart disease. Wyeth, the manufacturer of Redux, or dexfenfluramine—the "Fen" in Fen-Phen—has put aside $21 billion to cover costs and liabilities from litigation. Similar events played out, on a lesser scale, with Parke-Davis's diabetes drug Rezulin, and Wyeth's pain reliever Duract, which were taken off the market after being associated with life-threatening complications.

And what about reps themselves? Do they trust their companies to tell them about potential problems with their drugs? Not exactly. As one veteran rep, voicing a common sentiment, told me, "Reps are the last to know." Of course, for a rep to be detailing a drug enthusiastically right up to the day it is withdrawn from the market is likely to erode that rep's credibility with doctors. Yet some reps say they don't hear about problems until the press gets wind of them and the company launches into damage control. At that point, Slattery-Moschkau explains, "Reps learn verbatim how to handle the concern or objection in a way that spins it back in the drug's favor."

Some believe that the marketing landscape changed dramatically for both reps and doctors in 2002, after the Office of the Inspector General in the Department of Health and Human Services announced its intention to crack down on drug companies' more notorious promotional practices. With the threat of prosecution in the air, the industry began to take the job of self-policing a lot more seriously, and PhRMA issued a set of voluntary marketing guidelines.

Although most reps agree that the PhRMA code has changed things, not all of them agree that it changed things for the better. Some say that as long as reps feel pressure to meet quota, they will find ways to get around the rules. As one former rep pointed out, not all drug companies belong to PhRMA, and those that don't are, of course, not bound by PhRMA's guidelines. Jordan Katz says that things actually got worse after 2002. "The companies that tried to follow the guidelines lost a ton of market share, and the ones who didn't gained it," he says. "The bottom line is that if you don't pay off the doctors, you will not succeed in pharmaceuticals. Period."

A WORLD WITHOUT DOCTORS?

In 1997, John Lantos, a pediatrician and ethicist at the University of Chicago, wrote a book called *Do We Still Need Doctors?* We will always need health care, of course. But, as Lantos observes, it is not clear that we will always need to get our health care from doctors. Many of us already get it from other providers—nurses, physical therapists, clinical psychologists, nutritionists, respiratory therapists, and so on. The figure of "the doctor" is not cast in stone. It is really just a particular configuration of roles and duties and responsibilities, each of which can be changed.

Many have already been changed. Sometimes I think of my father as one of the last small-town, solo family doctors left in America. His kind of practice has been largely replaced by teams of specialists working in group practices underwritten by insurance companies and for-profit health-care chains. I doubt that any of the doctors my family has ever visited, except for a pediatrician who took care of our children when we lived in Montreal, would recognize us if they passed us in the street. Last year, while driving in Wisconsin, I filled up my car at a combination gas station, pharmacy, and walk-in medical clinic. I don't mean to complain. As long as our health insurance has been paid up, we have usually gotten good care. We simply live in a country that has decided that the traditional figure of the doctor is not worth preserving in the face of modern economics. Instead, we put our trust in the market.

Perhaps we are right to do so. We can get used to a world without doctors. As Lantos points out, we have gotten used to a world where we have shoes but no cobblers. We can copy documents without scriveners, make tools without blacksmiths, and produce books in the absence of bookbinders. We have left the old world behind, and for the most part, we don't miss it.

As the figure of the traditional doctor fades away, it is being replaced by a figure akin to the drug rep, one whose responsibilities are to compete as vigorously as possible in the medical marketplace. Patients are being replaced by "health-care consumers," who shop for the best medical bargains they can find. If it is true that the drug rep does not put my interests first, the same is true of everyone else in the marketplace; and we believe that such problems in the marketplace will be sorted out by the invisible hand. Buyers will stop buying from sellers who provide them with inferior goods. This model of medicine is not unlike that advocated thirty years ago by Robert Sade, a surgeon at my old medical school, the Medical University of South Carolina. Writing in *The New England Journal of Medicine*, Sade argued, "Medical care is neither a right nor a privilege; it is a service provided by doctors and others to people who wish to purchase it." He is now the vice chair of the AMA's Council of Ethical and Judicial Affairs.

Many doctors seem resigned to this shift. They see themselves as a beleaguered group whose lives are made miserable by third-party payers, personal-injury attorneys, and hospital bureaucrats. Whatever idealism they may have had about the practice of medicine is being pushed aside by the concrete realities of hustling in the new medical marketplace. Many academic physicians seem cowed by the power of the drug companies, upon whom some depend for research funding. For some, it's not so much a question of whether medicine has become a business as what kind of business it has become. When I talked recently to a gastroenterologist at an Ivy League medical school about his work as a thought leader for a variety of drug companies, he shrugged and said, "Better a whore than a concubine."

Which is not to say that pockets of resistance can't be found, especially among younger physicians and medical students. The American Medical Student Association may be the only mainstream medical organization with a principled position against taking industry gifts. It stands in striking contrast to the American Academy of Family Practice, which last year refused to grant exhibition space at its annual conference to No Free Lunch, a physician-led advocacy group that advises physicians to "Just say no to drug reps." The AAFP said that the group's goals were "not within the character and purpose" of the conference. But it allowed pharmaceutical companies, McDonald's, and the Distilled Spirits Council of the United States to exhibit. (It reversed its decision about No Free Lunch after protests by a number of AAFP members.)

Whether doctors and reps are all that different from one another is no longer clear. Doctors know a lot more about medicine, and drug reps dress a lot better, but these days both are Organization Men, small cogs in a vast health-care machine. They are just doing their jobs in a market-driven health-care bureaucracy that Americans have designed, and that we defend vigorously to critics elsewhere in the world. Like anyone else, doctors and reps are responding to the pressures and incentives of the system in which they work.

When Michael Oldani and I were having breakfast, he told me a story about a rep he interviewed for his dissertation. The rep had recently spent a day doing a "preceptorship," a practice in which a drug company pays doctors to let a rep shadow them while they see patients. This rep was shadowing a high-prescribing psychiatrist (she called him "Dr. C") at a med-check clinic. Med-check clinics are extremely busy sites where psychiatrists see large numbers of patients in quick succession, mainly to make sure that their medications are in proper order. At one point during the day, the rep said, a cheerful man in a wheelchair rolled into the office. Barely looking up from the stack of charts on his desk, Dr. C started quizzing the man about his medications. After a few minutes the man interrupted. "Look at me, Dr. C. Notice anything different?" Dr. C pushed his glasses up on top of his head and looked carefully at the patient for a few seconds before replying, "No, I don't. What's up?" The man smiled and said excitedly, "I got my legs cut off!"

After a moment of silence, Dr. C smiled. The man laughed. Neither seemed upset. In a few minutes the session ended, and the next patient came in.

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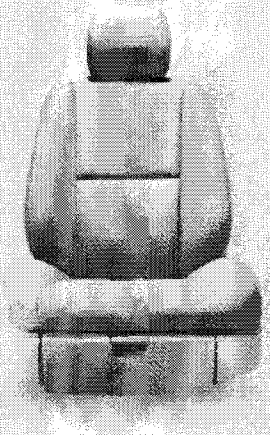

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Dr. Drug Rep

By DANIEL CARLAT

I. Faculty Development

On a blustery fall New England day in 2001, a friendly representative from Wyeth Pharmaceuticals came into my office in Newburyport, Mass., and made me an offer I found hard to refuse. He asked me if I'd like to give talks to other doctors about using Effexor XR for treating depression. He told me that I would go around to doctors' offices during lunchtime and talk about some of the features of Effexor. It would be pretty easy. Wyeth would provide a set of slides and even pay for me to attend a speaker's training session, and he quickly floated some numbers. I would be paid $500 for one-hour "Lunch and Learn" talks at local doctors' offices, or $750 if I had to drive an hour. I would be flown to New York for a "faculty-development program," where I would be pampered in a Midtown hotel for two nights and would be paid an additional "honorarium."

I thought about his proposition. I had a busy private practice in psychiatry, specializing in psychopharmacology. I was quite familiar with Effexor, since I had read recent studies showing that it might be slightly more effective than S.S.R.I.'s, the most commonly prescribed antidepressants: the Prozacs, Paxils and Zolofts of the world. S.S.R.I. stands for selective serotonin reuptake inhibitor, referring to the fact that these drugs increase levels of the neurotransmitter serotonin, a chemical in the brain involved in regulating moods. Effexor, on the other hand, was being marketed as a dual reuptake inhibitor, meaning that it increases both serotonin and norepinephrine, another neurotransmitter. The theory promoted by Wyeth was that two neurotransmitters are better than one, and that Effexor was more powerful and effective than S.S.R.I.'s.

I had already prescribed Effexor to several patients, and it seemed to work as well as the S.S.R.I.'s. If I gave talks to primary-care doctors about Effexor, I reasoned, I would be doing nothing unethical. It was a perfectly effective treatment option, with some data to suggest advantages over its competitors. The Wyeth rep was simply suggesting that I discuss some of the data with other doctors. Sure, Wyeth would benefit, but so would other doctors, who would become more educated about a good medication.

A few weeks later, my wife and I walked through the luxurious lobby of the Millennium Hotel in Midtown Manhattan. At the reception desk, when I gave my name, the attendant keyed it into the computer and said, with a dazzling smile: "Hello, Dr. Carlat, I see that you are with the Wyeth conference. Here are your materials."

She handed me a folder containing the schedule of talks, an invitation to various dinners and receptions and two tickets to a Broadway musical. "Enjoy your stay, doctor." I had no doubt that I would, though I felt a gnawing at the edge of my conscience. This seemed like a lot of money to lavish on me just so that I could provide some education to primary-care doctors in a small town north of Boston.

The next morning, the conference began. There were a hundred or so other psychiatrists from different parts of

the U.S. I recognized a couple of the attendees, including an acquaintance I hadn't seen in a while. I'd heard that he moved to another state and was making a bundle of money, but nobody seemed to know exactly how.

I joined him at his table and asked him what he had been up to. He said he had a busy private practice and had given a lot of talks for Warner-Lambert, a company that had since been acquired by Pfizer. His talks were on Neurontin, a drug that was approved for epilepsy but that my friend had found helpful for bipolar disorder in his practice. (In 2004, Warner-Lambert pleaded guilty to illegally marketing Neurontin for unapproved uses. It is illegal for companies to pay doctors to promote so-called off-label uses.)

I knew about Neurontin and had prescribed it occasionally for bipolar disorder in my practice, though I had never found it very helpful. A recent study found that it worked no better than a placebo for this condition. I asked him if he really thought Neurontin worked for bipolar, and he said that he felt it was "great for some patients" and that he used it "all the time." Given my clinical experiences with the drug, I wondered whether his positive opinion had been influenced by the money he was paid to give talks.

But I put those questions aside as we gulped down our coffees and took seats in a large lecture room. On the agenda were talks from some of the most esteemed academics in the field, authors of hundreds of articles in the major psychiatric journals. They included Michael Thase, of the University of Pittsburgh and the researcher who single-handedly put Effexor on the map with a meta-analysis, and Norman Sussman, a professor of psychiatry at New York University, who was master of ceremonies.

Thase strode to the lectern first in order to describe his groundbreaking work synthesizing data from more than 2,000 patients who had been enrolled in studies comparing Effexor with S.S.R.I.'s. At this time, with his Effexor study a topic of conversation in the mental-health world, Thase was one of the most well known and well respected psychiatrists in the United States. He cut a captivating figure onstage: tall and slim, dynamic, incredibly articulate and a master of the research craft.

He began by reviewing the results of the meta-analysis that had the psychiatric world abuzz. After carefully pooling and processing data from eight separate clinical trials, Thase published a truly significant finding: Effexor caused a 45 percent remission rate in patients in contrast to the S.S.R.I. rate of 35 percent and the placebo rate of 25 percent. It was the first time one antidepressant was shown to be more effective than any other. Previously, psychiatrists chose antidepressants based on a combination of guesswork, gut feeling and tailoring a drug's side effects to a patient's symptom profile. If Effexor was truly more effective than S.S.R.I.'s, it would amount to a revolution in psychiatric practice and a potential windfall for Wyeth.

One impressive aspect of Thase's presentation was that he was not content to rest on his laurels; rather he raised a series of potential criticisms of his results and then rebutted them convincingly. For example, skeptics had pointed out that Thase was a paid consultant to Wyeth and that both of his co-authors were employees of the company. Thase responded that he had requested and had received all of the company's data and had not cherry-picked from those studies most favorable for Effexor. This was a significant point, because companies sometimes withhold negative data from publication in medical journals. For example, in 2004, GlaxoSmithKline was sued by Eliot Spitzer, who was then the New York attorney general, for suppressing data hinting that Paxil causes suicidal thoughts in children. The company settled the case and agreed to make clinical-trial results public.

Another objection was that while the study was billed as comparing Effexor with S.S.R.I.'s in general, in fact most of the data compared Effexor with one specific S.S.R.I.: Prozac. Perhaps Effexor was, indeed, more effective than Prozac; this did not necessarily mean that it was more effective than the other S.S.R.I.'s in common use. But Thase announced that since the original study, he had analyzed data on Paxil and other meds and also found differences in remission rates.

For his study, Thase chose what was at that time an unusual measure of antidepressant improvement: "remission," rather than the more standard measure, "response." In clinical antidepressant trials, a "response" is defined as a 50 percent improvement in depressive symptoms, as measured by the Hamilton depression scale. Thus, if a patient enters a study scoring a 24 on the Hamilton (which would be a moderate degree of depression), he or she would have "responded" if the final score, after treatment, was 12 or less.

Remission, on the other hand, is defined as "complete" recovery. While you might think that a patient would have to score a 0 on the Hamilton to be in remission, in fact very few people score that low, no matter how deliriously happy they are. Instead, researchers come up with various cutoff scores for remission. Thase chose a cutoff score of 7 or below.

In his study, he emphasized the remission rates and not the response rates. As I listened to his presentation, I wondered why. Was it because he felt that remission was the only really meaningful outcome by which to compare drugs? Or was it because using remission made Effexor look more impressive than response did? Thase indirectly addressed this issue in his paper by pointing out that even when remission was defined in different ways, with different cutoff points, Effexor beat the S.S.R.I.'s every time. That struck me as a pretty convincing endorsement of Wyeth's antidepressant.

The next speaker, Norm Sussman, took the baton from Thase and explored the concept of remission in more detail. Sussman's job was to systematically go through the officially sanctioned "slide deck" — slides provided to us by Wyeth, which we were expected to use during our own presentations.

If Thase was the riveting academic, Sussman was the engaging populist, translating some of the drier research concepts into terms that our primary-care-physician audiences would understand. Sussman exhorted us not to be satisfied with response and encouraged us to set the bar higher. "Is the patient doing everything they were doing before they got depressed?" he asked. "Are they doing it even better? That's remission." To further persuade us, he highlighted a slide showing that patients who made it all the way to remission are less likely to relapse to another depressive episode than patients who merely responded. And for all its methodological limitations, it was a slide that I would become well acquainted with, as I would use it over and over again in my own talks.

When it came to side effects, Effexor's greatest liability was that it could cause hypertension, a side effect not shared by S.S.R.I.'s. Sussman showed us some data from the clinical trials, indicating that at lower doses, about 3 percent of patients taking Effexor had hypertension as compared with about 2 percent of patients assigned to a placebo. There was only a 1 percent difference between Effexor and placebo, he commented, and pointed out that treating high blood pressure might be a small price to pay for relief from depression.

It was an accurate reading of the data, and I remember finding it a convincing defense of Effexor's safety. As I look back at my notes now, however, I notice that another way of describing the same numbers would have been to say that Effexor leads to a 50 percent greater rate of hypertension than a placebo. Framed this way, Effexor looks more

hazardous.

And so it went for the rest of the afternoon.

Was I swallowing the message whole? Certainly not. I knew that this was hardly impartial medical education, and that we were being fed a marketing line. But when you are treated like the anointed, wined and dined in Manhattan and placed among the leaders of the field, you inevitably put some of your critical faculties on hold. I was truly impressed with Effexor's remission numbers, and like any physician, I was hopeful that something new and different had been introduced to my quiver of therapeutic options.

At the end of the last lecture, we were all handed envelopes as we left the conference room. Inside were checks for $750. It was time to enjoy ourselves in the city.

II. The Art and Science of Detailing

Pharmaceutical "detailing" is the term used to describe those sales visits in which drug reps go to doctors' offices to describe the benefits of a specific drug. Once I returned to my Newburyport office from New York, a couple of voice-mail messages from local Wyeth reps were already waiting for me, inviting me to give some presentations at local doctors' offices. I was about to begin my speaking — and detailing — career in earnest.

How many doctors speak for drug companies? We don't know for sure, but one recent study indicates that at least 25 percent of all doctors in the United States receive drug money for lecturing to physicians or for helping to market drugs in other ways. This meant that I was about to join some 200,000 American physicians who are being paid by companies to promote their drugs. I felt quite flattered to have been recruited, and I assumed that the rep had picked me because of some special personal or professional quality.

The first talk I gave brought me back to earth rather quickly. I distinctly remember the awkwardness of walking into my first waiting room. The receptionist slid the glass partition open and asked if I had an appointment.

"Actually, I'm here to meet with the doctor."

"Oh, O.K. And is that a scheduled appointment?"

"I'm here to give a talk."

A light went on. "Oh, are you part of the drug lunch?"

Regardless of how I preferred to think of myself (an educator, a psychiatrist, a consultant), I was now classified as one facet of a lunch helping to pitch a drug, a convincing sidekick to help the sales rep. Eventually, with an internal wince, I began to introduce myself as "Dr. Carlat, here for the Wyeth lunch."

The drug rep who arranged the lunch was always there, usually an attractive, vivacious woman with platters of gourmet sandwiches in tow. Hungry doctors and their staff of nurses and receptionists would filter into the lunch room, grateful for free food.

Once there was a critical mass (and crucially, once the M.D.'s arrived), I was given the go-ahead by the Wyeth reps to start. I dove into my talk, going through a handout that I created, based on the official slide deck. I

discussed the importance of remission, the basics of the Thase study showing the advantage of Effexor, how to dose the drug, the side effects, and I added a quick review of the other common antidepressants.

While I still had some doubts, I continued to be impressed by the 10 percent advantage in remission rates that Effexor held over S.S.R.I.'s; that advantage seemed significant enough to overcome Effexor's more prominent side effects. Yes, I was highlighting Effexor's selling points and playing down its disadvantages, and I knew it. But was my salesmanship going to bring harm to anybody? It seemed unlikely. The worst case was that Effexor was no more effective than anything else; it certainly was no less effective.

During my first few talks, I worried a lot about my performance. Was I too boring? Did the doctors see me as sleazy? Did the Wyeth reps find me sufficiently persuasive? But the day after my talks, I would get a call or an e-mail message from the rep saying that I did a great job, that the doctor was impressed and that they wanted to use me more. Indeed, I started receiving more and more invitations from other reps, and I soon had talks scheduled every week. I learned later that Wyeth and other companies have speaker-evaluation systems. After my talks, the reps would fill out a questionnaire rating my performance, which quickly became available to other Wyeth reps throughout the area.

As the reps became comfortable with me, they began to see me more as a sales colleague. I received faxes before talks preparing me for particular doctors. One note informed me that the physician we'd be visiting that day was a "decile 6 doctor and is not prescribing any Effexor XR, so please tailor accordingly. There is also one more doc in the practice that we are not familiar with." The term "decile 6" is drug-rep jargon for a doctor who prescribes a lot of medications. The higher the "decile" (in a range from 1 to 10), the higher the prescription volume, and the more potentially lucrative that doctor could be for the company.

A note from another rep reminded me of a scene from "Mission: Impossible." "Dr. Carlat: Our main target, Dr. , is an internist. He spreads his usage among three antidepressants, Celexa, Zoloft and Paxil, at about 25-30 percent each. He is currently using about 6 percent Effexor XR. Our access is very challenging with lunches six months out." This doctor's schedule of lunches was filled with reps from other companies; it would be vital to make our sales visit count.+

Naïve as I was, I found myself astonished at the level of detail that drug companies were able to acquire about doctors' prescribing habits. I asked my reps about it; they told me that they received printouts tracking local doctors' prescriptions every week. The process is called "prescription data-mining," in which specialized pharmacy-information companies (like IMS Health and Verispan) buy prescription data from local pharmacies, repackage it, then sell it to pharmaceutical companies. This information is then passed on to the drug reps, who use it to tailor their drug-detailing strategies. This may include deciding which physicians to aim for, as my Wyeth reps did, but it can help sales in other ways. For example, Shahram Ahari, a former drug rep for Eli Lilly (the maker of Prozac) who is now a researcher at the University of California at San Francisco's School of Pharmacy, said in an article in The Washington Post that as a drug rep he would use this data to find out which doctors were prescribing Prozac's competitors, like Effexor. Then he would play up specific features of Prozac that contrasted favorably with the other drug, like the ease with which patients can get off Prozac, as compared with the hard time they can have withdrawing from Effexor.

The American Medical Association is also a key player in prescription data-mining. Pharmacies typically will not

release doctors' names to the data-mining companies, but they will release their Drug Enforcement Agency numbers. The A.M.A. licenses its file of U.S. physicians, allowing the data-mining companies to match up D.E.A. numbers to specific physicians. The A.M.A. makes millions in information-leasing money.

Once drug companies have identified the doctors, they must woo them. In the April 2007 issue of the journal PLoS Medicine, Dr. Adriane Fugh-Berman of Georgetown teamed up with Ahari (the former drug rep) to describe the myriad techniques drug reps use to establish relationships with physicians, including inviting them to a speaker's meeting. These can serve to cement a positive a relationship between the rep and the doctor. This relationship is crucial, they say, since "drug reps increase drug sales by influencing physicians, and they do so with finely titrated doses of friendship."

III. Uncomfortable Moments

I gave many talks over the ensuing several months, and I gradually became more comfortable with the process. Each setting was somewhat different. Sometimes I spoke to a crowded conference room with several physicians, nurses and other clinical staff. Other times, I sat at a small lunch table with only one other physician (plus the rep), having what amounted to a conversation about treating depression. My basic Effexor spiel was similar in the various settings, with the focus on remission and the Thase data.

Meanwhile, I was keeping up with new developments in the research literature related to Effexor, and not all of the news was positive. For example, as more data came out comparing Effexor with S.S.R.I.'s other than Prozac, the Effexor remission advantage became slimmer -- more like 5 percent instead of the originally reported 10 percent. Statistically, this 5 percent advantage meant that only one out of 20 patients would potentially do better on Effexor than S.S.R.I.'s — much less compelling than the earlier proportion of one out of 10.

I also became aware of other critiques of the original Thase meta-analysis. For example, some patients enrolled in the original Effexor studies took S.S.R.I.'s in the past and presumably had not responded well. This meant that the study population may have been enriched with patients who were treatment-resistant to S.S.R.I.'s, giving Effexor an inherent advantage.

I didn't mention any of this in my talks, partly because none of it had been included in official company slides, and partly because I was concerned that the reps wouldn't invite me to give talks if I divulged any negative information. But I was beginning to struggle with the ethics of my silence.

One of my most uncomfortable moments came when I gave a presentation to a large group of psychiatrists. I was in the midst of wrapping up my talk with some information about Effexor and blood pressure. Referring to a large study paid for by Wyeth, I reported that patients are liable to develop hypertension only if they are taking Effexor at doses higher than 300 milligrams per day.

"Really?" one psychiatrist in the room said. "I've seen hypertension at lower doses in my patients."

"I suppose it can happen, but it's rare at doses that are commonly used for depression."

He looked at me, frowned and shook his head. "That hasn't been my experience."

I reached into my folder where I kept some of the key Effexor studies in case such questions arose.

According to this study of 3,744 patients, the rate of high blood pressure was 2.2 percent in the placebo group, and 2.9 percent in the group of patients who had taken daily doses of Effexor no larger than 300 milligrams. Patients taking more than 300 milligrams had a 9 percent risk of hypertension. As I went through the numbers with the doctor, however, I felt unsettled. I started talking faster, a sure sign of nervousness for me.

Driving home, I went back over the talk in my mind. I knew I had not lied — I had reported the data exactly as they were reported in the paper. But still, I had spun the results of the study in the most positive way possible, and I had not talked about the limitations of the data. I had not, for example, mentioned that if you focused specifically on patients taking between 200 and 300 milligrams per day, a commonly prescribed dosage range, you found a 3.7 percent incidence of hypertension. While this was not a statistically significant higher rate than the placebo, it still hinted that such moderate doses could, indeed, cause hypertension. Nor had I mentioned the fact that since the data were derived from placebo-controlled clinical trials, the patients were probably not representative of the patients seen in most real practices. Patients who are very old or who have significant medical problems are excluded from such studies. But real-world patients may well be at higher risk to develop hypertension on Effexor. +

I realized that in my canned talks, I was blithely minimizing the hypertension risks, conveniently overlooking the fact that hypertension is a dangerous condition and not one to be trifled with. Why, I began to wonder, would anyone prescribe an antidepressant that could cause hypertension when there were many other alternatives? And why wasn't I asking this obvious question out loud during my talks?

I felt rattled. That psychiatrist's frown stayed with me — a mixture of skepticism and contempt. I wondered if he saw me for what I feared I had become — a drug rep with an M.D. I began to think that the money was affecting my critical judgement. I was willing to dance around the truth in order to make the drug reps happy. Receiving $750 checks for chatting with some doctors during a lunch break was such easy money that it left me giddy. Like an addiction, it was very hard to give up.

There was another problem: one of Effexor's side effects. Patients who stopped the medication were calling their doctors and reporting symptoms like severe dizziness and lightheadedness, bizarre electric-shock sensations in their heads, insomnia, sadness and tearfulness. Some patients thought they were having strokes or nervous breakdowns and were showing up in emergency rooms. Gradually, however, it became clear that these were "withdrawal" symptoms. These were particularly common problems with Effexor because it has a short half-life, a measure of the time it takes the body to metabolize half of the total amount of a drug in the bloodstream. Paxil, another short half-life antidepressant, caused similar problems.

At the Wyeth meeting in New York, these withdrawal effects were mentioned in passing, though we were assured that Effexor withdrawal symptoms were uncommon and could usually be avoided by tapering down the dose very slowly. But in my practice, that strategy often did not work, and patients were having a very hard time coming off Effexor in order to start a trial of a different antidepressant.

I wrestled with how to handle this issue in my Effexor talks, since I believed it was a significant disadvantage of the drug. Psychiatrists frequently have to switch medications because of side effects or lack of effectiveness, and anticipating this potential need to change medications plays into our initial choice of a drug. Knowing that Effexor was hard to give up made me think twice about prescribing it in the first place.

During my talks, I found myself playing both sides of the issue, making sure to mention that withdrawal symptoms could be severe but assuring doctors that they could "usually" be avoided. Was I lying? Not really, since there were no solid published data, and indeed some patients had little problem coming off Effexor. But was I tweaking and pruning the truth in order to stay positive about the product? Definitely. And how did I rationalize this? I convinced myself that I had told "most" of the truth and that the potential negative consequences of this small truth "gap" were too trivial to worry about.

As the months went on, I developed more and more reservations about recommending that Effexor be used as a "first line" drug before trying the S.S.R.I.'s. Not only were the newer comparative data less impressive, but the studies were short-term, lasting only 6 to 12 weeks. It seemed entirely possible that if the clinical trials had been longer — say, six months — S.S.R.I.'s would have caught up with Effexor. Effexor was turning out to be an antidepressant that might have a very slight effectiveness advantage over S.S.R.I.'s but that caused high blood pressure and had prolonged withdrawal symptoms.

At my next Lunch and Learn, I mentioned toward the end of my presentation that data in support of Effexor were mainly short-term, and that there was a possibility that S.S.R.I.'s were just as effective. I felt reckless, but I left the office with a restored sense of integrity.

Several days later, I was visited by the same district manager who first offered me the speaking job. Pleasant as always, he said: "My reps told me that you weren't as enthusiastic about our product at your last talk. I told them that even Dr. Carlat can't hit a home run every time. Have you been sick?"

At that moment, I decided my career as an industry-sponsored speaker was over. The manager's message couldn't be clearer: I was being paid to enthusiastically endorse their drug. Once I stopped doing that, I was of little value to them, no matter how much "medical education" I provided.

IV. Life After Drug Money

A year after starting my educational talks for drug companies (I had also given two talks for Forest Pharmaceuticals, pushing the antidepressant Lexapro), I quit. I had made about $30,000 in supplemental income from these talks, a significant addition to the $140,000 or so I made from my private practice. Now I publish a medical-education newsletter for psychiatrists that is not financed by the pharmaceutical industry and that tries to critically assess drug research and marketing claims. I still see patients, and I still prescribe Effexor. I don't prescribe it as frequently as I used to, but I have seen many patients turn their lives around because they responded to this drug and to nothing else. +

In 2002, the drug industry's trade group adopted voluntary guidelines limiting some of the more lavish benefits to doctors. While the guidelines still allow all-expenses-paid trips for physicians to attend meetings at fancy hotels, they no longer pay for spouses to attend the dinners or hand out tickets to musicals. In an e-mail message, a Wyeth spokesman wrote that Wyeth employees must follow that code and "our own Wyeth policies, which, in some cases, exceed" the trade group's code.

Looking back on the year I spent speaking for Wyeth, I've asked myself if my work as a company speaker led me to do bad things. Did I contribute to faulty medical decision making? Did my advice lead doctors to make inappropriate drug choices, and did their patients suffer needlessly?

Maybe. I'm sure I persuaded many physicians to prescribe Effexor, potentially contributing to blood-pressure problems and withdrawal symptoms. On the other hand, it's possible that some of those patients might have gained more relief from their depression and anxiety than they would have if they had been started on an S.S.R.I. Not likely, but possible.

I still allow drug reps to visit my office and give me their pitches. While these visits are short on useful medical information, they do allow me to keep up with trends in drug marketing. Recently, a rep from Bristol-Myers Squibb came into my office and invited me to a dinner program on the antipsychotic Abilify.

"I think it will be a great program, Dr. Carlat," he said. "Would you like to come?" I glanced at the invitation. I recognized the name of the speaker, a prominent and widely published psychiatrist flown in from another state. The restaurant was one of the finest in town.

I was tempted. The wine, the great food, the proximity to a famous researcher — why not rejoin that inner circle of the select for an evening? But then I flashed to a memory of myself five years earlier, standing at a lectern and clearing my throat at the beginning of a drug-company presentation. I vividly remembered my sensations — the careful monitoring of what I would say, the calculations of how frank I should be.

"No," I said, as I handed the rep back the invitation. "I don't think I can make it. But thanks anyway."

Daniel Carlat is an assistant clinical professor of psychiatry at Tufts University School of Medicine and the publisher of The Carlat Psychiatry Report.

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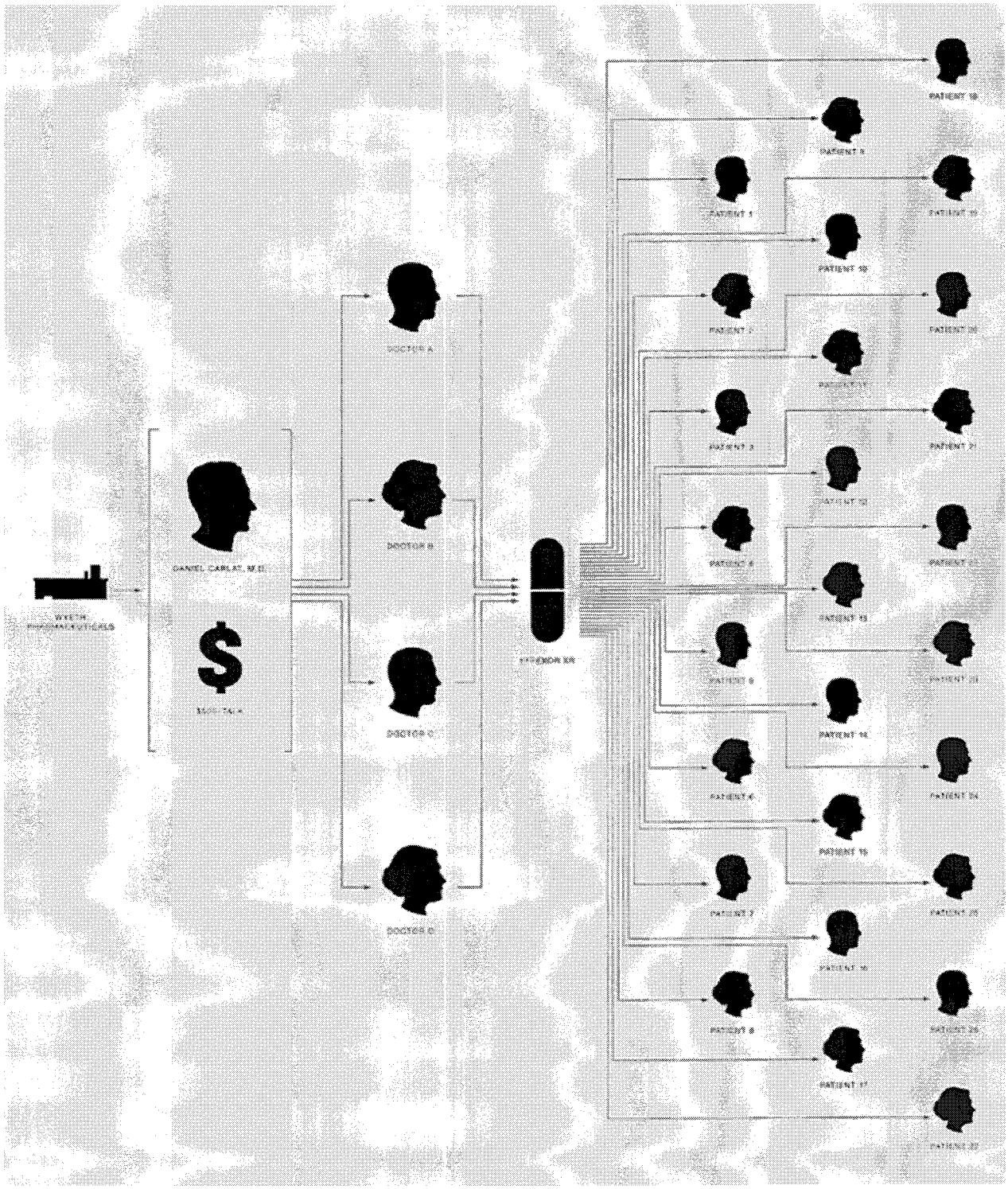

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May 9, 2007

Doctors Reap Millions for Anemia Drugs

By ALEX BERENSON and ANDREW POLLACK

Two of the world's largest drug companies are paying hundreds of millions of dollars to doctors every year in return for giving their patients anemia medicines, which regulators now say may be unsafe at commonly used doses.

The payments are legal, but very few people outside of the doctors who receive them are aware of their size. Critics, including prominent cancer and kidney doctors, say the payments give physicians an incentive to prescribe the medicines at levels that might increase patients' risks of heart attacks or strokes.

Industry analysts estimate that such payments — to cancer doctors and the other big users of the drugs, kidney dialysis centers — total hundreds of millions of dollars a year and are an important source of profit for doctors and the centers. The payments have risen over the last several years, as the makers of the drugs, Amgen and Johnson & Johnson, compete for market share and try to expand the overall business.

Neither Amgen nor Johnson & Johnson has disclosed the total amount of the payments. But documents given to The New York Times show that at just one practice in the Pacific Northwest, a group of six cancer doctors received $2.7 million from Amgen for prescribing $9 million worth of its drugs last year.

Yesterday, the Food and Drug Administration added to concerns about the drugs, releasing a report that suggested that their use might need to be curtailed in cancer patients. The report, prepared by F.D.A. staff scientists, said no evidence indicated that the medicines either improved quality of life in patients or extended their survival, while several studies suggested that the drugs can shorten patients' lives when used at high doses. Yesterday's report followed the F.D.A.'s decision in March to strengthen warnings on the drugs' labels.

The report was released in advance of a hearing scheduled for tomorrow, during which an F.D.A. advisory panel will consider whether the drugs are overused.

The medicines — Aranesp and Epogen, from Amgen; and Procrit, from Johnson & Johnson — are among the world's top-selling drugs, with combined sales of $10 billion last year. In this country, they represent the single biggest drug expense for Medicare and are given to about a million patients each year to treat anemia caused by kidney disease or cancer chemotherapy.

Dr. Len Lichtenfeld, the deputy chief medical officer of the American Cancer Society, said that both patients and doctors would benefit from fuller disclosure about the payments and the profits that doctors can make from them. "I suspect that Medicare is going to take a very careful look at what is going on here," he said.

Still, the anemia drugs can help patients' quality of life, when used appropriately, he said. "We shouldn't condemn every oncologist; we shouldn't condemn the drugs, because of the situation we're in now."

Federal laws bar drug companies from paying doctors to prescribe medicines that are given in pill form and purchased by patients from pharmacies. But companies can rebate part of the price that doctors pay for drugs, like the anemia medicines, which they dispense in their offices as part of treatment. The anemia drugs are injected or given intravenously in physicians' offices or dialysis centers. Doctors receive the rebates after they buy the drugs from the companies. But they also receive reimbursement from Medicare or private insurers for the drugs, often at a markup over the doctors' purchase price.

Medicare has changed its payment structure since 2003 to reduce the markup, but private insurers still often pay more. Combined with those insurance reimbursements, the rebates enable many doctors to profit substantially on the medicines they buy and then give to patients.

The rebates are related to the amount of drugs that doctors buy, and physicians that agree to use one company's drugs exclusively typically receive higher rebates.

Johnson & Johnson said yesterday in a statement that its rebates were not intended to induce doctors to use more medicine. Instead, the rebates "reflect intense competition" in the market for the drugs, the company said.

Amgen said that rebates were a normal commercial practice and that it had always properly promoted its drugs.

"Amgen is dedicated to patient safety," said David Polk, a spokesman. "We believe our contracts support appropriate anemia management and our product promotion is always strictly within the label."

Both companies' stocks fell yesterday after release of the F.D.A. report. Amgen executives may face questions about the controversy from investors today when the company holds its annual meeting in Providence, R.I.

Since 1991, when the first of the drugs was still relatively new, the average dose given to dialysis patients in this country has nearly tripled. About 50 percent of dialysis patients now receive enough of the drugs to raise their red blood cell counts above the level considered risky by the F.D.A.

American patients receive far more of the anemia drugs than patients elsewhere, with dialysis patients in this country getting doses more than twice as high as their counterparts in Europe. Cancer care shows a similar pattern. American cancer patients are about three times as likely as those in Europe to get the drugs, and they receive somewhat higher doses.

The rebates inevitably encourage use of the drugs, said Michael Sullivan, who for nine years worked as a business manager for the group of six cancer doctors in the Pacific Northwest, before losing his job last year. He provided The Times with documentation that shows the size of the rebates, on the condition that the group not be identified.

"Personally, I think rebates should go away," said Mr. Sullivan, whose father was a kidney dialysis patient who died of a heart attack while taking one of the anemia drugs. "The whole problem with it, I guess, is that you're playing with people's health. It's not the same as buying widgets."

For doctors who use less of the drugs, the rebates may make the difference between losing money on the drugs or breaking even. Mr. Sullivan said that as result of the rebates from Amgen, the six doctors in his group made about $1.8 million in net profit on the drugs they prescribed.

Unlike most drugs, the anemia medicines do not come in fixed doses. Therefore, doctors have great flexibility to increase dosing — and profits. Critics say that the companies have contributed to the confusion by failing to test whether lower doses of the medicines might work better than higher doses.

"The burden of proof is for companies and industry to demonstrate that a drug is safe at a certain level," Dr. Ajay Singh, an associate professor at Harvard Medical School. Dr. Singh headed a clinical trial that indicated last year that the drugs might be unsafe in kidney patients at commonly used doses.

Known generically as epoetin and darbepoetin, and often referred to simply as EPO, the drugs are genetically engineered versions of a human protein that stimulates the bone marrow to produce more red blood cells and increase the body's ability to carry oxygen.

Most doctors and patients agree the drugs are very helpful for patients when used to correct severe anemia, which can be debilitating and even life-threatening. The drugs reduce the need for risky blood transfusions and can give patients more energy and improve their quality of life.

"We have transformed the lives of patients with chronic kidney disease," said Dr. Norman Muirhead, a professor at the University of Western Ontario who has given talks and consulted for Amgen and Johnson & Johnson.

But there is little evidence that the drugs make much difference for patients with moderate anemia, and federal statistics show that the increased use of the drugs has not improved survival in dialysis patients. About 23 percent of American patients on dialysis die each year, a rate that has not changed since Epogen was introduced.

Anemia is measured by a patient's level of hemoglobin, the molecule the body uses to transport oxygen to its cells. Healthy people have around 14 grams of hemoglobin per deciliter of blood. Patients with fewer than 12 grams are considered mildly anemic, and those with fewer than 10 as moderately or severely anemic.

The labels on the drugs, as currently approved by the F.D.A., encourage doctors to aim for a hemoglobin level of 10 to 12. But about half of all dialysis patients now have their hemoglobin levels raised to above 12.

Critics of the drugs say their increased use has been driven by profit. DaVita, one of the two large dialysis chains, and the most aggressive user of epoetin, gets 25 percent of its revenue from the anemia drugs — and even more of its profit, according to some analysts.

Dr. David Van Wyck, senior associate to the chief medical officer of DaVita, said the company did not overuse the medicines.

Doctors determine how much to use, Dr. Van Wyck said. "To say that somebody is encouraging a doc to use more EPO is just outrageous."

Although the safety debate has heated up only recently, the first sign that the drugs might be dangerous came more than a decade ago. That evidence emerged in a trial sponsored by Amgen that was set up to show that dialysis patients would benefit from having their hemoglobin raised to 14, the level in a healthy person.

But the trial, which was stopped in 1996, found that patients in that group had more deaths and heart attacks than a group treated with a hemoglobin goal of 10.

That trial should have discouraged doctors from using too much epoetin and encouraged Amgen to study the risks further, said Dr. Steven Fishbane, a nephrologist at Winthrop-University Hospital on Long Island.

Instead, use of epoetin continued to soar. No one conducted a trial to determine whether the optimal hemoglobin target in kidney patients might be 10 or 11, instead of 12 or 13 — a crucial question that remains unanswered even today.

Dr. Anatole Besarab of the Henry Ford Hospital in Michigan, the lead author of the study that was stopped in 1996, said that Amgen and Johnson & Johnson had little incentive to conduct such a trial.

Dr. Robert M. Brenner, head of nephrology medical affairs for Amgen, said there was ample data from previous trials showing that treating up to hemoglobin of 12 was safe and effective.

Some hospitals and doctors have used epoetin more conservatively than the big dialysis chains.

Dr. Ronald A. Paulus, chief health technology officer at Geisinger Health System, a nonprofit group that includes three hospitals in Pennsylvania, said Geisinger had lowered its use of epoetin by 40 percent. Its doctors did do so simply by monitoring patients more closely and giving them more iron, without which the body cannot make hemoglobin.

Dr. N. D. Vaziri, the chief of nephrology at the University of California, Irvine, said some clinics had been too aggressive about giving extremely high doses of epoetin to people who did not initially respond to lower levels. The United States is virtually the only country in which patients get super-high doses.

"You create a toxicity situation," said Dr. Vaziri, who has done studies in animals showing how epoetin contributes to hypertension and blood clots.

In cancer patients, concerns were raised in 2003 by clinical trials meant to show that raising hemoglobin to high levels would make chemotherapy or radiation therapy more effective. Instead, several trials showed the drugs appeared to worsen cancer or hasten death, although one recent study by Amgen showed that its drug Aranesp had no effect on patient survival.

The conflicting studies are among the issues the F.D.A. advisory committee is expected to discuss tomorrow. Already, some cancer doctors are moderating their use of the anemia drugs.

Dr. Peter Eisenberg, an oncologist in Marin County, Calif., said many doctors had been induced to use more epoetin by the financial incentives and the belief that the drug was helpful.

"The deal was so good," he said. "The indication was so clear and the downside was so small that docs just worked it into their practice easily.

"Now it's much scarier than that," he said. "We could really be doing harm."

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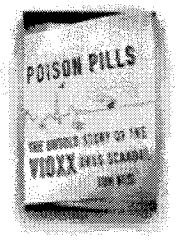
Former Pharma Pitchman: Beware of New Drugs

An insider speaks up on the Vioxx scandal—and reveals common tactics that dupe patients and doctors alike

By Sarah Baldauf
Posted September 18, 2008

Tom Nesi, author of the new book *Poison Pills: The Untold Story of the Vioxx Drug Scandal*, wants you to know what you're getting into when you pop a newly approved, heavily marketed prescription drug. A longtime director of public affairs at the pharmaceutical company Bristol-Myers Squibb, Nesi has more than 30 years' experience in medical communications and strategy. Now a writer and consultant, he comes off as no shill for the industry he once served.



Author Tom Nesi

His book focuses on the cautionary tale of Vioxx, the prescription painkiller that was pulled from the market after doctors belatedly realized that it caused heart, blood, and kidney problems—including some that were fatal. His broader objective, though, is to help consumers take advantage of good medicines while sidestepping the harm some can cause.

You say the most expensive drug you can take is a free sample. How is that?

They're very seductive—they're free. Merck distributed 17 million samples to 25,000 physicians and 375,000 patients. The problem is that if you've been doing fine on a 20-cent pill, you get the free sample for a month or two, then you have to go to the drugstore to fill the prescription and then it costs you $3 a pill.

You argue that in the context of pharmaceuticals, new is not always better. Why?

It's extremely important that people understand that, as extensively as a drug is tested before it's approved [by the Food and Drug Administration], it's still tested on a very small

population. It's also tested on a very select population. Drug companies don't go out to try to find the sickest patients to test their drugs on.

[With older drugs], not only is there more data but more usage experience. Doctors know how to use it—they become familiar with it. An example in the pain market: When some of these non-steroidal anti-inflammatories were released, like Motrin and Aleve, they were actually given at doses that were too high. As the years go by, [drugs] can actually become safer.

As a veteran drug marketer, you warn consumers to beware huge marketing campaigns for new drugs. In fact, you urge people to ask their doctors for proof that new drugs are superior to older ones before accepting a prescription for the newer medicine.

I would say the larger the marketing campaign, the more you should use caution. I would also say if there are good drugs in a category—in a type of illness that you suffer from—that have been out there for a while, there's no reason not to use those first.

How long should a drug be on the market before you try it?

I don't think it hurts to wait a few years. If you are in acute need, if you're just suffering horrible pain, you've tried everything under the sun and you need a new drug, well, that's entirely different than if you're satisfied. I would say, if you're satisfied with your current therapy, stay with it.

You caution women, in particular, to find out about a new drug's safety before taking it.

We know that some drugs interfere with reproduction. Any woman who is planning to get pregnant, or who potentially could get pregnant, should definitely discuss that with their doctor.

How often do doctors actually recommend their patients stop taking a prescription that works for them and start a newer drug instead? And how often do patients ask to change a medication they're doing well on?

It happens all the time. There are whole huge campaigns based on what they call switching behavior. A classic example that has just earned billions of dollars for no apparent reason: There was a drug I worked on, a very good drug called Prilosec, for treating heartburn, and

AstraZeneca, the company that had the patent, wanted to keep making money after Prilosec went off [patent], so they came up with a successor drug called Nexium, which is "the little purple pill." I remember working with a colleague [who, after looking at the preliminary data,] was just astounded and said, "Nexium doesn't work any better."

The Vioxx scandal is the main focus of your book. You contend that while the drug's maker, Merck, said it was collecting more data on Vioxx, thousands of people may have died. Is the lesson here to be skeptical when a pharmaceutical company says, "Not all the data are in yet" on a new drug?

Exactly. Some studies simply just get dropped. A lot of data just never gets published. There are ways of presenting data where not even the most sophisticated investigator could really tell what the data was really saying. One of the most disconcerting things, we know that there were more deaths among Alzheimer's patients who took Vioxx. The Alzheimer's trials for Vioxx were sort of published, but not with the complete data sets.

This book seems the antithesis, in some ways, of your life's work. Why did you write it?

My wife died about six years ago. She was very young, and she died of brain cancer. I went through experimental drugs, the talking to doctors—just about everything you can think of—and I found out that it was bogus. [Marketing medicines] was my life's career, and it forced me to really [re-]evaluate. I just didn't want to get out there anymore and tell people such-and-such a drug was a miracle compound when I knew that, (a) it wasn't, and (b) even if it was helping people, it was destroying their quality of life. So it caused me an entire career change—it just changed not just my career but my entire life. We're being duped.

Tags: FDA | marketing | prescription drugs | Merck | Vioxx

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Though Most Physicians Support a Ban on Collecting Prescribing Information, Only a Fraction Have Used PDRP to Restrict Rx Data Access

Business Wire. New York: Feb 21, 2007.

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Fifth graph of release dated Feb. 21, 2007 should be replaced with the following corrected graph:

PDRP is the AMA's new measure that gives physicians some control over access to their prescribing information. Under PDRP, physicians are able to opt out of having their individual prescribing data released to pharmaceutical sales representatives and their first-line managers.

The corrected release reads:

THOUGH MOST PHYSICIANS SUPPORT A BAN ON COLLECTING PRESCRIBING INFORMATION, ONLY A FRACTION HAVE USED PDRP TO RESTRICT RX DATA ACCESS

More than half of physicians support a total ban on collecting personal prescribing information and want more aggressive actions taken to protect their prescribing privacy, according to TNS Healthcare research released today. In

spite of these strong feelings, just 4% have used the AMA's Prescription Data Restriction Program (PDRP) to opt out of having their prescribing information released to pharmaceutical sales representatives, and only 29% plan to take advantage of the opt-out option. The largest group of physicians--44%--say they will wait and decide later what to do about PDRP.

Opt-out plans vary widely across specialty groups. Endocrinologists are most likely to take action through PDRP, with 47% either having already opted out or planning to do so. On the other end of the spectrum, neurologists appear least likely to respond to PDRP, with just under a quarter either having already opted out or planning to take action.

"There is a discrepancy between the amount of concern physicians express about protecting their prescribing privacy and their plans to take action through PDRP," says Andrew Brana, Consultant, Sales Performance Services for TNS Healthcare. "For instance, gastroenterologists have among the highest percentage of doctors in favor of more aggressive action to protect prescribing privacy, with a full 60% in favor of a total ban on prescribing data. Yet just 5% have opted out through PDRP, and only 32% have any plans to take advantage of the opt-out option.

"The large number of physicians taking a 'wait and see' approach--ranging from 39% of neurologists to 49% of psychiatrists--indicates that doctors are still unsure of whether PDRP is the right answer to the issue. Although the vast majority of physicians--79%--say they are uncomfortable knowing that sales reps have data on their prescribing behavior, only a small fraction of these doctors have used PDRP to block sales rep access to their prescription records."

PDRP is the AMA's new measure that gives physicians some control over access to their prescribing information. Under PDRP, physicians are able to opt out of having their individual prescribing data released to pharmaceutical sales representatives and their first-line managers.

PDRP Awareness High across All Specialties

Although few physicians have taken action, most are aware of PDRP. TNS Healthcare unaided awareness research shows that more than 80% of physicians know about the new program, even though few have acted on it.

Over-Aggressive Sales Tactics Linked to PDRP Action

The factor that appears most closely linked to physicians' PDRP opt-out plans is their experience with overly aggressive sales tactics. Overall, 38% of doctors report being victims of overly aggressive sales pitches. That percentage soars to 51% for endocrinologists--the specialty with the highest proportion of physicians planning to opt out through PDRP. Conversely, just 13% of neurologists report experiencing overly aggressive sales tactics--with neurologists also showing the smallest proportion of doctors planning to take action through PDRP.

Primary care physicians fall in between those two extremes, with 39% reporting overly aggressive sales tactics. They also fall in between in terms of their PDRP activity, with just about a third either having opted out or planning to opt out of providing their prescribing data to sales reps.

Physicians Much More Comfortable Sharing Their Own Prescribing Data

Although most physicians favor a ban on collecting prescribing data from secondary sources, such as pharmacies, the majority of doctors are comfortable sharing that information themselves with pharmaceutical companies. An overwhelming 85% would be willing to provide information on their prescribing practices to the pharmaceutical industry through market research questionnaires.

Most physicians also would be comfortable having pharmaceutical companies share this self-reported information with their field forces. About two-thirds of primary care physicians, cardiologists, neurologists and gastroenterologists say they would be willing to have pharmaceutical companies provide self-reported prescribing information to sales representatives. Endocrinologists are significantly less comfortable, with just 43% saying they would be willing to share self-reported prescribing practices with reps.

"Endocrinologists' hesitancy to share even self-reported information with reps most likely links back to their negative sales experiences," says Jonathan Kay, COO of TNS Healthcare. "More than half report overly-aggressive sales practices, perhaps explaining the deeper concerns endocrinologists have about reps having access to any kind of prescribing data--even self reported."

1,000 Physicians Weigh in on Their PDRP Plans

TNS Healthcare's findings are based on a January 2007 Internet survey of 1,001 doctors--500 primary care physicians, 100 cardiologists, 100 neurologists, 100 gastroenterologists, 100 endocrinologists and 101 psychiatrists. All physicians were recruited from TNS Healthcare's J Street Physician Internet panel.

About TNS...

TNS is a market information group:

-- The world's largest provider of custom research and analysis

-- A leader in political and social polling

-- A major supplier of consumer panel, media intelligence and TV and radio audience measurement services.

TNS operates across a global network in over 70 countries, providing internationally consistent, up-to-the-minute and high quality information and analysis.

The group's employees deliver innovative thinking and excellent service to local and multi-national clients worldwide. In the custom business, they combine in-depth sector knowledge with expertise in the areas of new product development, positioning and segmentation research, brand and advertising research and stakeholder management.

TNS' strategic goal is to be recognized as the global leader in delivering value added information and insights that help our clients make more effective decisions.

TNS is the sixth sense of business.

About TNS Healthcare...

TNS Healthcare provides market research consulting to the worldwide pharmaceutical, biotech and medical device industries, as well as health-focused ad agencies, media and analysts. It offers globally consistent solutions and custom advisory services to support product introductions; brand, treatment and sales performance optimization; and physician and DTC promotional assessment.

Informing decisions across the life cycle, TNS Healthcare offers action-ready insights for pre-launch landscaping, market and opportunity assessment, segmentation, positioning, message and campaign creation, pricing, forecasting, attitude and awareness measurement and post-launch tracking. It delivers information across stakeholders--including physicians, patients and consumers--to help companies anticipate and impact customers' behaviors. TNS Healthcare provides both qualitative and quantitative offerings, using traditional and on-line methodologies, combining worldwide reach with local expertise.

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Prescription Data Used To Assess Consumers

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Records Aid Insurers but Prompt Privacy Concerns

By Ellen Nakashima
Washington Post Staff Writer
Monday, August 4, 2008; A01

Health and life insurance companies have access to a powerful new tool for evaluating whether to cover individual consumers: a health "credit report" drawn from databases containing prescription drug records on more than 200 million Americans.

Collecting and analyzing personal health information in commercial databases is a fledgling industry, but one poised to take off as the nation enters the age of electronic medical records. While lawmakers debate how best to oversee the shift to computerized records, some insurers have already begun testing systems that tap into not only prescription drug information, but also data about patients held by clinical and pathological laboratories.

Traditionally, insurance companies have judged an applicant's risk by gathering medical records from physicians' offices. But the new tools offer the advantage of being "electronic, fast and cheap," said Mark Franzen, managing director of Milliman IntelliScript, which provides consumers' personal drug profiles to insurers.

The trend holds promise for improved health care and cost savings, but privacy and consumer advocates fear it is taking place largely outside the scrutiny of federal health regulators and lawmakers.

Ingenix, a Minnesota-based health information services company that had $1.3 billion in sales last year -- and Wisconsin-based rival Milliman -- say the drug profiles are an accurate, less expensive alternative to seeking physician records, which can take months and hundreds of dollars to obtain. They note that consumers authorize the data release and that the services can save insurance companies millions of dollars and benefit consumers anxious for a decision.

"Some insurers can make a decision in the same day, or right on the spot," Franzen said. "That's the real 'value-add.' "

But the practice also illustrates how electronic data gathered for one purpose can be used and marketed for another -- often without consumers' knowledge, privacy advocates say. And they argue that although consumers sign consent forms, they effectively have to authorize the data release if they want insurance.

"As health care moves into the digital age, there are more and more companies holding vast amounts of patients' health information," said Joy Pritts, research professor at Georgetown University's Health Policy Institute. "Most people don't even know these organizations exist. Unfortunately the federal health privacy rule does not cover many of them. . . . The lack of transparency with how all of this works is disturbing."

Ingenix and Milliman create the profiles by plumbing rich databases of prescription drug histories kept by pharmacy benefit managers (PBMs), which help insurers process drug claims. Ingenix, for instance, has servers in the PBM data centers, updating the drug files as frequently as once a day, said John Stenson, senior vice president of consulting for Ingenix, which is a division of UnitedHealth Group. The corporation also owns UnitedHealthcare, the nation's second-largest insurer.

When an insurer makes an online query about an applicant, Ingenix or Milliman's servers scour the data and within minutes or less return reports to a central server at the company. The server aggregates the information going back as far as five years, including the drugs and dosages prescribed, dates filled and refilled, the therapeutic class and the name and address of the prescribing doctor.

Then comes the analysis.

Ingenix's MedPoint tool provides insurers a "pharmacy risk score," or a number that represents an "expected risk" for a group of people, such as 30- to 35-year-old women who have taken prescription drugs, Stenson said. Higher scores imply higher medical costs.

Milliman's IntelliScript codes drugs red, yellow or green, according to the insurer's instructions, with red signaling the greatest risk, Franzen said. Red codes could include the so-called AIDS cocktail drugs and cancer medications, he said.

The companies receive data only on individuals who are in clients in PBMs' databases, generally excluding, say, people who pay for drugs in cash. The profiles cost insurers about $15 a search. IntelliScript gets about 1 million queries from insurers a year, largely individual health insurers.

The system can save money for insurers, said Richard Dick, an entrepreneur who built the database system that Ingenix acquired in 2002.

For instance, if MedPoint produces a report that an individual has been on the highest dose of the cholesterol-reducing drug Zocor for 18 monts, the insurer "would be able to know that you have a very high, near-intractable cholesterol problem," Dick said, and could avoid a costly blood test.

From a business standpoint, it makes no sense for an insurer to sell a plan with a $200 monthly premium if the company knows that the consumer is taking medications that cost $400 every six months, industry experts said. That is why having access to an "objective" source of third-party information is valuable, said Tia Goss Sawhney, a Chicago area health insurance actuary who has used both companies' tools. "Though most people tell the truth most of the time, there are people out there who don't, who leave out something that's incredibly relevant, who may even be able to defraud a company," she said. "That's important because ultimately the people who tell the truth have to pay for those who don't."

Franzen, whose firm expects revenue of $575 million this year, said his clients tell him that about 10 percent of applicants do not disclose pertinent medical conditions in their applications that are later revealed by prescription drug history.

Some health experts worry that insurance companies can make faulty assumptions by looking at prescription drug records, because many drugs have multiple uses. "I had a patient on Amitriptyline for migraines and they were denied life insurance because it's also an antidepressant," said physician Kate Atkinson of Amherst, Mass. "I had to explain it wasn't being used for depression." Another patient was on Prozac -- not for depression, but for menopausal hot flashes. "I wrote an appeal letter, and they still wouldn't give it to her," Atkinson said.

Services such as MedPoint are just "one of many tools" underwriters use to make coverage decisions, said Tyler Mason, a spokesman for UnitedHealthcare, which uses MedPoint. A high-risk score on a profile will often lead to requests for more information from the applicant, he said.

Ingenix and Milliman officials stress that they provide data only with the patient's consent, as required by the Health Insurance Portability and Accountability Act (HIPAA), a 1996 law that governs personal health records information. But HIPAA does not give the Department of Health and Human Services the ability to directly investigate or hold accountable entities, such as pharmacy benefit managers or companies such as Ingenix and Milliman, who are not covered by HIPAA.

A health privacy proposal pending in Congress would expand federal officials' ability to regulate such "downstream" organizations, audit their activities and impose civil fines. The bill also includes a prohibition on the sale of electronic medical records.

Tim Sparapani, senior legislative counsel at the American Civil Liberties Union, said that the products that Ingenix and Milliman are marketing represent the "commodification" of electronic medical records by third parties. "We've got to stop these practices before the marketplace is fully developed and patients lose all control over their medical information," he said.

The field is growing rapidly. Realtime Solutions Group, a company in Woodridge, Ill., is testing whether lab data can be aggregated with prescription and other data for underwriting purposes. The firm is working with two major commercial labs and three large insurers, using thousands of real applicants. Initial results are promising enough that the company plans to proceed to the data-analysis stage, company co-founder Tedd Determan said.

"A lot of insurance companies are starting to use this type of data," said Determan, who co-founded IntelRx, a company that mined prescription databases and was sold to Milliman in 2005. "They said, 'All right. Prescription data is working, let's go and look at other types of data, too.' It's because of the success of one, that we're going after others."

In February, the Federal Trade Commission issued an order saying that MedPoint and IntelliScript are consumer reports under the Fair Credit Reporting Act, so the companies must notify insurers that consumers denied insurance on the basis of these reports have the right to request a copy of the report and that errors be corrected. The FTC's order followed a settlement of allegations that the companies violated the credit-reporting law by failing to provide such notice to insurers.

Bob Gellman, an independent privacy consultant in Washington, said the FTC's decision not to fine the companies sends "the message that it is okay to ignore the law." That, he said, "is absolutely outrageous."

As more health records become electronic, he said, more parties will compete to sell more comprehensive patient data to insurers, driving down data prices. "It will all likely be lawful," Gellman said, "but consumers will likely continue to have no real meaningful choices if they want insurance."

Dick, who conceived the idea of linking the pharmacy databases for underwriting purposes a decade ago, said the pharmacy benefit managers understood the system's privacy implications. He said their attitude seemed one of, " 'Ooh, this is a 60 Minutes' story in the making.' Generally, they wanted to make it a super-secret database, restricted to underwriting."

But now, he said, "there's a huge case for it being opened up for all legitimate access," whether for a patient in an emergency room or for federal government purposes. The key, he said, is full transparency.

He said he has created a privacy tool that requires users to consent before specific data, such as prescription histories, can be released. To work, he said, the tool must be independent of all who hold the data.

"Otherwise," he said, "you have the fox in charge of the henhouse."

Staff researcher Magda Jean-Louis contributed to this report.

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ISSUE BRIEF:

THE SALE OF PHYSICIAN PRESCRIBING DATA RAISES HEALTH CARE COSTS—THE NATIONAL PHYSICIANS ALLIANCE CALLS FOR A BAN

NATIONAL PHYSICIANS ALLIANCE

Databases about physicians' prescribing practices have been created, sold, and used without physicians' knowledge or consent.

- Pharmacies compile databases that show how many and which medications individual physicians prescribe; these databases are sold to Healthcare Information Organizations (HIOs). HIOs combine this information with data from the Physician Masterfile, purchased from the American Medical Association (AMA).
- The Physician Masterfile contains information on virtually every physician in the United States *including the two-thirds of physicians who are not AMA members.*
- This combined data set is then sold to pharmaceutical companies. These companies arm their drug detailers with the prescribing data of physicians in their area so they can target individual physicians with finely tuned sales pitches.
- A study from the Kaiser Family Foundation in 2001 found nearly three-quarters of physicians disapprove of this practice.[1]

This raises the cost of health care by promoting inappropriate and expensive prescribing.

- This practice is bad for public health because it raises costs to patients by promoting inappropriate prescribing of expensive drugs. Pharmaceutical representatives—who have personal relationships with many physicians and their office staff—routinely persuade physicians to prescribe newer and more expensive medications when cheaper and equally good or sometimes even better alternatives exist.
- The prescribing data allows drug detailers to tailor their marketing messages to individual physicians and use carefully selected data to convince doctors to change their prescribing to a particular company's product.
- While retail data is commonly sold in many fields, the relationship between a physician and patient is a unique one. Physicians are entrusted by society to act in their patients' best interests, yet physicians are demonstrably influenced by the marketing strategies of drug detailers.[2] The best way to ensure that physicians retain the trust of patients is to warrant it, by eliminating this commercial intrusion into the doctor-patient relationship. Medical decision-making must remain scientific and objective.

The AMA, pharmacies, and pharmaceutical companies all have a financial interest in the status quo.

- The AMA received **$44.5 million in 2005** from sales of data from the Masterfile.[3]
- Pharmacies and HIOs clearly benefit from the system. One of the leading HIOs, IMS Health, had revenues of **$1.75 billion in 2005.**[3]

Recent efforts have begun to address this problem.

- New Hampshire passed a law in 2006 that bans the sale of physician-specific prescribing data.
- The American Medical Association recently began the Prescribing Data Restriction Program (PDRP). The PDRP allows physicians to prevent their own prescribing data from being released to pharmaceutical detailers, or to "opt-out."
- The California Medical Association, working with IMS Health, is planning to start a program in 2007 that will allow physicians to access their own prescribing information but that continues to permit pharmaceutical companies to purchase prescribing data.

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The AMA's opt-out program falls short. A complete ban is needed on the sale of prescribing data.

- Many physicians do not and will not know that the AMA's opt-out program exists.
- If physicians want their prescribing data sold to pharmaceutical companies, they should have to "opt-in."
- The AMA only allows physicians to opt-out for three years; it will be difficult for physicians to remember to opt-out repeatedly.
- Even if physicians opt-out using the AMA's PDRP, pharmaceutical companies can still purchase the data from the AMA. The opt-out only means that pharmaceutical companies have agreed not to release individual provider information to their drug detailers, but there is no law that prevents them from doing so.
- The AMA's Masterfile helps pharmaceutical corporations target their detailing practices. However, even without the Masterfile, companies will be able to obtain some information from pharmacies about physicians' prescribing practices. Thus, more global protection is needed than what the AMA can offer with its opt-out program.

The National Physicians Alliance supports a legislative ban on the sale of physician prescribing data for commercial and marketing purposes.

- A ban on the sale of prescribing data is good for patient care and will save money by reducing the aggressive marketing by drug companies that contributes to inappropriate and more expensive prescriptions.
- Legitimate, noncommercial uses of prescribing data such as clinical and health services research can and should be exempted. For example, government agencies or university researchers should be able to use the data to evaluate prescribing practices.
- The NPA supports legislation modeled after New Hampshire HB 1346 enacted June 30, 2006.

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THE EVIDENCE GAP

The Minimal Impact of a Big Hypertension Study

By ANDREW POLLACK

The surprising news made headlines in December 2002. Generic pills for high blood pressure, which had been in use since the 1950s and cost only pennies a day, worked better than newer drugs that were up to 20 times as expensive.

The findings, from one of the biggest clinical trials ever organized by the federal government, promised to save the nation billions of dollars in treating the tens of millions of Americans with hypertension — even if the conclusions did seem to threaten pharmaceutical giants like Pfizer that were making big money on blockbuster hypertension drugs.

Six years later, though, the use of the inexpensive pills, called diuretics, is far smaller than some of the trial's organizers had hoped.

"It should have more than doubled," said Dr. Curt D. Furberg, a public health sciences professor at Wake Forest University who was the first chairman of the steering committee for the study, which was known by the acronym Allhat. "The impact was disappointing."

The percentage of hypertension patients receiving a diuretic rose to around 40 percent in the year after the Allhat results were announced, up from 30 to 35 percent beforehand, according to some studies. But use of diuretics has since stayed at that plateau. And over all, use of newer hypertension drugs has grown faster than the use of diuretics since 2002, according to Medco Health Solutions, a pharmacy benefits manager.

The Allhat experience is worth remembering now, as some policy experts and government officials call for more such studies to directly compare drugs or other treatments, as a way to stem runaway medical costs and improve care.

The aftereffects of the study show how hard it is to change medical practice, even after a government-sanctioned trial costing $130 million produced what appeared to be solid evidence.

A confluence of factors blunted Allhat's impact. One was the simple difficulty of persuading doctors to change their habits. Another was scientific disagreement, as many academic medical experts criticized the trial's design and the government's interpretation of the results.

Moreover, pharmaceutical companies responded by heavily marketing their own expensive hypertension drugs and, in some cases, paying speakers to publicly interpret the Allhat results in ways that made their products look better.

"The pharmaceutical industry ganged up and attacked, discredited the findings," Dr. Furberg said. He eventually resigned in frustration as chairman of the study's steering committee, the expert group that continues to oversee analysis of data from the trial. One member of that committee received more than $200,000 from Pfizer, largely in speaking fees, the year after the Allhat results were released.

There was another factor: medicine moves on. Even before Allhat was finished, and certainly since then, new drugs appeared. Others, meanwhile, became available as generics, reducing the cost advantage of the diuretics. And many doctors have shifted to using two or more drugs together, helped by pharmaceutical companies that offer combination pills containing two medicines.

So Allhat's main query — which drug to use first — became "an outdated question that doesn't have huge relevance to the majority of people's clinical practices," said Dr. John M. Flack, the chairman of medicine at Wayne State University, who was not involved in the study and has consulted for some drug makers.

Dr. Sean Tunis, a former chief medical officer for Medicare, remains an advocate for comparative-effectiveness studies. But, as Allhat showed, "they are hard to do, expensive to do and provoke a lot of political pushback," said Dr. Tunis, who now runs the nonprofit Center for Medical Technology Policy, which tries to arrange such trials.

"There's a lot of magical thinking," he said, "that it will all be science and won't be politics."

Expensive Pills

Promising better ways to treat high blood pressure, drug companies in the 1980s introduced a variety of medications, including ones known as calcium channel blockers and ACE inhibitors.

Although there was no real evidence the newer pills were better, diuretics fell to 27 percent of hypertension prescriptions in 1992, from 56 percent in 1982. Use of the more expensive pills added an estimated $3.1 billion to the nation's medical bill over that period.

So the National Heart, Lung and Blood Institute, part of the federal National Institutes of Health, decided to compare the various drugs' ability to prevent heart attacks, strokes and other cardiovascular problems. "This was a big-bucks issue," said Dr. Jeffrey Cutler, the Heart, Lung and Blood Institute's project director for the study.

Allhat — short for the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial — began enrolling patients with high blood pressure, age 55 and older, in 1994, with more than 42,000 people eventually participating. Patients were randomly assigned one of four drugs: a diuretic called chlorthalidone; an ACE inhibitor called lisinopril, which AstraZeneca sold as Zestril; a calcium channel blocker, amlodipine, sold by Pfizer as Norvasc; and an alpha blocker, doxazosin, which Pfizer sold as Cardura.

Cardura was added only after Pfizer, which had already agreed to contribute $20 million to the trial's costs, increased that to $40 million, Dr. Cutler said.

Early Trouble Signs

Pfizer's bet on Cardura proved a big mistake. As the Allhat data came in, patients taking Cardura were nearly twice as likely as those receiving the diuretic to require hospitalization for heart failure, a condition in which the heart cannot pump blood adequately. Concerned, the Heart, Lung and Blood Institute announced in March 2000 that it had stopped the Cardura part of the trial.

What happened next provided the first signs that the Allhat evidence might not be universally embraced.

Rather than warn doctors that Cardura might not be suited for hypertension, Pfizer circulated a memo to its sales representatives suggesting scripted responses they could use to reassure doctors that Cardura was safe, according to documents released from a patients' lawsuit against the company.

And in an e-mail message unearthed in those same court documents, a Pfizer sales executive boasted to colleagues that company employees had diverted some European doctors attending an American cardiology conference from hearing a presentation on the Allhat results and Cardura. "The good news," the message said, "is that they were quite brilliant in sending their key physicians to sightsee rather than hear Curt Furberg slam Pfizer once again!"

Pfizer declined to comment on the messages.

The Food and Drug Administration waited a year before convening a meeting of outside experts to discuss Cardura's safety. At that session, some of the experts sharply challenged the conclusions of the Allhat organizers. They argued that the heart failure cases might have been false readings and that an inadequate dose of Cardura had been used in the trial.

By the end of the daylong meeting, Dr. Robert J. Temple, a senior F.D.A. official, was clearly exasperated by the experts' varying interpretations of a supposedly definitive trial.

"This is the largest and best attempt to compare outcomes we are ever going to see," he said. "And people are extremely doubtful about whether it has shown anything at all."

The committee decided that there was no need to issue an urgent warning to doctors and patients about Cardura.

Cardura sales held up in 2000. But the next year, worldwide sales fell to $552 million, from $795 million. Prescriptions for all alpha blockers fell 22 percent from 1999 to 2002 after having risen before then, according to one study.

Pfizer's decision to stop promoting Cardura in late 2000, after the drug lost patent protection, was a factor in the decline. But Allhat clearly was, too.

Cost-Benefit Analysis

The main Allhat results were announced in December 2002 at a news conference in Washington and published in The Journal of the American Medical Association.

In the primary target outcome of the trial — the prevention of heart attacks — the three remaining drugs were proved equal. But patients receiving the Norvasc calcium channel blocker from Pfizer had a 38 percent

greater incidence of heart failure than those on the diuretic. And those receiving the ACE inhibitor from AstraZeneca had a 15 percent higher risk of strokes and a 19 percent higher risk of heart failure.

Moreover, the diuretic cost only about $25 a year, compared with $250 for an ACE inhibitor and $500 for a calcium channel blocker. So the diuretic was declared the winner.

But some hypertension experts accused the government of overstating the case for the diuretics, as a way to cut medical spending.

"There was a feeling there was a political and economic agenda as much as a scientific agenda," said Dr. Michael Weber, a professor of medicine at the Health Science Center at Brooklyn, part of the State University of New York, who had been an investigator in the study but afterward became one of its leading critics. "They pushed beyond what the data allowed them to say."

Critics said the rules of the trial had favored the diuretics. If the first drug did not adequately lower blood pressure — as happened in more than 60 percent of cases — a second drug could be added. But that second drug was usually a type that worked better with diuretics than with ACE inhibitors.

There were also more new cases of diabetes among the patients who took diuretics, although experts argued over how meaningful that finding was.

Adding fuel to the debate, an Australian study released two months after Allhat found an ACE inhibitor superior to a diuretic. The proper lesson to draw from Allhat, some critics contended, was that what matters most is how much blood pressure is lowered, not which drug is used to do it. For these and other reasons, European hypertension experts discounted Allhat.

Allhat's proponents discounted the Australian study as less authoritative, and they dismissed the other criticisms.

Still, the arguments "muddied the waters," said Dr. Randall S. Stafford of Stanford, who studied the effect of Allhat on prescriptions. "The message," he said, "was no longer as clear to physicians."

Science Moves On

By the time the Allhat results were released, lisinopril, the ACE inhibitor, had become generic. That meant AstraZeneca and Merck, which sold a version of the compound as Prinivil, had less interest in defending their drugs.

Not so Pfizer. Norvasc was the best-selling hypertension treatment in the world, with sales of $3.8 billion in 2002, and Pfizer's second-biggest drug behind the cholesterol medication Lipitor.

The company set out to accentuate the positive. In a news release after the Allhat results were announced, it said that Norvasc was found to be "comparable to the diuretic in fatal coronary heart disease, heart attacks and stroke." And in a medical journal advertisement, it proclaimed "ALL HATs off" to its drug.

Neither the news release nor the ad, however, included the 38 percent greater risk of heart failure with Norvasc in the Allhat study.

Nor did Hank McKinnell, then Pfizer's chief executive, mention heart failure in lauding the results during his quarterly earnings conference call with analysts a few weeks after the Allhat report was released. "Contrary to what you might have read in the press," Mr. McKinnell said, "Allhat is extremely positive for Norvasc. It will be our job to explain that to the medical community."

Dr. Paul K. Whelton, president of Loyola University Health System and the current chairman of the Allhat steering committee, said that Pfizer and other drug companies "took what was in their best interest and ran with those, and conveniently didn't mention other things."

Pfizer defends its actions. Dr. Michael Berelowitz, the head of Pfizer's global medical organization, said that in the trial's design, heart failure was merely one component of a broader measure of various cardiovascular problems. And in that broader measure, Dr. Berelowitz said, there was no difference between Norvasc and the diuretic. Also, he said, the label for Norvasc already contained a precaution about heart failure.

"Further action regarding the heart failure finding was therefore not considered necessary," he said in a statement in response to questions.

Pfizer was not the only company promoting its drugs. The drug giant Novartis, for example, was spending heavily to market Diovan, a leader among a class of hypertension drugs called angiotensin receptor blockers, which were too new to have been included in Allhat. Diovan, which had more than $5 billion in sales last year, sells for $1.88 to $3.20 a pill on drugstore.com, compared with 8 to 31 cents for a diuretic.

No company, though, was spending money to promote generic diuretics. So the federal Heart, Lung and Blood Institute recruited Allhat investigators, provided them with training and sent them to proselytize fellow physicians. In all, 147 investigators gave nearly 1,700 talks and reached more than 18,000 doctors and other health care providers.

But it was a coffee-and-doughnuts operation compared with the sumptuous dinners that pharmaceutical companies used to market to doctors. Moreover, the steering committee's outreach program did not get under way until about three years after the results were published.

Dr. Stafford of Stanford said the outreach seemed to have had a slight effect on increasing the use of diuretics.

The results of Pfizer's efforts are easier to quantify. Norvasc sales continued to grow to $4.9 billion in 2006, falling only after the drug lost patent protection in the United States in 2007.

Tangles and Strife

Tensions about industry influence reached even the study's own steering committee. Dr. Furberg, the chairman, bluntly accused some members of the committee of being agents of the industry.

One member, Dr. Richard H. Grimm Jr. of the University of Minnesota, had been receiving tens of thousands of dollars a year from Pfizer since at least 1997, according to reports that pharmaceutical companies file in that state.

In 2003, the year after the Allhat results were published, Dr. Grimm's payments from Pfizer soared to more than $200,000 — an increase that The New York Times reported in 2007.

Dr. Grimm said in a recent interview that about half those fees in 2003 came from giving about 100 Pfizer-sponsored talks to doctors about Allhat. Dr. Grimm said he gave mainly the standard Allhat-sanctioned talk. But instead of saying diuretics were outright better than the other drugs, he said they were as good or better.

Meanwhile, Dr. Grimm had led an effort to remove Dr. Furberg from his position on the grounds that he had not been impartial.

"He had a vendetta against the calcium channel blockers," Dr. Grimm said. Dr. Furberg had been publicly questioning the safety of those drugs based on some studies he did in the 1990s. The effort to oust Dr. Furberg failed in 2001. But in August 2004, Dr. Furberg resigned as chairman, contending that there had not been enough effort to disseminate the Allhat message.

Dr. Whelton, who took over as chairman, said that the study's message was never compromised by industry ties on the steering committee.

"Curt is a wonderful guy who is a crusader," said Dr. Whelton, who did not have industry ties and was not involved in the effort to unseat Dr. Furberg. "He has certainly rubbed a lot of people, even good friends, the wrong way."

Changing Practice

Experts see several lessons to be learned from Allhat.

One is that "all trials have flaws" that leave the results open to interpretation, said Dr. Robert M. Califf, a cardiologist at Duke who served on the safety monitoring committee of Allhat.

Another is that providing doctors information is "necessary, but not sufficient" to urge them to change their practices, said Dr. Carolyn M. Clancy, director of the federal Agency for Healthcare Research and Quality, which itself conducts studies comparing different medical treatments.

And while insurers can influence practice through reimbursement policies, they did not seem to have pushed strongly for diuretics after Allhat, in part because some of the other drugs had become generic.

Even the cost-conscious medical system at the Department of Veterans Affairs did not require diuretics, because too many doctors would probably have requested exceptions, said Dr. William C. Cushman, chief of preventive medicine at the department's medical center in Memphis.

Dr. Cushman, a member of the Allhat steering committee, said diuretic use in the system was still "much lower" than he thought it should be.

Dr. Clancy said that her agency was now mainly using insurance records to judge how treatments perform. While clinical trials are the gold standard, she said, they are costly and time-consuming.

And, she added, "You might be answering a question that by the time you are done, no longer feels quite as

relevant."

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PUSHING PILLS
Mining Prescription Records for Fun and Profit
California has become a battleground in a debate over how Big Pharma's access to prescription data affects patient care and the price of drugs

Jake Whitney
Sunday, August 6, 2006

One afternoon in early 2002, Dr. Brad Drexler, an obstetrician in Healdsburg, got a visit from a pharmaceutical sales representative. The drug rep was from a company called Berlex, and the drug she was selling was Yasmin, a birth control pill that had been on the market for about a year.

Unlike some physicians, Drexler enjoyed visiting with drug reps, and saw them routinely; only in rare instances did he refuse to speak with them. The visit with the Berlex rep that day was typically pleasant. The rep was so friendly, in fact, that she thanked Drexler for all the prescriptions he had been writing for Berlex's pharmaceuticals.

Drexler found the statement odd. He wasn't in the habit of divulging to salespeople how often he prescribed their company's drugs, so he wondered just how the rep knew. Drexler called local pharmacies and asked the pharmacists if they had any knowledge of drug reps gaining access to prescription records. But they were as befuddled as he was.

Then one day, a rep with whom Drexler was particularly friendly spilled the beans. He told Drexler that he and his fellow reps were provided with detailed prescription information, which was stored in their laptops, on every physician in their sales territory.

"It bothered me in two ways," Drexler said. "One, that this practice was so hidden that neither I nor any of the pharmacists I spoke with knew it occurred. And two, because this potentially changed the equation between doctor and drug rep." He added, "I felt like I lost a lot of privacy that day."

The discovery prompted Drexler to take his concerns to the California Medical Association, where he had been a member of its House of Delegates. He introduced a resolution there calling for the CMA to oppose drug company access to prescription records.

Today, three years after Drexler's resolution, California has become a key battleground in a growing debate over how drug companies' access to prescription data affects both patient care and the price of pharmaceuticals. A pilot program, to be launched imminently with 100 doctors, may determine just

how easy, or difficult, it will be in the future for pharmaceutical companies to access this information.

Drug companies have been buying prescription records since the 1990s, yet the practice is still not widely known. Even many doctors don't know it occurs.

According to a Kaiser Family Foundation survey taken in 2001, 34 percent of doctors did not know that drug companies had access to their prescription writing history. In 2004, a survey sponsored by the American Medical Association found that number to have shrunk to about 25 percent. And, like Drexler, the more doctors learn of the practice, the more they try to stop it.

The imminent pilot program had its genesis in 2003, when, spurred by physician complaints and encouragement from the CMA, Assemblywoman Wilma Chan, D-Oakland, presented Assembly Bill 262 to the California Legislature. AB 262 would have banned statewide the use of prescription data for marketing purposes.

Despite strong support from the CMA, opposition to Chan's bill was intense. Between its introduction in February 2003 and its demise in August 2004, AB 262 was amended 13 times to mollify various interest groups. Concessions were made allowing prescription data to be collected for research purposes -- the bill's opponents' chief argument as to the benefits of the practice -- but, according to Chan, lobbying from the pharmaceutical industry and data mining companies, especially IMS Health, crushed it.

Data mining companies such as IMS Health play the role of middleman in tracking prescription records. These firms buy records from pharmacy chains and other sources before repackaging them and selling them to drug companies. When pharmacy chains sell the records, however, they do not include patient names and, in some cases, the doctors who wrote the prescriptions. So drug companies turn to a surprising source to complete the prescription profiles: the AMA.

The AMA leases its "physicians' Masterfile" to data mining companies and, through them, subleases it to pharmaceutical companies. This Masterfile contains personal and professional information, including the Drug Enforcement Agency number on all doctors practicing in the United States. And since every prescription written in the United States must include the prescribing physician's DEA number, drug companies use these physician-unique numbers on the Masterfile to match prescription records to doctors.

How important are the profiles to drug reps? "An enormous help," said Kathleen Slattery-Moschkau, whose 2005 film "Side Effects" is loosely based on her 10 years peddling pills for pharmaceutical giants Johnson & Johnson and Bristol-Myers Squibb. "They allow reps to enter doctors' offices armed and dangerous."

Slattery-Moschkau said that when she was a rep she was given reports on every doctor within her sales territory by drug class, as well as "numerous other reports, such as the 'Heavy Hitter List,'" which

would include the top physicians her company was trying to "convert."

She said the profiles helped her decide which doctors "were worthy of spending my monthly budgets on for lunches, dinners, days at the spa, etc." Overall, she said, the reports "were a great tool for determining which marketing tactics worked best."

Jamie Reidy, a former Pfizer rep who chronicled his days selling Viagra in his 2005 memoir "Hard Sell," put it bluntly: "Prescription data was our greatest tool in planning our approach to manipulating doctors." But the pharmaceutical industry maintains that prescription profiles are collected primarily for research and for other reasons beneficial to patients.

The Pharmaceutical Research and Manufacturers Association, in an e-mailed statement prepared by Senior Vice President Ken Johnson, said that banning the practice (West Virginia, Arizona, Hawaii and New Hampshire are also considering or have considered legislation to ban or restrict it) "could chill important research that protects and improves public health."

The statement added that the data "can be analyzed by researchers to identify poor prescribing habits," and then cited a study by the Centers for Disease Control and Prevention that used the data to examine antibiotic use to help prevent antibiotic resistance and "reduce unnecessary prescribing." The statement concluded that, "Analyzing prescribing data is another way to make sure patients all over the country receive the best possible care."

The AMA shares this position. Its policy is that the data is collected for research, for locating doctors to participate in clinical trials, to assist in distributing drug samples and in case of a drug recall.

Robert Musacchio, the AMA's vice president of publishing and business services, said that as a general rule his organization has no problem with the data being used for marketing purposes, as long as it is not used to "overtly influence the physician/patient relationship."

But critics point to insider revelations like those of Reidy and Slattery-Moschkau as proof that drug companies use the data precisely in this way: to influence doctors' prescription writing. Drexler said it was just this potentiality that engendered his 2003 resolution. He said his concerns were that visits by drug reps, "could be used to inappropriately reward doctors who were prescribing the company's products."

And that with prescription data in their hands, "the potential existed for reps to influence doctors." When asked whether Drexler's fears were merited, Reidy said yes, that reps "totally reward doctors," but not so it's obvious. He illustrated: "Say Dr. X is prescribing a lot of Zithromax (a Pfizer antibiotic) when he used to prescribe Amoxicillin for similar conditions. If the rep rewards him by giving him gift certificates to Morton's Steakhouse and saying things like, 'Thanks for all the business,' then suddenly Dr. X may feel sleazy and stop writing for Zithromax. On the other hand, he may realize what's going on and start asking the rep for gift certificates to Peter Luger Steakhouse."

Physicians' staffs are also targets, Reidy said, especially nurses. He said that in his case he would take nurses out to happy hour where he would thank them for their help in encouraging Dr. X to prescribe Zithromax. Reidy said this would make the nurses feel as if they were a part of his "team," and they'd "know that if the doctor keeps writing Zithromax they'll be having regular happy hours."

Dr. Sharon Levine, an executive director with Kaiser Permanente, the nation's largest HMO, said that it is because of tactics like these that Kaiser's doctors are prohibited from accepting personal gifts from reps (they are allowed to accept gifts that could benefit their practice -- i.e. they can accept a pen, but not a gift certificate to Morton's), and have never made their prescription records available to drug companies.

Studies support these concerns. A 2000 study published in the European Journal of Clinical Pharmacology, for example, found that increased interaction with drug reps led physicians to prescribe against their patients' best interests. A 2003 study in the American Journal of Bioethics found that when a person accepts a gift, no matter how small, "the obligation to directly reciprocate, whether or not the recipient is conscious of it, tends to influence behavior."

And then there's the cost. Drug companies lay out hefty sums for the profiles. IMS Health, just one of a handful of data mining companies, generated $1.7 billion in revenues last year, $847 million from its "Sales Force Effectiveness Offerings." Critics say pharmaceutical companies should be spending that money seeking new medications. (The major pharmaceutical companies generally spend more than twice as much on marketing as they do on research and development. In 2005, for example, Pfizer spent $17 billion globally on "selling, information and administration" and $7.4 billion on research and development.)

Levine said that the high cost of the profiles manifests itself on drug prices in two ways. Not only is the high cost reflected directly in higher drug prices, but the data is used to persuade doctors to prescribe expensive, brand-name drugs -- often when much cheaper generics would do -- which jacks up co-pays and insurance premiums. Physician privacy is another concern. Dr. Zoe Berna, a family practitioner in Vacaville, is against drug companies gaining access to her records because she thinks she should be free to write prescriptions without salespeople looking over her shoulder. "I definitely feel (drug company access to prescription records) is an invasion of my privacy," she said. Berna added that she would support an outright ban of the release of the data.

In California, at least, that possibility may have died along with AB 262.

But, according to Dr. Jack Lewin, the CMA's chief executive officer, though Chan's bill failed to become law, it initiated almost two years of negotiations among the AMA, IMS Health and the CMA, at the end of which a happy compromise was reached.

Lewin went as far as to assert that the results of the compromise would benefit physicians more so than Chan's bill would have. "We could have gotten (AB 262) passed in any event, except we think we

have the better option now," Lewin said in an e-mail.

"The better option" is a new program, unique to the state, built around three main facets.

The primary feature is an "opt out" mechanism that will allow doctors to choose whether or not drug companies may access their physician-specific data.

Second, for those physicians who do not use the "opt out" mechanism, IMS will be required to send them the same data package containing their personal prescription profile it sends to drug companies. In addition, IMS will provide reports comparing the "opting in" physician's prescription patterns with those of area doctors who share the same specialty.

Third, physicians who "opt in" will be e-mailed, on a quarterly basis, an unbiased educational newsletter about the latest medications and developments in their field.

Lewin said that a pilot of the new program is imminent. The statewide rollout is scheduled for January 2007.

The AMA launched its own "opt out" program on July 1. According to Musacchio, the AMA's Physician Data Restriction Program (PDRP) allows physicians to request their individual prescribing data be hidden from pharmaceutical sales representatives -- similar to the California program, but minus the requirements of IMS Health. (In both programs drug companies would continue to have access to aggregated prescription data, including the data of the physicians who have "opted out.")

A spokesperson for IMS Health said in an e-mail that the company supports the AMA's PDRP program, and that the California compromise "will give physicians better insights into their own practices and those of their peers, helping to drive improvements in patient care."

Critics, however, assert that both programs suffer from an inherent flaw: with so many doctors still oblivious to the practice in the first place, the reliance on an "opt out" mechanism is ludicrous -- you can't "opt out" of something you don't know exists.

One of the harshest critics, especially of the AMA's program, is New Hampshire state Rep. Cindy Rosenwald, D-Nashua, who in May pushed a bill through the New Hampshire legislature that would ban statewide the release of prescription data for all commercial purposes. Gov. John Lynch signed the bill June 30, making it the first such legislation in the nation.

Rosenwald said the PDRP program doesn't go nearly as far, and suggested it was simply an effort by the AMA to prevent more bills like hers, and more compromises such as California's. Pointing out that the AMA generates millions of dollars per year with the lease of its Masterfile (the AMA would not comment on how much it made), Rosenwald said, "The AMA has absolutely no incentive to stop the practice."

(Mussachio said that the AMA recognizes that there has been inappropriate use of the data, but there was no need for an outright ban because the PDRP program gives physicians a choice. He added that a lot of younger physicians like being presented with the data because it helps them measure their "performance.")

So what did Drexler think of these "opt out" programs, particularly the California compromise he may have helped engender after an innocent encounter with a birth control rep more than three years ago?

"I still believe drug company access to physician data should be banned," he said, adding that it may be time to "rethink (his) attitude" toward drug reps. He concluded, "but the compromise is a good thing, because it's the best we could get."

New York freelancer Jake Whitney's work has appeared in New York magazine, the Long Island Press and Guernicamag.com.

http://sfgate.com/cgi-bin/article.cgi?f=/chronicle/archive/2006/08/06/CMGTSJU4NT1.DTL

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Drug marketing techniques may be risking patient safety

Analysis: What can we learn from drug marketing efficiency?

With new drugs being reviewed by regulatory agencies and then released onto the market faster than ever before, patients' safety is being compromised, warns a study published on bmj.com today.

Dr David Kao from the University of Colorado Health Sciences Center, argues that while drug regulatory bodies are under pressure to make new drugs available more quickly, there are concerns that the deadlines for approving drugs have shifted the focus away from safety.

Kao reviews trends in drug approval times in the United States, and suggests how drug marketing techniques could be used to improve the way new drugs are monitored.

Previous research has shown that drugs approved in the US during the two months before the mandated deadline were more likely to be withdrawn for safety reasons or to carry a warning.

Today's marketing techniques are so sophisticated, says Kao, that once a drug has been approved the products can be released on websites within 90 minutes. He cites the example of Merck's new treatment (sitagliptin) for hyperglycaemia (high blood sugar levels)—within 14 days of approval 188 million patients or 73% of the insured US population had been targeted by the marketing campaign.

The danger with so many people trying a new drug very quickly, argues Kao, is that it can expose large numbers of patients to unknown risks. When Merck's anti-inflammatory drug Vioxx (rofecoxib) was withdrawn from the market for safety reasons it had been available for five years and 20 million patients had been exposed to it.

Regulatory agencies have been criticised for their dependence on drug companies for funding. The agencies often collect fees from drug companies so that they can hire staff to review the drugs more quickly. The European Agency for the Evaluation of Medicinal Products receives 75% of its funding in this way, 43% of the US Food and Drug Administration (FDA) budget is similarly derived, and the UK's Medicines and Healthcare Products Regulatory Agency is completely funded by drug companies.

The author believes that the systems for reporting adverse drug reactions must be improved and suggests using the very same effective drug marketing techniques to do this. For example, laws in the US already compel TV adverts to instruct patients experiencing negative side effects to report their symptoms to the FDA. This could be expanded to include campaigns dedicated to drug safety monitoring.

Kao concludes by saying that the only drug monitoring system that will minimise unknown risks must involve all the key players in healthcare, including doctors, regulatory bodies, drug companies and patients.

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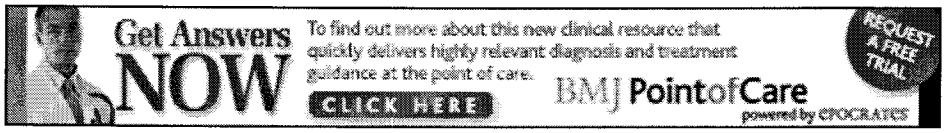

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Analysis

What can we learn from drug marketing efficiency?

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*The time it takes new drugs to penetrate the market is shrinking. **David Kao** suggests how drug companies' techniques could be used to improve safety surveillance systems*

Institutions responsible for monitoring drug safety have been criticised widely after the withdrawal of drugs such as rofecoxib because of safety concerns. An estimated 20 million patients received prescriptions for rofecoxib over five years before the drug was withdrawn, and events attributable to rofecoxib may number in tens to hundreds of thousands.[1] Regulatory bodies such as the US Food and Drug Administration have simultaneously been under pressure to reduce drug approval times to ensure timely availability of new drugs. However, concerns have been expressed that deadlines for approving drugs have reduced the focus on safety.[2 3 4]

New efficiencies in drug marketing exacerbate the problem because rapid adoption of new drugs can quickly expose large numbers of patients to unknown risks. Here, I review trends in drug approval times in the United States, the mechanism by which this has been achieved, and concerns raised by this approach. I then discuss an example of the speed with which a new product may be adopted once approved and suggest improvements to drug safety surveillance systems.

Trends in drug approval

Faced with staffing and budget limitations on drug approval, the US Congress passed the Prescription Drug User Fee Act in 1992. This authorised the FDA to collect fees from drug manufacturers and use the revenue to hire additional staff to review drugs and improve its administrative infrastructure. In return, the FDA established goals of reviewing 90% of priority new drug applications within six months and 90% of standard new drug applications within 12 months. As a result, the mean review time in the US decreased from 33.6 months during 1979-86 to 16.1 months during 1997-2002.[5] The act has been renewed three times since 1992, and revenues collected from industry now account for 43% of the FDA budget for drug oversight.[6] Similarly, the European Agency for the Evaluation of Medicinal Products receives 75% of its funding in this manner, and the United Kingdom's Medicines and Healthcare Products Regulatory Agency is entirely funded by user fees.[7 8 9]

Critics have voiced concern over the dependence of regulatory agencies on drug companies for operational funding.[2 10] Although drug approval times have decreased overall, the relation between this trend and subsequent postmarketing safety problems is less clear.[7] Drug withdrawal rates have not increased overall since the US act, but a recent study showed that

drugs approved in the US in the two months before the mandated deadline are more likely than those approved at other times to be withdrawn for safety reasons, to carry a subsequent black box warning, or to have at least one dosage voluntarily discontinued by the manufacturer. Because drugs approved more than three months before or just after the deadline were not associated with the same degree of subsequent safety problems, the authors concluded that the deadlines may increase the likelihood of unexpected safety problems.[4]

Deficits in postmarketing safety monitoring may, in turn, prevent these safety concerns from being discovered for years after approval. Depending on the success of the product, this can mean widespread exposure of patients to risk. Rapid acceptance of new products without concomitant improvements in postmarketing surveillance can only exacerbate this risk.

Sitagliptin launch

Merck's novel treatment for hyperglycaemia, sitagliptin, provides a good example of the speed with which companies can now get new products to market. The FDA approved sitagliptin 3.8 years after the drug's discovery; this compares with five years for rofecoxib and an industry average of 14.2 years between 1990 and 1999. Once the drug was approved Merck began a multifaceted marketing campaign that capitalised on sitagliptin being a new class of drug (oral dipeptyl peptidase-IV inhibitor). Within 48 hours, education forums were delivered, sales representatives had their first doctor contacts, and broadcasts were made by webcast and satellite to thousands of healthcare providers and investigators. The product website was functional within 90 minutes of approval, and within eight days, Merck had reached 70% of target doctors and made first deliveries of sitagliptin to pharmacies. Within 14 days, discussions were completed with managed care organisations covering around 188 million patients or 73% of the insured US population.

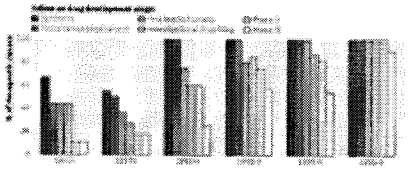
The company also formed a partnership with the American Diabetic Association to produce educational materials and patient guidebooks and to train diabetes educators with the goals of prompting undiagnosed patients to seek testing and to identify cases in which treatment goals are not being met.[11] Since about a third of diabetic patients are undiagnosed and half of diagnosed patients are not meeting treatment goals, these strategies increase the potential market. Emphasis on the versatility of the drug as both single and add-on treatment also makes the drug marketable to nearly any patient with type 2 diabetes.

The success of this campaign was evident quickly. One month after FDA approval, one survey found that sitagliptin accounted for 14% of all new prescriptions given for type 2 diabetes drugs by primary care doctors. Among endocrinologists, 20% of new prescriptions for type 2 diabetes were for sitagliptin, compared with 22% for exenatide, 19% for rosiglitazone, and 16% for metformin.[12] Merck estimates that by the end of 2007, three million prescriptions had been written, and sitagliptin had become the second most prescribed branded oral hypoglycaemic drug in the US. Merck reports a steady increase in sales of sitagliptin from $42m (£28m; €33m) in the final quarter of 2006 to $272m in the first quarter of 2008, putting sitagliptin on course for $1bn in annual sales in its second year of release.[13]

Marketing motivations and methods

The time required to bring a new product to market in the US has been decreasing for the past 20 years.[14] For drug manufacturers, rapid deployment and adoption are necessitated by shifts in industry economics and public demand. Companies continually face the threat of loss of revenue because of expiring patents, and administrative and legal costs of withdrawn or suspended products can add millions of dollars to companies' annual expenditures.[11 15 16] Spending on drug research and development is aimed primarily at developing novel products to replace these losses, ideally with new classes of drugs.

The importance of developing new products and the advantage of being the first in a class is reflected by the decrease in time between approval of new class drugs and follow-on drugs over the past 30 years. Most drug classes now have at least one competitor in advanced stages of development at the time that the first drug in the class is approved, and more follow-on drugs are in development at the time that the first in the class is approved than ever before (figure↓). Furthermore, the mean and median interval of marketing exclusivity have decreased from highs of 8.2 and 10.2 years respectively (n=9 drugs) during the 1960s to 1.8 and 1.2 years from 1995-8 (n=18 drugs, $P<0.0001$ and $P=0.0005$, respectively).[5] Once FDA approval is received, companies must act quickly to establish dominance before a competitor becomes available.



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Proportion of therapeutic classes with at least one follow-on drug in development at time the first in class was approved[5]

Recent years have seen major changes in drug marketing strategies facilitated by the evolution of mass media and prompted by changes in the relationships between manufacturers, doctors, and patients. Doctors are more aware of the effect of marketing on prescription practices, and concerns regarding conflicts of interest have led to changes in institutional policy in many settings, making traditional marketing to doctors more challenging.[17] These changes have resulted in marketing budgets being moved to campaigns directed at funders and, where permitted, consumers.[11] In countries such as the UK, where direct advertising to patients is prohibited, the public may still access internet resources designed for patients in other countries.

Public health initiatives regarding disease awareness and education have become important vehicles for increasing public demand for drugs, and engagement of healthcare funders is also a priority to ensure availability and coverage of costly new products for patients. The success of these strategies has been magnified by new mass media technologies, and companies are capitalising on their favourable cost-benefit ratio. This is exemplified by Merck's discussion in their 2006 and 2007 annual business briefings of the efficiency of techniques such as video detailing and of their transition to multichannel marketing campaigns using web, video, and customisable, unbranded education resources to engage potential customers.[11] These techniques enable drug companies to reach more potential customers faster than ever before. In most cases, this is not harmful and can benefit many patients in need of new treatment options. Nevertheless, improved infrastructure for postmarketing surveillance will be crucial to minimise risk to users of these new products.

Monitoring drug safety

Many groups have criticised the FDA for the time taken to publicise suspected risks associated with approved products like rofecoxib. As a result, the Federal Drug Administration Amendments Act of 2007 included a 50% increase in fees collected in association with the Prescription Drug Users Fee Act, with $29.2m designated specifically for surveillance of drug safety. FDA postmarket surveillance relies heavily on the Adverse Event Reporting System, which collects spontaneous reports from manufacturers, providers, and consumers that are reviewed by scientists at the Center for Drug Evaluation and Research. This database is publicly available and updated quarterly, although it is difficult to extract meaningful datasets and the data are of variable quality. The World Health Organization Collaborating Centre for International Drug Monitoring, also called the Uppsala Monitoring Centre, integrates reports collected by similar systems in 83 member countries into a single database called Vigibase, which in June 2007 contained about 3.87 million cases.[18] Vigibase is not publicly available, although it is possible to purchase extracts of this database for about $2500 (€1600) per drug entity and reports of analyses are sent periodically to member pharmacovigilance centers.

Most adverse event reporting systems rely on voluntary reporting of clinical observations and therefore are sensitive to many biases. Lack of associated data on usage also makes it difficult to determine the true frequency of adverse events identified, and observers have called for development of an active postmarketing surveillance system wherein cohorts of patients are followed after starting a new treatment.[19] Nations with centralised healthcare systems have some established infrastructure to support such systems, but most use a much smaller volume of drugs than the US. The initial draft of the FDA's five year drug safety plan discusses acquiring data from organisations that have prescribing information such as drug sales databases and the Centers for Medicare and Medicaid Services to generate higher quality utilisation and longitudinal outcomes data, with the goal of building a database of 100 million patients by 2012.[20] It has been estimated that with a dataset of this size, the increased cardiovascular risk associated with rofecoxib could have been detected independently after two to three months rather than as a result of ongoing clinical trials several years after approval.[21] In addition, the FDA

can now require drug companies to participate in postmarketing safety surveillance, greatly expanding potential resources for monitoring drug safety. Still, these improvements are expected to take several years, and the $29.3m budget allocated for developing drug safety monitoring represents only 1% of that spent on advertising and 0.1% of total annual drug sales in the US.[19 20]

Suggestions

Emerging marketing techniques use several methods that might also be used to engage a wider audience in monitoring drug safety. The 2007 FDA Amendments Act includes some examples such as the requirement that television advertisements must instruct patients experiencing negative side effects to report their symptoms to the FDA.[22] Other techniques might also prove useful. For example, public health initiatives sponsored by drug companies have helped providers to raise disease awareness. Expanding this collaboration to include campaigns dedicated to drug safety surveillance could provide healthcare professionals with the marketing expertise and infrastructure to track utilisation patterns. Merck has described a shift towards a "value based partnership"' marketing model that builds product loyalty by rewarding customers with individual benefits in the form of convenience and improved health outcomes.[11] Maximising the direct benefit to individual patients and providers from participating in drug safety surveillance programmes might similarly increase voluntary involvement. Reporting a single adverse event provides little direct benefit to the reporting individual, but the development of tools for managing prescriptions, which in turn communicate with broad utilisation monitoring systems, provides patients and doctors with personal incentives to take an active role in drug safety monitoring by giving a useful service in return for their participation. A multifaceted approach to postmarketing surveillance of drug safety involving all stakeholders in healthcare including providers, payers, regulatory agencies, and patients seems likely to hold the most promise for maximising the benefits of pharmaceutical advancements while minimising unknown risks.

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Physicians and the Pharmaceutical Industry

Is a Gift Ever Just a Gift?

Ashley Wazana, MD

Context Controversy exists over the fact that physicians have regular contact with the pharmaceutical industry and its sales representatives, who spend a large sum of money each year promoting to them by way of gifts, free meals, travel subsidies, sponsored teachings, and symposia.

Objective To identify the extent of and attitudes toward the relationship between physicians and the pharmaceutical industry and its representatives and its impact on the knowledge, attitudes, and behavior of physicians.

Data Sources A MEDLINE search was conducted for English-language articles published from 1994 to present, with review of reference lists from retrieved articles; in addition, an Internet database was searched and 5 key informants were interviewed.

Study Selection A total of 538 studies that provided data on any of the study questions were targeted for retrieval, 29 of which were included in the analysis.

Data Extraction Data were extracted by 1 author. Articles using an analytic design were considered to be of higher methodological quality.

Data Synthesis Physician interactions with pharmaceutical representatives were generally endorsed, began in medical school, and continued at a rate of about 4 times per month. Meetings with pharmaceutical representatives were associated with requests by physicians for adding the drugs to the hospital formulary and changes in prescribing practice. Drug company–sponsored continuing medical education (CME) preferentially highlighted the sponsor's drug(s) compared with other CME programs. Attending sponsored CME events and accepting funding for travel or lodging for educational symposia were associated with increased prescription rates of the sponsor's medication. Attending presentations given by pharmaceutical representative speakers was also associated with nonrational prescribing.

Conclusion The present extent of physician-industry interactions appears to affect prescribing and professional behavior and should be further addressed at the level of policy and education.

JAMA. 2000;283:373-380 www.jama.com

THERE ARE FEW ISSUES IN MEDICINE that bring clinicians into heated discussion as rapidly as the interaction between the pharmaceutical industry and the medical profession.[1-4] More than $11 billion is spent each year by pharmaceutical companies in promotion and marketing, $5 billion of which goes to sales representatives.[5,6] It has been estimated that $8000 to $13 000 is spent per year on each physician.[7,8] The attitudes about this expensive interaction are divided and contradictory. One study[9] found that 85% of medical students believe it is improper for politicians to accept a gift, whereas only 46% found it improper for themselves to accept a gift of similar value from a pharmaceutical company. Most medical associations have published guidelines to address this controversy. Perhaps the intensity of the discussion is related to the potential consequences were it confirmed that gifts influence prescription of medication that results in increasing cost or negative health outcomes.

This article addresses the question by way of a critical examination of the evidence. Two review articles[10,11] have addressed the factors affecting drug prescribing, but only 1 has focused on the impact of the physician-industry interaction on the behavior of physicians.[12] This article critically examines the literature and highlights articles with rigorous study methods.

METHODS

Studies were identified by searching MEDLINE for articles from 1994 to the present, using the expanded Medical Subject Headings *conflict of interest* and *drug industry*, limiting the search to articles in English while excluding review articles, letters, and editorials; each identified study was cross-referenced; a database of 400 articles gathered by the Medical Lobby for Appropriate Marketing[13] was searched; and 5 key informants were sought for their bibliographies on the topic.

A total of 538 studies that provided data on any of the main study questions were targeted for retrieval. Of the 29 studies that were published in peer-reviewed journals and identified as potentially relevant (containing quantitative data on 1 of 3 facets of physician-industry interactions), 10 were from MEDLINE and 19 from other sources. The data extractor (A.W.) was not blinded to the authors of the studies.

Those with an analytical design (having a comparison group) were considered to be of higher methodological quality.

See also p 391.

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Table 1. Interaction, Attitudes, and Impact of the Interaction Between the Medical Profession and the Pharmaceutical Industry*

Study, y	Site	Population (n)	Interactions	Measure
		Prepost Study		
Bowman and Pearle,[14] 1988	Washington, DC	Physicians attending CME (150)	CME	Impact on prescribing
		Cohort Studies		
Spingarn et al,[15] 1996	Philadelphia, Pa	Internal medicine residents (22 case, 53 control)	Teachings	Impact on prescribing
Orlowski and Wateska,[16] 1992	Cleveland, Ohio	Hospital physicians	Travel, CME	Impact on prescribing
		Case-Control Studies		
Chren and Landefeld,[17] 1994	Cleveland, Ohio	Faculty physicians (36 case, 69 control)	PR, meals, travel, honoraria, research	Frequency and impact on formulary addition requests
Bowman,[18] 1986	Washington, DC	2 CME with different sponsors (5, 6)	Honoraria	Impact on content
		Cross-sectional Studies		
Gibbons et al,[19] 1998	Washington, DC	Physicians and residents (268)	Gifts, samples, meals, travel, teachings	Attitudes
Sandberg et al,[20] 1997	Chicago, Ill	Fourth-year medical students (205)	Gifts	Frequency and impact on attitudes
Mahood et al,[21] 1997	Canada	Family medicine program directors (16)	Samples, teachings, CME, research	Frequency
Hopper et al,[22] 1997	Detroit, Mich	Primary care residents (28) and faculty (14)	PR, gifts	Attitudes
Sergeant et al,[23] 1996	Ontario	Family medicine residents (262)	PR, gifts, meals, CME	Frequency and attitudes
Caudill et al,[24] 1996	Kentucky	Primary care physicians (1603)	PR, promotional material	Frequency, attitudes, and impact on attitudes and prescribing
Strang et al,[25] 1996	Canada	Physicians (550)	PR, gifts, samples, meals, travel	Frequency and attitudes
Hodges,[26] 1995	Toronto, Ontario	Psychiatry clerks and residents (105)	PR, gifts, samples, teachings, CME	Frequency, attitudes, and impact on attitudes
Ziegler et al,[27] 1995	California	Internal medicine residents (27)	PR, teachings	Frequency, attitudes, and impact on knowledge
Andaleeb and Tallman,[28] 1995	Pennsylvania	Faculty physicians and osteopathic practitioners (95)	PR	Impact on attitudes
Poirier et al,[29] 1994	Pennsylvania	Physicians chair of P&T committee (26)	PR, gifts, samples, meals, promotional material	Attitudes
Thomson et al,[30] 1994	New Zealand	Family physicians (67)	PR, gifts, samples, CME, promotional material, travel	Frequency, attitudes, and impact on attitudes
Brotzman and Mark,[31] 1993	United States	Family medicine residents (122 case, 143 control)	PR, meals, CME	Impact on attitudes
Reeder et al,[32] 1993	United States	Emergency medicine chief residents (87)	PR, gifts, samples, meals, travel, teachings	Frequency and attitudes
Keim et al,[33] 1993	United States	Emergency residents (1385) and directors (80)	PR, gifts, meals, travel, teachings	Frequency and attitudes
Banks and Mainous,[34] 1992	Kentucky	Faculty physicians (169)	PR, gifts, samples, meals, travel, CME	Attitudes
Brotzman and Mark,[35] 1992	United States	Family medicine program directors (328)	PR, samples, teachings, gifts, promotional material	Frequency
Bucci and Frey,[36] 1992	United States	Family practice program directors (325)	PR, gifts, samples, meals, CME, teachings	Frequency and attitudes
Lichstein et al,[37] 1992	United States	Internal medicine program directors (444)	PR, meals, samples, travel, CME	Frequency and attitudes
McKinney et al,[38] 1990	Minnesota	Internal medicine residents and faculty (425)	PR, gifts	Frequency and attitudes
Lurie et al,[39] 1990	United States	Internal medicine residents and faculty (484)	PR, meals, travel, honoraria, research	Frequency, attitudes, and impact on formulary requests
Peay and Peay,[40] 1988	Adelaide, Australia	Physicians (59 case, 29 control)	PR	Impact on prescribing
Bower and Burkett,[41] 1987	United States	Family medicine physicians (317)	PR	Impact on prescribing
Haayer,[42] 1982	Twente, Holland	Family medicine physicians (118)	PR	Impact on prescribing

*PR indicates pharmaceutical representative; CME, continuing medical education; and P&T, pharmacy and therapeutics.

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RESULTS

A total of 29 studies[14-42] were identified (TABLE 1). Of these, 16 addressed the extent of the physician-industry interaction, 16 identified the attitudes of physicians toward the interaction, and 16 evaluated the effect of the interaction on the practitioner.

Interaction Between Medical Professionals and the Pharmaceutical Industry

All 16 studies* identified (TABLE 2) used self-reporting cross-sectional survey designs, and all but 1[17] used a mailed survey. The response rate ranged from 30%[24] to 100%.[21] Most authors claimed that the response rate was consistent with that obtained in similar studies and that a self-report design would tend to underreport the actual frequency of interaction because of underestimates in recall or a social desirability bias.

Interactions with the industry were found to start as early as medical school[26] and to continue well into practice. Most physicians met with pharmaceutical representatives about 4 times a month,[25,27,30-32] and the frequency tended to stabilize during residency. Residents do not differ significantly from faculty[38,39] in the frequency with which they experience this interaction. Thomson et al[30] found decreased availability of peer physicians ($r = 0.36$, $P<.05$) and a positive attitude toward the pharmaceutical representative ($r = 0.39$, $P<.05$) to be the only predictors of the number of contacts.

The frequency with which physicians benefit from industry-sponsored meals [39] and samples [39] decreases as they enter practice, while frequency of receiving honoraria, [39] conference travel,[25] and research funding[25] increases. Both populations frequently use promotional material.[23] One study found that residents receive 6 gifts a year,[26] with no comparable data for physicians. All interactions were generally permitted except for lunch rounds,[21] pharmaceutical representative speakers,[21,37] and promotionalmaterial,[21,36] which were more controversial. As many as 85% of programs had policies on interactions.[21,23,33,35-37]

*References 17,20,21,23-27,30,32,33,35-39.

Attitudes Toward the Interaction

All 16 studies† reported here (TABLE 3) used a self-report design with similar rates of response and limitations.

Residents and physicians have similar attitudes about pharmaceutical representatives. They believe that representatives provide accurate information about their drugs[25] and are equivocal in their beliefs that representatives could provide accurate information on established or alternative drugs.[24-26,38] Most believe that representatives prioritize product promotion above patients' welfare[25] and are likely to use unethical practices.[22,33] Residents are less likely than physicians are to endorse the influence of the interaction on their behavior.‡

Most deny that gifts could influence their behavior[19,24,26,32,34,38] and are equivocal about the ethics of such a practice,[22,33] with residents more likely to admit that without gifts, their interactions with pharmaceutical representatives would be reduced.[24,26,38] Similarly, respondents agree that conference[37] and lunch rounds[27] attendance would decrease without industry-paid meals. Samples, continuing medical education (CME), and conference travel funding are felt to exert more influence (40% to 55%) than promotional material does (22%).[19,29,34] Each interaction elicited ethical concerns; travel funding generated the most concern (48%[29] to 75%[19]). Most physicians also agree that pharmaceutical representative speakers should be banned.[24,38] Residents' opinions are divided.[24,26] Programs with concerns about these interactions were more likely to be military, nontraditional, or to have another source of funding.[37]

Effect of Interaction

Sixteen studies§ were identified (TABLE 4) that assessed the impact of the physician-industry interaction on the knowledge, attitudes, and prescribing practices of physicians. Studies used cross-sectional, case-control, or preinteraction and postinteraction methods to assess the impact of particular interactions.

†References 19, 22-27, 29, 30, 32-34, 36-39.
‡References 22, 24, 25-27, 29, 33, 34, 38, 39.
§References 14-18, 20, 24, 26-28, 30, 31, 39-42.

Interactions With Pharmaceutical Representatives

There was an independent association between meetings with pharmaceutical representatives and formulary addition requests for the drug of the representative's company, both with respect to control physicians who did not meet representatives and with respect to requests for other companies' drugs.[17,39] Most of the requested drugs presented little or no therapeutic advantage over existing formulary drugs, but the merit of the requests was not related to interactions with the pharmaceutical industry. This, as well as the strength, consistency, specificity, and independence of the results, make it unlikely that the interaction occurred because the physician was already convinced of that drug's influence.[17]

Interactions with pharmaceutical representatives were also found to impact the prescribing practice of residents and physicians[39] in terms of prescribing cost,[24] nonrational prescribing,[42] awareness, preference and rapid prescribing of new drugs,[40] and decreased prescribing of generic drugs.[41] These findings were independent of other variables in all but 1 study,[41] in which such an analysis was not done.

Attitudinal outcomes were examined in matched residency programs with and without restrictions on interactions. Exposure to pharmaceutical representatives was highly associated with a perception of the benefits of such an interaction and the appropriateness of other interactions. Whether exposure to pharmaceutical representatives or to critical faculty role models influences residents' attitudes remains unknown.[31] There were other correlates of positive attitudes,[24,28,30] but the directionality of these latter associations is not as clear as with the above quasi-experimental study.[31]

Gifts

Receiving a gift[20] and the number of gifts received[26] correlated with the belief that pharmaceutical representatives have no

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Table 2. Interaction Between the Medical Profession and the Pharmaceutical Industry*

Measure	Residents	Physicians
	Overall	
Policy, % of programs	Limited,[21,23,33,35-37] 25[21] to 86[23]	
	Interaction with PR	
Interaction	51% of residents[23] (83% of programs [1-3/wk])[32]	85%[30] to 87%[17]
Frequency	0.25/mo[26] to 3.1/mo[38] (higher than in fourth year)[26] Brief: 1.5/mo[39] to 8.7/mo[27] Extended: 0.3/mo[39] to 3.5/mo[27]	3 to 4/mo (NS)[30,38] Brief: 1.6/mo[39] Extended: 0.6/mo (NS)[39]
Policy, % of programs Permitted ad lib Limited Prohibited	 84[30,37] 64[33] to 79[36] 34[33]	
	Gifts	
Interaction	80% of medical students received a book[20] (90% of programs[32])	
Frequency	6/y (average value $60)[26]	
Policy, % of programs Permitted	 86 to 89[35,36]	
	Samples	
Interaction	66% of residents (66% of programs[32])	86%[25]
Frequency	2/y[26] to 2.4/y[39] (interns, 4.8/y; $P<.02$)[26]	1.3/y (fewer than residents; $P<.001$)[39]
Policy, % of programs Permitted	 71 to 94[35-37]	
	Promotional Material	
Interaction	91% of residents patient education items[23] 52% of residents seeking drug information from PR[27] (82% of programs)[35]	
Frequency		5.4% Daily 31% Weekly 48% Monthly 14% Yearly[19]
Policy, % of programs Permitted	 43[36], 62[21]	
	Industry-Paid Meals	
Interaction	80% of residents [26] (80% of programs[32])	41%[20]
Frequency	14/y[26] to 15/y[39] (interns, 31/y; $P<.05$)	2.3/y (fewer than residents; $P<.001$)[39]
Policy, % of programs Permitted	 88[36]	
	Conference Travel	
Interaction	3% of residents [26]	42%[25]
	Lunch Rounds and PR Speakers	
Interaction	54% of programs[32]	
Frequency	Attended lunch rounds (20/y)[27]	
Policy, % of programs Permitted	 38 lunch rounds[21] 38 to 86 PR speakers[21,35,37]	
	CME Funding	
Policy, % of programs Permitted	 88[36,37]	
	Honoraria	
Frequency		1.2/y[39]
	Research Funding	
Frequency, %		54%[25]
Policy, % of programs Permitted	 69[36]	

*PR indicates pharmaceutical representative; CME, continuing medical education; and NS, not significantly different from residents. Blank spaces indicate data do not apply or were not collected.

impact on prescribing behavior; receiving gifts of high relevance to practice was also associated with a positive attitude.[30] The former association was independent of the student's ability to recall the donor.

Samples

Accepting samples was associated with awareness, preference and rapid prescription of a new drug,[40] and a positive attitude toward the pharmaceutical representative.[30]

Industry-Paid Meals

There was an independent association between benefiting from sponsored meals and formulary addition requests for any drug[39] that was clearly dose-related.[17]

Funding for Travel or Lodging to Attend Educational Symposia

Accepting funding to attend a symposium was independently associated with increased formulary addition requests for the sponsor's drug.[17] This interaction was also found to impact hospital prescribing practices 2 years after 2 groups of physicians accepted all-expenses-paid trips to a drug-sponsored symposium. This occurred despite the continued prescribing of the 2 drugs that the new ones were to replace and the lack of concern about the interaction among all but 1 beneficiary.[16] The physicians were not randomly selected, thus raising the unlikely possibility that physicians more partial to the sponsor's drug chose to participate. It is nonetheless striking to note that the changes occurred at an institutional level.

Pharmaceutical Representative Speakers

Resident exposure to pharmaceutical representative speakers at lunch rounds was associated with dissemination and learning of inaccurate information about the sponsor's and competitor's drug.[27] Attendance at rounds given by a physician pharmaceutical representative was associated with appropriate and inappropriate treatment decisions by attending residents, independent of

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variables including the resident's memory of the presenter's affiliation.[15] Although not a randomized trial, the factors leading to attendance seemed unrelated to the outcome.[15]

CME Sponsorship

Drug company CME, sponsorship affected presentation content in that the sponsor's drug was always preferentially highlighted, although the same drugs were discussed in each event.[18] Changes in prescribing practice (self-reported) in favor of the sponsor's drug were also found.[14] The participants were not randomized, but it is unlikely that their self-selection reflected a bias for the sponsor's drug. The consistent findings across all events also minimize the lack of control groups. These were findings in settings where industry guidelines were applied.

Honoraria, Research Funding, Employment

Accepting a drug company honorarium to present data on a new therapy and receiving research support were independently associated with a formulary addition request for the sponsor's drug as well as any drug.[17,39] One study examined the impact of employment but did not find it significant.[13]

COMMENT

Limitations

MEDLINE was not personally searched before 1994 and other databases were not searched. However, 1 of the studies examined[12] searched MEDLINE and HEALTH from 1978 to 1993, and the methods ensured a thorough exploration of the published literature.

Industry-Physician Interaction

Residents and physicians interact with the pharmaceutical industry frequently and in multiple settings and fashions, beginning as early as medical school. Residents benefit more from drug-sponsored meals, whereas physicians receive more honoraria, conference travel, and research funding. Both meet equally often with pharmaceutical representatives.

Table 3. Attitudes Toward the Physician–Pharmaceutical Industry Interactions*

Measure	Residents	Physicians
Interaction With PR		
Knowledge and technique		
Adequate/accurate knowledge overall		20%[29] to 35%[25]
of their drug		65%[25]
of new drugs	32%[26]; LS, 2.8[38]	LS, 2.8[38] to 3.6[24]
of established drugs	25%[26]; LS, 2.9[38]	LS, 2.7[38] to 3.5[24]
of alternatives		19%[25]
Fairly portray their product		20%[25]
Provide misleading information	44%[27]	
May use unethical practice	74%[33]; LS, 3.2[22]	LS, 3.7 ($P = .04$)[22]
Goal is product promotion		92%[25]
Value		
PR support CME	77%[26]; LS, 4.0[38]	LS, 3.9[24] to 4.2[38]
Positive	29% to 85%[26,27,32]; LS, 2.4[38] to 3.7[22]	LS, 2.1 to 3.7[22,30,38]
Influence behavior	25% to 49%[23,26,27,33,39]; LS, 1.8[22] to 2.5[38]	58%[34] to 70%[25]; LS, 1.75 to 3.2[22,24,38]
Concerned about influence		52% to 68%[29]
Too much contact	LS, 2.8[22]	LS, 3.4 ($P = .003$)[22]
Plan to interact with PR in the future	76.1%[23]	
Policy		
Should be allowed to interact with PR	82.3%[23]	
Gifts		
Influence behavior	8% to 27%[19,26,32]; LS, 1.7[38]	8 to 13%[19,26]; LS, 1.6 to 1.8[24,38]
Inappropriate/unethical	4% to 49%[19,33]	4% to 88%[19,29]
Ethical for gifts with/without patient benefit	LS, 3.9/LS, 2.8[22]	LS, 4.0/LS, 2.5[22]
Leads to higher costs of drugs	35.9%[23]	
Would maintain same contact without gifts	45%[26]; LS, 2.8[39]	LS, 2[24] to 4.0[39] ($P<.05$)
Samples		
Inappropriate	12%[33] to 33%[19]	33%[19] to 60%[29]
Influential	55%[19]	42%[34] to 55%[19]
Should be offered		86%[25]
Promotional Material		
Useful	58.4%[25]	
Influential	22%[19]	22%[19]
Inappropriate		12%[19] to 60%[29]
Industry-Paid Meals		
Influential	24%[19]	24%[34,19]
Unethical	33%[19]	12%[27] to 33%[19]
CME attendance would decline without		
Should be allowed		21%[25]
Conference Travel		
Inappropriate	39%[33] to 75%[19]	48% to 75%[29,19,30]
Influential	42%[19]	42%[19]
Partial/full funding should be allowed		47%/15%[25]
Lunch Rounds and PR Speakers		
Appropriate	10%[19] to 11%[27]	10%[19]
Influential	12%[19]	12%[19]
Attendance would be same without lunch	0%[27]	
Should be banned	10%[26]; LS, 3.7[39]	LS, 3.5[39] to 4.2[24]
CME Funding		
Influential		40%[34]
Content should be chosen by physicians	92.5%[23]	

*Results for residents and physicians do not significantly differ unless identified by P values. LS indicates Likert scale: "strongly agree"-5, "agree"-4, "neutral"-3, "disagree"-2, "strongly disagree"-1. PR indicates pharmaceutical representative; CME, continuing medical education. Blank spaces indicate data do not apply or were not collected.

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Physicians and residents were similarly skeptical of the motives and comprehensive knowledge of pharmaceutical representatives but expressed a similar lack of concern about the influence of gifts, promotional material, meals, and lunch rounds. They had similar concerns about pharmaceutical representative speakers, CME funding, and conference funding; physicians were more concerned than were residents about the influence of representatives. All admitted that contact with representatives and attendance at educational events would decline were it not for gifts and meals.

Outcome of Interaction

Although some positive outcomes were identified (improved ability to identify the treatment for complicated illnesses), most studies found negative outcomes associated with the interaction. These included an impact on knowledge (inability to identify wrong claims about medication), attitude (positive attitude toward pharmaceutical representatives; awareness, preference, and rapid prescription of a new drug), and behavior (making formulary requests for medications that rarely held important advantages over existing ones; nonrational prescribing behavior; increasing prescription rate; prescribing fewer generic but more expensive, newer medications at no demonstrated advantage.)

No study used patient outcome measures. Studies demonstrating an effect on research findings[43-47] were excluded because they were not limited to physicians or to clinical activity. Some detected an influence of some interactions using self-report measures but were limited by the aforementioned biases and were less informative than the analytic studies reporting specific outcomes. However, most of these studies examined only 1 interaction or the effect of 1 intervention at a time, even if the effect of these interactions was posited as being cumulative. One study gave a high estimate for the effect of 2 interactions but had not entered this finding into the regression analysis.[17]

Most studies found a significant association that was consistent and strong for all interactions examined and which was biologically plausible and coherent with

Table 4. Effect of Physician–Pharmaceutical Industry Interactions on the Practitioner*

Interaction	Outcome	Findings
Interaction with PR	Attitude	Exposure to PR associated with positive perception of PR (β = .638; P = .02) (R),[31] perception of appropriateness of other interactions (r = 0.706; P = .02) (R)[31] Perceived support by PRs (r = 0.384; P<.01),[28] the availability (r = 0.30; P<.001) and applicability (r = 0.30; P<.001) of PR information and of the PRs themselves (r = 0.54; P<.001),[24] and receiving practical prescribing information[30] associated with positive perception of PR (P)
	Formulary request	"Request made at suggestion of PR in the last year" (R, 4%; P, 20%)[39] Contact with PR associated with increased likelihood of request for PR's drug vs those who did not meet PR (OR, 3.4; 95% CI, 1.8-6.6), and vs request for other company's drug (OR, 4.9; 95% CI, 3.2-7.4) (P)[17]
	Prescribing	Frequency of contact associated with change of practice (R, r = 0.049, P = .003; P, r = 0.016, P = .003),[39] higher prescribing cost (r = 0.155; P<.01) (P),[24] and rapid prescription of a new drug (r = 0.35; P<.002) (P)[40] Relying on PR associated with decreased likelihood of prescribing generic by 66% (P)[41] and less rational prescribing (r = 0.195; P<.03) (P)[42]
Gifts	Attitudes	Receiving a gift[20] and number of gifts received (r = 0.24; P<.04)[26] are associated with belief that PRs have no impact on behavior (R) Receiving high-relevance gifts is associated with positive attitude toward gifts (P)[30]
Samples	Attitudes	Positive attitude toward the PR (P)[30]
	Prescribing	Awareness, preference, and rapid prescription of a new drug (r = 0.35; P<.002) (P)[40]
Industry-paid meals	Formulary request	Increased likelihood of request for any drug (r = 0.089; P = .03)[39]; 8% of requesting physicians vs 3% of controls "occasionally" shared meals; 14% vs 1% "often" shared meals (P<.01) (P)[17]
Conference travel	Formulary request	Increased likelihood of request for sponsor's drug (OR, 7.9; 95% CI, 1.1-55.6) vs controls who did not benefit (P)[17]
	Prescribing	4.5- to 10-fold increase in preconference prescribing rate of sponsor drug (compared with 2.5- to 3.5-fold national rate increase) (P)[16]
PR speakers	Knowledge	Learning of inaccurate information (only 26% able to identify inaccurate claims) (R)[27]
	Prescribing	Appropriate treatment for complications of discussed illness (OR, 8.4; 95% CI, 2.1-38.9) (R)[15] Inappropriate treatment (higher cost, more invasive) for milder forms of the discussed illness (100% vs 79% of those not in attendance; P = .03) (R)[15]
CME funding	Content	More frequent mention (2.5 to 3 times) of positive effects of sponsor's medication and negative or equivocal effects of competitor's (P<.05) (P)[18]
	Prescribing	Highest increase (5.5% to 18.7%) in the rate of prescription of the drugs made by the CME sponsor, while decrease or smaller increase in rate of competitor's drug (P<.05) (P)[14]
Honoraria	Formulary request	Increased likelihood of request for any drug (r = 0.178; P = .003),[39] from those who benefit "occasionally" (OR, 4.0; 95% CI, 1.0-16.8) and "often" (OR, 29.1; 95% CI, 3.4-246.6) (P)[17] Increased likelihood of request for sponsor's drug vs controls who did not benefit (OR, 3.9; 95% CI, 1.2-12.7), and vs request for other company's drugs (OR, 2.2; 95% CI, 1.1-4.2) (P)[17]
Research funding	Formulary request	Increased likelihood of request for any drug (r = 0.102; P<.05)[39]; 61% of requesting physicians vs 29% of controls benefited (P = .002) (P)[17] Increased likelihood of request for sponsor's drug (OR, 9.5; 95% CI, 2.6-35.7) vs controls who did not benefit (P)[17]

*CME indicates continuing medical education; PR, pharmaceutical representative; P, physicians; R, residents; S, students; OR, odds ratio; and CI, confidence interval.

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other theories[48] (TABLE 5). Dose response was demonstrated in all interactions in which it was examined. Some studies were even able to establish specificity by identifying a stronger endorsement of a company's product, although nonspecific outcomes (eg, decreased prescription of nongeneric products, more expensive and less rational treatment) are just as meaningful. The independence of the association was established with a matched analysis or multivariate analysis in all but CME and gifts, although, the bias in the case of CME funding seems small. Nonetheless, the temporal direction of the association was established for only 4 interactions: an increase in the physician prescribing rate of the CME sponsor's drug[14]; an increase in hospital prescribing rate of the conference travel sponsor's drug[16]; increased nonrational prescribing choice of the sponsor's drug after related resident teaching given by physician pharmaceutical representatives[15]; and an association between interactions with pharmaceutical representatives and positive attitudes toward them.[31] This latter association is limited by the possibility of a confounder responsible for the differences in attitudes among the 2 groups of residents. The causal directions of all other studies are not as clear, suggesting that interactions could have followed the outcomes. Chren and Landefeld[17] argue that their findings demonstrate the impact of interactions with pharmaceutical representatives, honoraria, and sponsored research. There are no ideal data to date, but the literature points to important concerns for 3 interactions with physicians: pharmaceutical representative speakers, CME sponsorship, and conference travel. Many less rigorous studies also detected the impact of the interactions with pharmaceutical representatives. These outcomes occurred despite physicians' forgetting the sponsors' names[15,20] or physicians' beliefs that they could not be influenced.[16]

Policy Implications

Several professional societies,[53-57] have developed guidelines to modulate the interaction between physicians and the pharmaceutical industry. Despite the guidelines' recommendation that students and residents should be informed about them, there was a lack of awareness. Among residents, only 23%[23] to 50%[32] knew about them, whereas 62% of physicians knew of at least 1 guideline.[19] Also, enrollment in a program with guidelines affected whether they would accept gifts, but having read the national guidelines and awareness of the program's policy did not.[23] Enrollment in a program with guidelines also affected the frequency of and attitude toward these interactions.[31] Whether it was the guidelines themselves or the presence of critical faculty who served as role models that influenced the interactions cannot be elucidated from these studies. Only a few training programs have proposed their own guidelines (35% of US internal medicine programs,[37] 58% of US family medicine[35] programs, 61% of US emergency medicine programs,[33] and 25% of Canadian family medicine programs[21]) and fewer distribute these guidelines[21] or give formal instruction on them.[23]

Finally, most such guidelines allow for physician–pharmaceutical representative interaction whereas subsidies for travel and other amenities at a symposium can only be given to residents. This article questions the adequacy of the guidelines for many of the above interactions, specifically, the lack of guidelines regarding resident–pharmaceutical representative interaction, the efficacy of the guidelines for industry-sponsored CME events, and the allowance of industry-sponsored conference travel for residents despite the fact that these have been disallowed for physicians. This is of great concern in terms of travel scholarships, for which residents have conference subschedules designed by a group of mentors hired by the same industry sponsor and are immersed in this group for the duration of the conference. Concerns about CME could be addressed by prioritizing the Association of American Medical Colleges guidelines and concerns by other authors.[58] Also, the American College of Physicians' suggestion that physicians should be guided in making decisions about their activities by whether they would be willing to have their interactions known does not address the fact that physicians do not always comprehend how interactions affect them.

Another attempt to address growing concern about physician-industry interaction has been the introduction of practical training. Twenty-five percent[37] to

Table 5. Hill Criteria for Causality and Industry-Physician Interactions[48]*

	Consistency†	Strength	Specificity‡	Dose-Response	Biological Plausibility§	Coherence	Temporal Relationship	Experiment[31]
Interaction with PR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Gifts	Yes	Yes	...	Yes	Yes	Yes	...	Yes
Samples	Yes	Yes	...	Yes	Yes	Yes	...	...
Industry-paid meals	Yes	Yes	...	Yes	Yes	Yes	...	...
PR speakers	Yes	Yes	...	...	Yes	Yes	Yes	...
CME funding	Yes	Yes	...	...	Yes	Yes	Yes	...
Conference travel	Yes	Yes	Yes	Yes	Yes	Yes	Yes	...
Honoraria	Yes	Yes	Yes	Yes	Yes	Yes	...	...
Research funding	Yes	Yes	Yes	Yes	Yes	Yes	...	...

*Ellipses indicate data were not collected. CME indicates continuing medical education.
†More than 1 study found an effect for each interaction.
‡Only 1 study examined specificity and defined it as increased likelihood of choosing product of sponsor over competition in association with interaction.[25]
§Mechanism: for gifts, meals, honoraria, and travel subsidy[49]; interaction with pharmaceutical represtative (PR)[50-52]; research funding[43-47]; the mechanisms for all other interactions are reviewed in the text.

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75%[21] of programs taught about industry marketing techniques and critical appraisal of industry product claims. Yet these attempts left many residents wanting: family medicine, psychiatry, emergency medicine, and internal medicine residents wanted more teaching[26,33,38] both in medical school (45%) and residency (60.6%).[21] Reports of some programs that have been implemented are optimistic,[9,22,33,59-62] However, 2 of the studies are older[9,60] and another program[62] was conducted infrequently. Also, only short-term effects on attitude and knowledge were examined, leaving the impact on long-term behavior unknown. Clearly, there is a need for systematic interventions. Positive changes in prescription patterns and physician knowledge[40,63,64] associated with such alternatives as academic detailing and industry-independent drug information mailings suggest other avenues for action.

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The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JUNE 29, 2006

For Sale: Physicians' Prescribing Data

Robert Steinbrook, M.D.

Since the early 1990s, health care information companies have bought electronic records of prescriptions from pharmacies and other sources and linked them with information about doctors that is licensed from the Physician Masterfile of the American Medical Association (AMA). These information companies, the largest of which is IMS Health of Fairfield, Connecticut, have then compiled and sold individual physicians' prescribing data to pharmaceutical manufacturers. The business is lucrative. But a growing number of physicians have rebelled after becoming aware that drug companies have access to their data — in some cases because zealous sales agents have confronted them with their prescribing histories.[1] The abuses have occurred despite "best practice guidelines" from the AMA that include admonitions that industry and its representatives should keep prescribing data confidential, that companies should prohibit disclosure "by sales representatives to any other party," and that "the use of prescribing data to overtly pressure or coerce physicians to prescribe a particular drug is absolutely an inappropriate use."

The ferment has had several consequences. First, the AMA has created a Prescribing Data Restriction Program (see box). Physicians are now able to deny all sales representatives access to their individual prescribing data. The restriction is limited to sales representatives and their direct supervisors; physicians will not be able to deny access to other officials at pharmaceutical companies.[2]

Second, the California Medical Association (CMA), in conjunction with IMS Health, is planning a program that will allow physicians who do not restrict access to their information to see their own data, comparative data, and educational material that will focus on prescribing for common diseases as well as categories of medications that are heavily prescribed. After pilot testing is completed this year, the program is expected to be available in 2007. The CMA is likely to make the program available to all California physicians, not just association members. Eventually, similar programs may be available to physicians in other states.

Third, some states may enact legislation that would supersede the AMA program. They may ban outright the use and sale, for most commercial purposes, of prescription data in which prescribers are identified. Typically, the use of

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The Prescribing Data Restriction Program

The AMA's Prescribing Data Restriction Program (www.ama-assn.org/ama/pub/category/12054.html) allows physicians in the United States, regardless of whether they are members of the AMA, to deny all pharmaceutical sales representatives access to their individual prescribing data. The Web-based system also allows physicians to report concerns about the inappropriate use of prescribing data by a specific pharmaceutical-company representative or a specific company and to make "general observations" about the uses of the data. The program became available in May 2006.

"Restricted data" are defined as "any product-level data regarding the prescribing practices of an identifiable physician who has [restricted access to his or her data]. This includes measures of prescription volume in absolute and percentage terms, the associated dollar value of a physician's prescribing, any indicators of change in these measures, as well as any means of ranking, benchmarking, or grouping physicians that may reveal prescribing habits for a particular product."[2] Efforts to identify the individual physicians associated with restricted prescribing information are also prohibited.

A restriction is valid for three years and can then be reinstated; it can be removed at any time. A restriction applies equally to all sales representatives, regardless of their company. Pharmaceutical manufacturers are required to check the program database at least quarterly; it may take as long as 90 days from each such check for them to cut off their sales representatives' access to data newly marked as restricted. The new program is separate from other restrictions that physicians can already place on the uses of their Masterfile data, such as the "no contact" list, which prevents doctors from receiving solicitations through the mail.

The AMA says that it will gauge compliance by monitoring physicians' complaints and that companies with isolated infractions will receive warnings. Those with a pattern of abuse may lose access to the data altogether.[2]

such data for marketing, promotion, or any activity related to sales agents would be prohibited. However, the noncommercial use of an individual's prescribing data for health care research or public health purposes would be permitted, as would the commercial use of data in which providers were not identified and were grouped by ZIP Code, geographic area, or specialty. In 2003 and 2004, a legislative ban was seriously considered in California at the request of the CMA. After the CMA and IMS Health agreed to develop the forthcoming program, the ban was not enacted. Earlier this year, the New Hampshire legislature approved a ban. As of mid-June, the legislation was on its way to Governor John Lynch, who has said he will sign it. The restrictions would go into effect immediately.

The Masterfile includes current and historical data on physicians from the time of their undergraduate medical education onward; the database encompasses information not only about AMA members, but also about nonmembers and many graduates of foreign medical schools who reside in the United States. As of December 2004, the Masterfile contained data on 820,000 living physicians. It does not contain prescribing data.

Companies that license data from the Masterfile are subject to AMA rules and regulations. According to a recent article by Robert Musacchio, of the AMA, and Robert Hunkler, of IMS Health, the rules of the new program "allow the industry to retain access to prescribing data for most purposes, but they require companies to police their own sales forces."[2] They warned that unless companies "comply in letter and spirit with the requirements," they "will sabotage the success of the program and pave the way for legislation that imposes stricter measures on the industry."

The current controversy is about collecting and selling physicians' prescribing information, not data that identify patients, whose confidentiality is protected under the Health Insurance Portability and Accountability Act. Prescribing data can be linked to individual physicians in various ways — by means of Drug Enforcement Administration registration numbers, state medical license numbers, or internal identifiers used by pharmacies, for instance.

According to a national survey of physicians conducted by the Gallup Organization for the AMA in 2004, 77 percent were aware that pharmaceutical companies had access to physicians' prescribing data, and 66 percent opposed the release of these data to sales representatives. However, 68 percent believed that the release of the data had "neither a particularly positive nor a particularly negative impact on their medical practices"; 77 percent indicated that their concern would be alleviated if they were given the choice of preventing the release of their prescribing data to sales representatives.[3]

Of course, prescribing data have other uses, some of which have little to do with marketing. For example, they can be used by public health agencies and in studies about drug interactions, prescribing trends, long-term effects of medication, and the prevention of medical errors. In a 2004 report, the Board of Trust-

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ees of the AMA, while acknowledging the concern about the release of prescribing data and their commercial uses, noted that pharmaceutical companies believe they "would struggle without the data, resulting in physicians seeing an increase in sales calls, less targeted educational information, and fewer or less relevant drug samples. The public good uses of the data would be severely cut back or eliminated as [health care information organizations] would no longer have a financial incentive to maintain the data."[3]

In 2005, IMS Health had operating revenue of $1.75 billion, substantially all from sales to the pharmaceutical industry, according to its annual report.[4] Forty-eight percent was from "sales force effectiveness offerings," which include "sales territory reports and prescription tracking reports." Pharmaceutical manufacturers use such reports to decide how much to pay their sales representatives as well as for many other purposes. IMS Health collects information on about 70 percent of all prescriptions filled in community pharmacies and projects nationally representative data. Some organizations, such as Kaiser Permanente, do not make their prescription data available because they object to their use in influencing prescribing patterns; the limit, however, applies only to prescriptions filled in their pharmacies.

In 2005, the AMA received $44.5 million in revenue — about 16 percent of its total revenue — from the sale of database products.[5] The association does not release information indicating what percentage of its database revenue comes from licenses to IMS Health and its competitors, such as Dendrite International, Verispan, and Wolters Kluwer.

Prohibiting the release of prescribing data to sales representatives will not put an end to another practice to which some physicians object: the use of such data by managed care or pharmacy benefit managers. These entities have sources of information that are independent of the AMA Masterfile. It also will not stop visits from sales agents, which doctors have always had the right to refuse, nor will it curtail the marketing of drugs. According to the AMA, the potential effects of restricted release may include a reduction in the number of "offers physicians currently receive from the pharmaceutical industry, such as drug samples, CME programs and speaking engagements."

Although broad notification efforts are planned, many physicians remain unaware that they can restrict access to their data, so it is impossible to predict how many will do so, or whether the monitoring system to prevent abuses will be effective. Programs that would let physicians view their data along with comparative data and educational materials are not yet available, so their features and value are not known. It is also uncertain whether all physicians in the United States will eventually have access to them. If the AMA were to stop licensing the Masterfile to aid the compiling of prescribing data, it would separate itself from the practice, but its revenue would decline, and health care information companies would no doubt seek to obtain similar data from other medical societies and commercial entities. Finally, fueled by general objections to the practice, other states may follow New Hampshire and enact broad bans on using and selling prescribing data. Thus, the fallout from this controversy is likely to remain uncertain for at least several years.

An interview with Dr. Jack Lewin, chief executive officer of the California Medical Association, can be heard at www.nejm.org.

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September 2008

Prescription Drug Trends

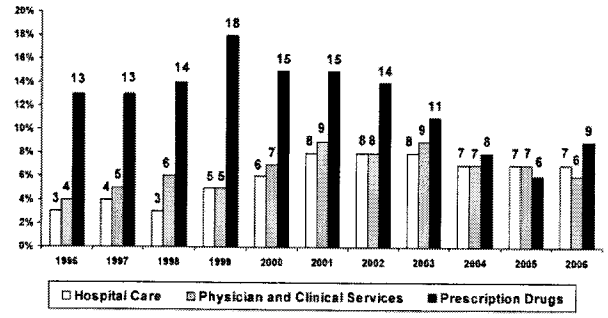
Overview

Prescription drugs are vital to preventing and treating illness and in helping to avoid more costly medical problems. Rising costs and implementation of the Medicare Part D drug benefit in 2006 have highlighted the need for a better understanding of the pharmaceutical market and for new approaches to address increasing prescription costs.

Rising Expenditures for Prescription Drugs

Spending in the US for prescription drugs was $216.7 billion in 2006, more than 5 times the $40.3 billion spent in 1990.[1] Although prescription drug spending has been a relatively small proportion of national health care spending (10% in 2006, compared to 31% for hospitals and 21% for physician services), it has been one of the fastest growing components, until recently growing at double-digit rates compared to single-digit rates for hospital and physician services. In 2006, the annual rate of increase in prescription spending was 9%, compared to 7% for hospital care and 6% for physician services[2] (Figure 1).

Figure 1: Average Annual Percentage Change in Selected National Health Expenditures, 1996-2006



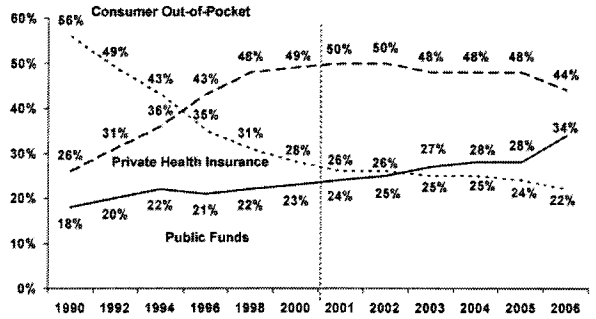
Source: Kaiser Family Foundation calculations using National Health Expenditure historical data from Centers for Medicare & Medicaid Services, http://www.cms.hhs.gov/NationalHealthExpendData/.

Prescription spending growth slowed from 1999 to 2005 because of the increased use of generic drugs, the increase in tiered copayment benefit plans, changes in the types of drugs used, and a decrease in the number of new drugs introduced.

The growth in drug spending in 2006 resulted from 1) increased use of prescription drugs, attributed to the implementation of Medicare Part D, new indications for existing drugs, strong growth in several therapeutic classes, and increased use of specialty drugs; 2) lower rebates from drug manufacturers; and 3) changes in the therapeutic mix of drugs.[3]

The share of prescription drug expenses paid by private health insurance increased substantially over the past sixteen years (from 26% in 1990 to 44% in 2006), contributing to a decline in the share that people paid out-of-pocket (from 56% in 1990 to 22% in 2006). The government's share of expenditures remained fairly constant. However, the implementation of the Medicare Part D drug program in 2006 substantially changed the mix of funding sources, as the government's share rose from 28% in 2005 to 34% in 2006, the private insurance portion fell from 48% to 44%, and the consumer out-of-pocket share declined from 24% to 22% (Figure 2).

Figure 2: Percent of Total National Prescription Drug Expenditures by Type of Payer, 1990-2006



Notes: Consumer Out-of-Pocket includes direct spending by consumers for health care goods and services not covered by a health plan and cost-sharing amounts (coinsurance, copayments, deductibles) required by public and private health plans. It does not include consumer premium payments and cost sharing paid by supplementary Medicare policies, which are included in the Private Health Insurance category. May not add to 100% due to rounding.

Source: Kaiser Family Foundation calculations using National Health Expenditure historical data from Centers for Medicare & Medicaid Services, http://www.cms.hhs.gov/NationalHealthExpendData/.

Within public funds, the funding shares changed from 7% Medicare and 68% Medicaid in 2005, to 53% Medicare and 26% Medicaid in 2006 (Figure 3).

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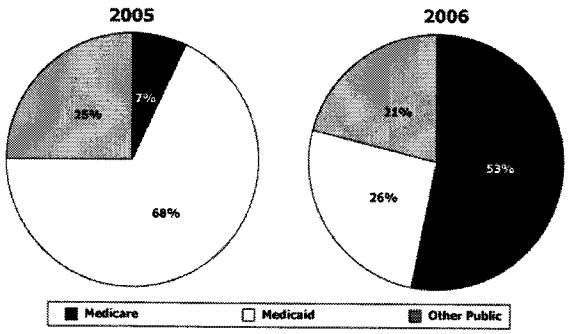
Figure 3: Distribution of Total Public Prescription Drug Expenditures by Type of Payer, 2005 and 2006



Notes: "Medicaid" includes federal and state funds for Medicaid and the Medicaid State Children's Health Insurance Program (SCHIP) expansion; "Other Public" includes other federal, state, and local expenditures and the Medicaid SCHIP program.

Source: Kaiser Family Foundation calculations using National Health Expenditures historical data from Centers for Medicare & Medicaid Services, http://www.cms.hhs.gov/NationalHealthExpendData/.

Factors Driving Changes in Prescription Spending

Three main factors drive changes in prescription drug spending: changes in the number of prescriptions dispensed (utilization), price changes, and changes in the types of drugs used.

Utilization. From 1997 to 2007, the number of prescriptions purchased increased 72% (from 2.2 billion to 3.8 billion), compared to a US population growth of 11%. The average number of retail prescriptions per capita increased from 8.9 in 1997 to 12.6 in 2007.[4] The percent of the population with a prescription drug expense in 2005 was 59% for those under age 65, and 91% for those 65 and older; the proportions of these populations with a drug expense has changed little since 1997, when they were 59% and 86%, respectively.[5]

Price. Prescription drug prices increased at the same rate in 2006 as in 2005 (3.5%).[6] Retail prescription prices[7] (which reflect both manufacturer price changes for existing drugs and changes in use to newer, higher-priced drugs) increased an average of 6.9% a year from 1997 to 2007 (from an average price of $35.72 to $69.91), more than two and a half times the average annual inflation rate of 2.6% over the same period. The average brand name prescription price in 2007 was over 3 times the average generic price ($119.51 vs. $34.34). Of the average retail prescription price of $69.91, manufacturers received 78%, retailers received 19%, and wholesalers received 4% in 2007.[8]

Changes in Types of Drugs Used. Prescription drug spending is affected when new drugs enter the market and when existing medications lose patent protection. New drugs can increase overall drug spending if they are used in place of older, less expensive medications; if they supplement rather than replace existing drugs treatments; or if they treat a condition not previously treated with drug therapy. New drugs can reduce drug spending if they come into the market at a lower price than existing drug therapies; this can occur when a new drug enters a therapeutic category with one or two dominant brand competitors. New drug use is affected by the number of new drugs (new molecular entities) approved by the US Food and Drug Administration; approvals have fluctuated over the past decade, with 39 approvals in 1997, 27 in 2000, 20 in 2005, and 18 in 2006.[9]

Drug spending is also typically reduced when brand drugs lose patent protection and face competition from new, lower cost generic substitutes. FDA analysis shows that generic competition is associated with lower drug prices: on average, the first generic competitor prices its product only slightly lower than the brand-name manufacturer; the second generic manufacturer reduces the average generic price to nearly half the brand name price; prices continue to fall but more slowly as additional generic manufacturers market the product. For products with a large number of generics, the average generic price falls to 20% of the branded price and lower.[10]

Approximately three-quarters of FDA-approved drugs have generic counterparts. In 2007, 21% of total prescription drug sales and 65% of total prescriptions dispensed were generic medicines. Generic sales grew 8% from 2005 to 2006.[11] Federal legislation allowing FDA approval of generic substitutes for brand name biologic drugs was introduced in 2007 but has not as yet been enacted.

Advertising. Both prescription use and shifts to higher-priced drugs can be influenced by advertising. After increasing every year since 1996, the total amount manufacturers spent on advertising declined from 2004 to 2005 (from $11.9 billion to $11.4 billion), rose to $12.0 billion in 2006, and fell to $10.4 billion in 2007. The share directed toward consumers (through advertising on

television, radio, magazines, newspapers, and outdoor advertising) decreased from 2006 to 2007 (from $4.8 to $3.7 billion), and the share directed toward physicians (through the sales activities of pharmaceutical representatives and through professional journals) also decreased (from $7.2 to $6.7 billion). Spending for consumer advertising in 2007 was over 4 times the amount spent in 1996 ($3.7 billion vs. $0.8 billion), while 2007 physician advertising was almost 2 times the 1996 amount ($6.7 billion vs. $3.5 billion).[12] The FDA and Congress are considering changes to prescription advertising rules.

Profitability. From 1995 to 2002, pharmaceutical manufacturers were the nation's most profitable industry (profits as a percent of revenues). They ranked 3rd in profitability in 2003 and 2004, 5th in 2005, 2nd in 2006, and 3rd in 2007, with profits of 15.8% compared to 5.7% for all Fortune 500 firms in 2007.[13] Prescription drug sales were $286.5 billion in 2007, an increase of 3.8% over 2006, the smallest growth rate since 1961. IMS Health attributes slower sales growth to loss of exclusivity of brand name medicines, fewer new product approvals, the leveling of year-over-year growth from the Medicare Part D program, and the impact of safety issues.[14]

Insurance Coverage for Prescription Drugs

Lack of insurance coverage for prescription drugs can have adverse effects. An April 2008 survey found that uninsured nonelderly adults (ages 18-64) are more than twice as likely as insured nonelderly adults to say that they or a family member did not fill a prescription (45% vs. 22%) or cut pills or skipped doses of medicine (38%vs.18%) in the past year because of the cost.[15]

Prescription drug coverage comes from a variety of private and public sources:

Employer Coverage. Employers are the principal source of health insurance in the United States, providing coverage for 177 million (59%) of Americans in 2007.[16] Sixty percent of employers offered health insurance to their employees in 2007, and 65% of employees in those firms are covered by their employer's health plan.[17] Other employees may have obtained coverage through a spouse. Nearly all (98%) of covered workers in employer-sponsored plans had a prescription drug benefit in 2007.[18]

Medicare. Prior to January 1, 2006, the traditional Medicare program (the federal health program for the elderly and disabled) did not provide coverage for outpatient prescription drugs. As a result, about one-quarter (27%) of seniors age 65 and older, and one-third of poor (34%) and near-poor (33%) seniors, had no drug coverage in 2003.[19] The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a voluntary Medicare outpatient prescription drug benefit (known as Part D), effective January 1, 2006, under which the 44 million Medicare beneficiaries can enroll in private drug plans. These plans vary in benefit design, covered drugs, and utilization management strategies.

Department of Health and Human Services (HHS) data show that as of January 2008, approximately 90% of Medicare beneficiaries had drug coverage: 25.4 million beneficiaries had Medicare Part D drug coverage from either a stand-alone prescription drug plan (17.4 million, including 6.2 million low-income seniors and people with disabilities, known as dual eligibles, who were transferred from Medicaid drug coverage to Medicare Part D drug coverage), a Medicare Advantage drug plan (7.6 million), or other Medicare health plan types (0.4 million). Another 10.2 million beneficiaries had coverage from creditable employer or union retiree plans including FEHB and TRICARE retiree coverage. And an estimated 4.0 million beneficiaries had creditable drug coverage from the VA and other sources. About 4.6 million beneficiaries did not have creditable coverage (were not enrolled in a Part D drug plan or a source of creditable coverage).[20]

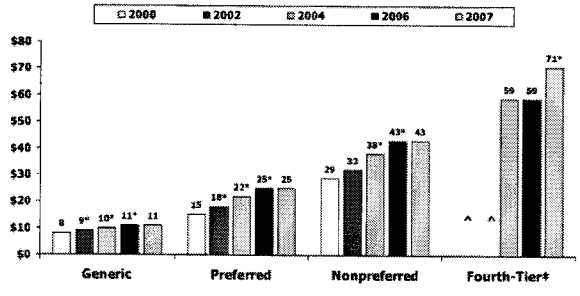
Medicaid. Medicaid is the joint federal-state program that pays for medical assistance to 60 million low-income individuals and is the major source of outpatient pharmacy services to the low-income population. All state Medicaid programs provide coverage for prescription drugs, although there are important differences in state policies with regard to copayments, preferred drugs, and the number of prescriptions that can be filled. Approximately 6 million dual eligibles were transferred from Medicaid drug coverage to Medicare Part D drug coverage in January 2006;

they represented an estimated 14% of Medicaid beneficiaries and accounted for about 45% of Medicaid prescription drug spending in FY2003.[21] Since January 1, 2006, states have been required to make payments to Medicare to help finance Medicare drug coverage for the transferred and future dual eligibles.

Responses to Increasing Prescription Costs
A variety of public and private strategies have been implemented to attempt to contain rising costs for prescription drugs, as described below.

Utilization Management Strategies. Health plans have responded to increasing prescription drug costs by excluding certain drugs from coverage, using quantity dispensing limits, and increasing enrollee cost-sharing amounts. In 2007, three-quarters (75%) of workers with employer-sponsored coverage had a cost-sharing arrangement with 3 or 4 tiers, over 2½ times the proportion in 2000 (27%).[22] Copayments for nonpreferred drugs (those not included on a formulary or preferred drug list) increased 48% from an average of $29 in 2000 to $43 in 2007. Copayments for preferred drugs (those included on a formulary or preferred drug list, such as a brand name drug without a generic substitute) increased by 67%, from an average of $15 in 2000 to $25 in 2007 (Figure 4).

Figure 4: Among Covered Workers with Three or Four-Tier Prescription Drug Cost Sharing, Average Copayments, 2000-2007



*Estimate is statistically different from estimate for the previous year shown at p<.05.

^Fourth-Tier drug copay information was not obtained prior to 2004.

Source: Kaiser/HRET Survey of Employer-Sponsored Health Benefits, 2000-2007, Exhibit 9.4, http://www.kff.org/insurance/7672/index.cfm

Discounts and Rebates. Private and public drug programs negotiate with pharmaceutical manufacturers (often using contracted organizations known as pharmacy benefit managers) to receive discounts and rebates which are applied based on volume, prompt payment, and market share. Manufacturers who want their drugs covered by Medicaid must provide rebates to state Medicaid programs for the drugs they purchase; many states have also negotiated additional rebates, known as supplemental rebates.

Several government agencies, including the Department of Veterans Affairs, the Defense Department, the Public Health Service, and the Coast Guard, participate in a program known as the Federal Supply Schedule through which they purchase drugs from manufacturers at prices equal to or lower than those charged to their "most-favored" nonfederal purchasers. In order to participate in Medicaid, another program, the Section 304B Program, requires manufacturers to provide drugs to certain nonfederal entities (such as community health centers and disproportionate share hospitals) at reduced prices. Federal legislation to expand this program was introduced in 2007 but has not as yet been enacted.

Medicaid. Historically, prescription drugs have been one of the fastest-growing Medicaid services. The Deficit Reduction Act of 2005 gave states more authority to control Medicaid drug spending through increased cost sharing for non-preferred drugs, changes in the way Medicaid pays pharmacists, allowing pharmacists to refuse prescriptions for beneficiaries who don't pay their cost sharing, and inclusion of authorized generic drugs in the calculation of "best price" for drugs. A 2006 survey of 50 states+DC found that more than half had Medicaid pharmacy cost containment measures in place in FY2006, including preferred drug lists and prior authorization programs (about 75% of states), supplemental rebates from manufacturers (about 70% of states), and state Maximum Allowable Cost programs for generic and multi-source brand drugs (about 60%); smaller proportions of states were members of multi-state purchasing coalitions (about 25%) or had limits on quantities dispensed per prescription (about 20%).[23] BY 2007, most states had already implemented many of these approaches, so new action to control drug spending slowed.[24]

The Centers for Medicare & Medicaid Services issued a rule (known as the AMP Rule) in July 2007 that would have set limits on federal government

reimbursements to states for Medicaid prescriptions; however, in December 2007, a US District Court issued a preliminary injunction against this change. Several bills have been introduced in Congress to address this issue.

Medicare. The Medicare Part D drug benefit shifted spending from the private sector and Medicaid to Medicare, making Medicare the nation's largest public payer of prescription drugs in 2006, when Medicare spending rose to 18% of total US prescription spending from 2% in 2005.[25] Under the Medicare Part D legislation, Medicare is prohibited from directly negotiating drug prices or rebates with manufacturers, but will rely on the private Part D drug plans to negotiate these discounts/rebates. In early 2007, the 110th Congress considered but did not pass legislation to allow or require Medicare to negotiate drug prices with drug makers.

Purchasing Pools. Some public and private organizations have banded together to form prescription drug purchasing pools to increase their purchasing power through higher volume and shared expertise. Examples include joint purchasing by the Department of Defense and VA; multi-state bulk buying pools through which states purchase drugs for their Medicaid, state employees, senior/low-income/uninsured pharmacy assistance programs, or other public programs; and individual state purchasing pools.[26]

Consumers. Consumers are turning to a variety of methods to reduce their prescription costs,[27] including requesting cheaper drugs or generic drugs from their physicians and pharmacies, using the Internet and other sources to make price comparisons, using the Internet to purchase drugs, buying at discount stores, buying over-the-counter instead of prescribed drugs, buying drugs in bulk and pill-splitting, using mail-order pharmacies,[28] and using pharmaceutical company or state drug assistance programs. Over half of physicians say they frequently talk with patients about the out-of-pocket costs of medicines they prescribe, 62% say they switch patients to less expensive drugs, and 58% say they give patients office samples.[29]

Importation. The high cost of prescriptions has led some to suggest that individuals be permitted to purchase prescription products from distributors in Canada or other countries (called "importation," or "reimportation" if the drug is manufactured in the US). Although it is generally not lawful for individuals or commercial entities such as pharmacies or wholesalers to purchase prescription drugs from other countries, the government does not always act to stop individuals from purchasing drug products abroad. Importation of pharmaceutical products from Canada through Internet sales and travel to Canada totaled about $700 million in sales in 2003, or 0.3% of total US prescription sales. An equivalent amount of prescription drugs was estimated to have entered the US from the rest of the world, mostly through the mail and courier services.[30] P.L. 109-295 (enacted in 2006) allows US residents to transport up to a 90-day supply of qualified drugs from Canada to the US. Actual savings amounts, drug safety, and marketplace competition and pricing are importation issues being debated.

Outlook for the Future

HHS projects US prescription drug spending to increase from $216.7 billion in 2006 to $515.7 billion in 2017, a 138% increase in 11 years. The average annual increase in drug spending from the previous year is projected to drop from 8.5% in 2006 to 6.7% in 2007 because of a deceleration in drug price growth, and then rise to 9.6% in 2017, or an 8.2% average annual increase over the 11-year period. Drug spending as a percent of overall health spending is projected to increase from 10% in 2006 to 12% in 2017. HHS projects that over the next decade, drug spending growth will accelerate due to a leveling off of growth in the use of generic drugs, rising utilization rates, and a mild acceleration in new drugs coming onto the market.[31]

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[1] All spending amounts in this report are in current dollars (i.e., not adjusted for inflation).

[2] Centers for Medicare & Medicaid Services, National Health Expenditure Accounts, Historical, http://www.cms.hhs.gov/NationalHealthExpendData/.

[3] Aaron Catlin et al., "National Health Spending In 2006: A Year Of Change For Prescription Drugs," *Health Affairs* 27, no. 1, (January/February 2008).

[4] Kaiser Family Foundation calculations using data from IMS Health, http://www.imshealth.com (About Us, Press Room, US Top-Line Industry Data), and Census Bureau, http://www.census.gov. The per capita number may differ from the number reported at KFF's website www.statehealthfacts.org because of differing data sources which use different retail pharmacy definitions (e.g., IMS Health includes mail order, Verispan does not).

[5] Agency for Healthcare Research and Quality, Medical Expenditure Panel Survey Component Data, "Prescription Medicines – Mean and Median Expenses per Person With Expense and Distribution of Expenses by Source of Payment," table 2, 1997 and 2005, http://www.meps.ahrq.gov/mepsweb/.

[6] Aaron Catlin et al., "National Health Spending In 2006: A Year Of Change For Prescription Drugs," *Health Affairs* 27, no. 1, (January/February 2008).
[7] Retail prescription prices reflect the prices paid by insured and uninsured patients, and do not reflect rebates, discounts, and other payments that in effect lower the cost of prescriptions.
[8] Kaiser Family Foundation calculations using data from the National Association of Chain Drug Stores, "Industry Facts-at-a-Glance," http://www.nacds.org (based on data from IMS Health), and Consumer Price Index, US City Average, All items, from the Bureau of Labor Statistics, http://www.bls.gov.
[9] US Food and Drug Administration, http://www.fda.gov/cder/rdmt/; 2004-2007 data include new BLAs (biologic license applications) for therapeutic biologic products transferred from FDA's Center for Biologics Evaluation and Research to its Center for Drug Evaluation and Research.
[10] US Food and Drug Administration, Center for Drug Evaluation and Research, "Generic Competition and Drug Prices," http://www.fda.gov/cder/ogd/generic_competition.htm.
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[12] IMS Health, http://www.imshealth.com (About Us, Press Room, 2007 US Top-Line Industry Data); Kaiser Family Foundation, *Prescription Drug Trends, a chartbook*, (July 2000), ex. 3.13, http://www.kff.org/rxdrugs/3019-index.cfm. The data on spending for advertising directed towards physicians excludes the retail value of drug samples left at sales visits to physicians' offices, which totaled about $16 billion in 2004, the last year such data were available online from IMS Health.
[13] Fortune 500 online, http://money.cnn.com/magazines/fortune/fortune500/2008/performers/industries/profits/index.html, and personal communication; April issues of *Fortune* magazine.
[14] "Moderating Growth Reflects Impact of Patent Expirations, Fewer Product Approvals, Maturing Medicare Part D Program, and Safety Issues," IMS Health Press Release (March 12, 2008), http://imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_83470499,00.html.
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[16] US Census Bureau, *Income, Poverty and Health Insurance Coverage in the United States: 2007* (August 2008), Table C-1, p. 61, http://www.census.gov/prod/2008pubs/p60-235.pdf.
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[19] Dana Gelb Safran et al., "Prescription Drug Coverage And Seniors: Findings From A 2003 National Survey," *Health Affairs*, Web Exclusive (April 19, 2005): W5-160, http://www.kff.org/medicare/med041905pkg.cfm.
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[31] Sean Keehan et al., "Health Spending Projections Through 2017: The Baby-Boom Generation Is Coming To Medicare," *Health Affairs*, Web Exclusive (February 26, 2008), w145-w155.

For More Information:
In addition to the Kaiser Family Foundation reports found in the Endnotes above, this Fact Sheet (#3057-07) and the following reports are available on the Foundation's website at www.kff.org: *Trends and Indicators in the Changing Health Care Marketplace* (#7031), *Prescription Drug Trends—A Chartbook Update* (#3112), *Cost Containment Strategies for Prescription Drugs: Assessing the Evidence in the Literature* (#7295), *Follow the Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain* (#7296), *Medicare Prescription Drug Benefit Fact Sheet* (#7044-08), *Medicare Payments and Beneficiary Costs for Prescription Drug Coverage* (#7620), *Resources on the Medicare Prescription Drug Benefit, Medicaid and Outpatient Prescription Drugs* (#1609-03), *Federal Policies Affecting the Cost and Availability of New Pharmaceuticals* (#3254), and *Retiree Health Benefits Examined: Findings from the Kaiser/Hewitt 2006 Survey on Retiree Health Benefits* (#7587). See also www.statehealthfacts.org for state-specific prescription drug utilization and sales (under Health Costs & Budgets); www.kaiserEDU.org (Prescription Drugs) for a Tutorial, Issue Modules, and SmartLinks on prescription drugs; and http://facts.kff.org/ (search for Prescription Drugs) for Fast Facts about prescription drugs.

Prepared by Janet Lundy of the Kaiser Family Foundation.

Target Article

All Gifts Large and Small

Toward an Understanding of the Ethics of Pharmaceutical Industry Gift-Giving

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Much attention has been focused in recent years on the ethical acceptability of physicians receiving gifts from drug companies. Professional guidelines recognize industry gifts as a conflict of interest and establish thresholds prohibiting the exchange of large gifts while expressly allowing for the exchange of small gifts such as pens, note pads, and coffee. Considerable evidence from the social sciences suggests that gifts of negligible value can influence the behavior of the recipient in ways the recipient does not always realize. Policies and guidelines that rely on arbitrary value limits for gift-giving or receipt should be reevaluated.

Key Words

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Healthcare professionals commonly receive small gifts such as pens and note pads from drug companies seeking to influence their prescribing practices. Gifts, both large and small, have been used by the pharmaceutical industry for almost a century to promote specific products and establish brand recognition (Shaughnessy, Slawson, and Bennet 1994; Clark 1989). The presumption is that large gifts, such as extravagant vacations, have the capacity to influence behavior, but gifts of *de minimis* monetary value, such as donuts and penlights, do not. Yet, while it might seem both logical and practicable to distinguish small gifts from larger, seemingly more problematic gifts, a large body of evidence from the social sciences shows that behavior can be influenced by gifts of negligible value.

Policy Background

In the 1980s the large cash payments and lavish gifts some physicians received from drug companies captured public attention (U.S. Senate 1990). There was concern that physician integrity was falling victim to commercial influence in ways that were costly to the healthcare system in terms of both dollars and public trust. Congressional hearings on pharmaceutical promotion led the American Medical Association (AMA) and the Pharmaceutical Research and Manufacturers of America (PhRMA) to adopt voluntary guidelines prohibiting the exchange of cash payments and gifts valued over $100 (Department of Health and Human Services 1991). Under these guidelines inexpensive gifts such as pens and notepads were expressly allowed providing they "relate" to medical practice. The Office of the Inspector General (OIG) of the U.S. Department of Health and Human Services (DHHS), in a set of studies examining marketing practices, questioned the extent to which those guidelines were being enforced and suggested that allowing small gifts might be contrary to the public interest (DHHS 1991; 1992).

Numerous studies of pharmaceutical marketing practices were performed during the 1990s. These studies suggest that the pharmaceutical industry exercised considerable influence over physician prescribing practices and formulary composition (Wazana 2000). The $12 billion spent annually by the industry on gifts and payments to physicians drew attention from the DHHS OIG and a large-scale study of marketing practices was budgeted for 2002. The study was to examine whether all drug company gifts present an inherent conflict of interest or even a violation of federal antikickback legislation (DHHS 2001). However, it was subsequently deleted from the OIG's research agenda (Robert Brown, personal communication, 2003).

In 2001 the AMA and PhRMA responded to the government's renewed interest in gift-giving by launching a joint educational campaign. Nine large pharmaceutical companies contributed a total of $675,000, and the AMA contributed $50,000 plus staff time in an effort to remind physicians, medical students, and pharmaceutical sales representatives of the importance of following the

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1990 guidelines (Okie 2001). During this time the American College of Physicians and the American Society of Internal Medicine issued a position paper that recognized the potential for small gifts to compromise clinical judgment but stopped short of calling for the practice to cease (Coyle 2002).

In May 2002 PhRMA issued a new, voluntary code for self-regulation of industry interactions with physicians. The code continues to allow for the exchange of gifts valued less than $100 but puts "items of minimal value" in their own category. Whereas gifts under $100 can be given only "on occasion" and must primarily benefit patients, gifts of minimal value, including calendars and stress dolls, should benefit medical practice and can be given with any frequency. Snacks and modest meals are permissible so long as they are consumed while listening to the sales pitch of a company representative (PhRMA 2002).

No studies have been conducted specifically on the effect of *de minimis* gifts on physician prescribing practices. This might be due in part to the presumption that the size or value of a gift correlates with its potential to influence the recipient. Thus the larger and more valuable the gift, the weightier are the ethical concerns raised about the industry's influence over physicians. Until recently *de minimis* gifts generated little moral or regulatory concern.

Today, groups such as Public Citizen (Tanner 2001), Physicians for a National Health Program (http://www.pnhp.org), American Medical Student Association (Romano 2002) and No Free Lunch (http://nofreelunch.org) oppose all industry gift-giving on the belief that the practice conflicts with the professional duties of physicians. The OIG has also issued draft compliance guidelines that suggest industry gift-giving might violate federal antikickback laws in that the gifts are given to influence prescriptions. From the government's perspective this is particularly problematic for patients receiving federal health coverage (DHHS 2002). The compliance guidelines are to be finalized in 2003.

The Issue of Small Gifts

The OIG and others have found that nearly all doctors accept small gifts from drug salespeople (OIG 1992; Wazana 2000). Drug companies use office trinkets and foodstuffs to entice physicians to speak with company representatives (Braithwate 1984; Lichstein, Turner, and O'Brien 1992; Hodges 1995; Ziegler, Lew, and Singer 1995; Jacobs 1999). The large majority of physicians meet with industry detailers several times a month (Lexchin 1989; Wazana 2000). Many physicians cite these gifts as the sole or among the top reasons for seeing drug detailers (Lexchin 1989; Jacobs 1999; Wazana 2000).

Gifts such as pens and notepads, typically emblazoned with product names, are called "reminder items," but their potential to influence prescribing extends beyond the advertisement they bear. Some physicians see industry gifts as a professional entitlement. This is particularly the case for those in the professionalization process where respect from a sales representative and a free meal are relished. Gifts and foods can be seen as a simple perk or a sign of career accomplishment and status.

Industry proponents assert that because physician-detailer interaction raises awareness of new products, the practice benefits patients. However, no evidence exists to support this claim. In contrast, research suggests that physicians rely heavily on detailers for information and that the more doctors rely on commercial sources of information, the less likely they are to prescribe drugs in a manner consistent with patient needs. Information provided by detailers is often biased, and sometimes dangerously misleading (Avorn, Chren, and Hartley 1982; Lexchin 1989; Ziegler, Lew, and Singer 1995). The reviews by Lexchin (1989; 1993) and Wazana (2000) correlate physician-detailer interactions with marked physician preferences for new products that hold no demonstrated advantage over existing ones, a decrease in the prescribing of generics, and a rise in both prescription expenditures and irrational and incautious prescribing.

Many physicians deny the potential for the receipt of small promotional items to undermine their professional objectivity (Gorski 1990; Hume 1990; Banks and Mainous 1992; Orlowski and Wateska 1992; Rosner 1992; Chren and Landefeld 1994; Shaughnessy, Slawson, and Bennet 1994; Thompson, Craig, and Barham 1994; Hodges 1995; Aldir et al. 1996; Gibbons et al. 1998; Roughead, Harvey, and Gilbert 1998; Davis 2000; Howard 2000; Wazana 2000; Steinman, Shlipak, and McPhee 2001; Woollard 2003). In fact, researchers have found that the more gifts a physician receives, the more likely he or she is to believe that they do not influence behavior (Hodges 1995). While medical professionals might believe themselves to be "more rational and critical" than the average person (Shaughnessy, Slawson, and Bennet 1994; Babcock and Loewenstein 1997), the success of pharmaceutical marketing illustrates that physi-

cians are as susceptible to target marketing as others (Coste 1999). Those who do not acknowledge the power of small gifts are the ones most likely to be influenced, because their defenses are down.

Small gifts play an important role in opening doors and promoting friendlier, more cooperative relationships between pharmaceutical sales representatives and physicians. Thus, as the following section explains, the effects of gifts on physician practices can be far greater than their minimal monetary value would imply.

The Effects of Gifts, Large and Small, on Behavior

Gift exchange underlies the human tendency to engage in networks of obligation (Gouldner 1960; Mauss 1954; Levi-Strauss 1969). When a gift or gesture of any size is bestowed, it imposes on the recipient a sense of indebtedness. The obligation to directly reciprocate, whether or not the recipient is conscious of it, tends to influence behavior. Many social scientists believe that the predilection to reciprocate is an adaptive mechanism that has helped bind and advance human societies by enabling exchanges of food, skills, and goods (Leakey and Lewin 1978).

The social rule of reciprocity imposes on the recipient an obligation to repay, in kind if possible, for favors, gifts, invitations, and the like (Levi-Strauss 1969; Cialdini 1993). For example, when someone does us a favor, we are expected to return the favor at some point down the road. Hence, the phrase *much obliged* is used as a synonym for *thank you.*

Feelings of obligation are not related to the size of the initial gift or favor. For example, the success secret of the world's record holder for car sales was to send mass-produced greeting cards to his customers every month printed with the simple phrase "I like you" (Cialdini 1993, 174). In another case, the owner of a pharmacy gave patrons a $0.50 key chain when they entered the store and the amount they spent on purchases increased 17% (Friedman and Herskovitz 1990). Similarly, when the Disabled American Veterans organization appeals for donations through direct-mail solicitation, the response rate is about 18% when no gift is included and 35% when the envelopes contain an unsolicited gift (e.g., inexpensive, customized address labels) (Cialdini 1993).

Food, flattery, and friendship are all powerful tools of persuasion, particularly when combined. Individuals tend to be more receptive to information when it is received while eating enjoyable food (Janis, Kay, and Kirshner 1965). This is why food is "the most commonly used technique to derail the judgment aspect of decision making" (Razran 1940). The positive feelings associated with good food are projected onto the people and messages experienced while eating. When salespeople combine food with flattery, recipients tend to like them more, regardless of what it is they have to say. Moreover, people are receptive to compliments even when they recognize that their source has a transparent agenda (Friedman and Friedman 1996). The act of dining helps to foster cozier working relationships that might help break down professional barriers between physicians and sales representatives. Positive social relationships are an effective way of engendering goodwill and making people want to reciprocate for gifts received (Perez, quoted in Rosenbloom 1989).

An amicable relationship, though, is not a prerequisite for compelled reciprocation. The reciprocity rule is so potent that people who are often disliked or distrusted, such as politicians and salespeople, can get people to comply with their wishes by imposing on them a small, unsolicited favor or gift (Cialdini 1993). This is exemplified by the "benefactor-before-beggar" strategy of the Hare Krishnas. Hare Krishnas commonly gathered in crowded airports and thrust trinkets, such as flowers and pamphlets, into the hands of passersby while saying, "this is our gift to you." Although recipients often tried unsuccessfully to refuse the small gift and ultimately threw it away, they were frequently so compelled to make a donation that the Hare Krishnas became quite wealthy. However, airport patrons' complaints about having to donate to the Krishnas resulted in airports prohibiting this mode of solicitation.

Airport patrons could have made the token gift giving of the Krishnas unprofitable by simply refusing to donate. The act of accepting a gift directly from another person without reciprocating is so socially uncomfortable, however, that to many it is preferable to avoid or ban the interaction altogether. Reciprocation is so highly valued a social norm that those who do not reciprocate are often regarded with disgust and assigned negative labels, such as "moocher," "ingrate," "free-loader" and "welsher." Regardless of the size of a gift, it is widely considered distasteful or bad form to take but make no effort to give in return (Cialdini 1993). Refusal either to accept a gift or to give a gift in return signifies a refusal to cooperate and is

often considered a declaration of conflict (Mauss 1954).

The natural tendency for people to accept gifts and kind gestures reduces their ability to choose to whom they wish to be indebted (Cialdini 1993). This is how the reciprocity rule can be exploited. Oftentimes, the initial actor in reciprocal relationships not only chooses the form of the initial favor but the form of the return favor as well. If physicians are to reciprocate for small gifts, they cannot do so in any form they please. They are essentially compelled to reciprocate by supporting their benefactor's products.

Small Gifts: The Cost of Doing Business?

In the business world, gifts are a valuable, time-honored marketing tool because they keep doors of communication open between cooperating parties. Medicine, in one view, is also a business. Some believe that modest gift-giving is appropriate and acceptable if it helps physicians be aware of and knowledgeable about the broad range of products available to them (Dodd and Dexter 1999; Benbow 1999). This is based on the premise that industry and physicians' interests do not conflict, because both are interested in learning how best to treat patients. It is also premised upon the shallow and contradictory assertion that, but for the gifts, physicians would not spend the time and energy to meet with information-providing salespeople even though what they have to gain can be helpful to their practice and their patients.

Laypersons' opinions regarding the acceptability of industry gifts are related to their perceptions of possible effects on prescribing behaviors and costs (Blake and Early 1995). Laypersons—like physicians—are likely to approve of physicians' receipt of small promotional items or gifts relevant to patient care and to disapprove of larger gifts and gifts that do not benefit patient care. In one study increased education (presumably excluding education in medicine) was correlated with the likelihood that laypersons would find certain gifts inappropriate (Mainous, Hueston, and Rich 1995). Patients tend to be aware that physicians accept gifts, unaware whether their own physicians accept gifts, and feel that gifts are more influential and less appropriate than do their physicians (Gibbons et al. 1998).

The ethical acceptability of small gifts should turn on the character of the gift as well as its potential consequences. One fundamental question is whether drug company gift-giving should be classified as a balanced exchange, where parties expect immediate and equal return, or as a negative exchange, where giving is motivated by profit so that parties seek to come out ahead in the transaction (Sahlins 1965). According to PhRMA, the exchange is balanced because gifts are given as compensation for the time physicians spend becoming educated about products (Dembner 2001). However, if the interests of physicians dovetail with those of industry, it follows that gifts are unnecessary because the valuable information provided to physicians is compensation enough for their time.

Industry gift-giving should, rather, be viewed as negative exchange because the practice is inherently profit-motivated, and the profit potential significantly exceeds the value of the gift. Drug companies are purely interested and invested in the products physicians prescribe, and they know and expect that their marketing practices will pay off with increased sales. Indeed, former president of Pfizer Pharmaceuticals G. Leubach was quoted as saying that marketing "is almost as scientific as anything we do" (Clark 1989).

Drug companies do not deduct the cost of such gifts as charity but as marketing expenses. For tax purposes business gifts are hardly considered gifts at all, because their giving does not arise out of a "detached and disinterested generosity" (Commissioner v. Duberstein 363 U.S. 733 [1949]). In this view, calling small tokens given as part of the sales activity of pharmaceutical firms "gifts" is disingenuous and a transparent attempt to be nonjudgmental. These "gifts" should be recognized for what they are: marketing wares.

While the benefits of promoting goodwill between physicians and the pharmaceutical industry cannot be discounted, the main objective of drug company gift-giving is to create relationships and interests on the part of recipient physicians that conflict with their primary obligation to act in the best interest of their patients. The practice is particularly problematic because favors and promotional items of negligible value can influence behavior in ways the recipient does not often realize. Research into the so-called "self-interest bias" has shown that it takes extraordinarily little to bias an individual's interpretation and processing of information as well as one's subjective judgments, including those dealing with ethics and fairness (Babcock and Loewenstein 1997).

The fundamental question is whether the risk of bias from small commercially-oriented gifts is acceptable. Implicit in many guidelines is the rec-

ognition that marketing wares create a conflict of interest but that the risk of bias from items of negligible value is small and, on net, worth taking because of the potential benefits offered by product marketing information. Guidelines establishing thresholds, such as the arbitrary amount of $100, are based on the belief that there is a direct "dose response"—that the risk of bias increases as the value of the gifted item increases. There is no level, however, below which it is guaranteed that marketing wares have no effect on the recipient.

The Need to Respond: Practical Considerations

Given that small gift-giving can influence clinical judgment in ways that conflict with physicians' fiduciary responsibilities, the question of how best to respond to the problem still remains. Changes in the standards of acceptable professional conduct and pharmaceutical marketing practices might be in order, ranging from disclosure of gift exchange to elimination of the practice altogether.

In June 2002 Vermont enacted legislation (Vt. Acts No. 127 [2001–2002]) that requires pharmaceutical companies to disclose gifts worth more than $25 to the state pharmacy board. According to "Review and Outlook: Green Mountain Drugs," published in the *Wall Street Journal,* 20 June 2002, Wisconsin, New York, and Maine are considering similar legislation. If gifts of all sizes are disclosed to federal or state regulators, valuable research can be conducted to determine the extent to which gift acceptance is associated with physicians' prescribing practices. Disclosure policies can also take the form of requiring physicians to inform patients receiving prescriptions that they have received gifts from the drug's manufacturer. Considering the extent to which physicians' offices are adorned with drug company trinkets, it is likely that patients are already aware of the *de minimis* gifts physicians receive. What they might not know is that these inexpensive penlights and notepads might actually undermine physician objectivity in ways that clash with their own medical and financial interests. Full disclosure, therefore, could also require physicians to inform patients of this potential bias. Such disclosure, however, would not neutralize the bias, nor would it assist patients who have little choice but to rely on physicians' judgments and little or no ability to combat the bias.

One obvious and compelling policy option in response to the evidence of the power of small gifts is to restrict or eliminate gift-giving or gift acceptance. Restrictions could take many forms, such as limiting the frequency of or settings for gift-giving, for example, to conferences or major holidays. Enforcement of restrictions or bans could take various forms, including FDA regulation or ties to state medical licensure through state antikickback and bribery laws. In light of the evidence that all gifts influence behavior, physicians and pharmaceutical firms could be sanctioned now for small gift exchange under current antikickback laws (Bulleit and Krause 1999). The federal government has already indicated that gift-giving practices may be criminalized because of the presumable effects on governmental drug expenditures (DHHS 2002).

On the other hand, some might argue that the regulation of gift-giving in medicine should be no stricter than it is in any other business context. In response we ask whether physicians aspire to be viewed more like corporate salespeople or like professionals beholden to the public trust. Most journalists are not permitted to accept gifts from information sources, and university professors are prohibited from accepting gifts from students before grades are issued (see http://www.presswise.org.uk/Washington%20Post.htm). Judges, National Basketball Association referees, and Major League Baseball umpires are all prohibited from accepting gifts of any size for any occasion from anyone with an interest in the outcomes of their judgments. Similarly, medical professionals ought to step up to the plate. When acting as patient advocates and trusted sources of information, physicians should carry out their professional activities in a way that minimizes the intrusion of avoidable conflicting interests.

We note that psychology research suggests that any imposed restrictions on physicians' professional behavior are likely to be ill-received and viewed as an affront to their personal integrity and professional freedom. Because people tend to desire freedoms more when faced with the threat of losing them (Worchell and Arnold 1973; Cialdini 1993), restrictions would not only irritate physicians who (over)value drug company gifts, but physicians who have historically been indifferent to them might find themselves valuing the gifts more. The exaggerated desire for restricted behavior increases when the restrictions apply to one group and not another (Cialdini 1993). Therefore, if physicians liken themselves to business professionals, restrictions on gift exchange would be viewed as unfair because medicine would seem the only sector of U.S. business prohibited from exchanging small

gifts. However, regulations barring the use of marketing wares would not, in actuality, regulate physician practices but only the sales practices of the pharmaceutical industry. To our minds, a ban on industry gift-giving would be inherently fair in that it would put all firms, including generics, on a level playing field.

Nonetheless, we recognize that gift-giving is the foundation of human interaction. If it engenders valuable social obligations that are definitional of relationships such as friendship and camaraderie, then regulating the gift relationship might compromise desirable, arguably essential, social relations. Government regulations might indeed be too crude and too heavy-handed an approach for micromanaging the fine lines between geniality and commercial inducement. For example, company-sponsored gifts to physicians clearly fall within the purview of government interest because they are ostensibly given for commercial purposes. In contrast, a true gift (one that is not subsidized by a company) that is given to a physician by a sales representative with whom a preexisting, interpersonal relationship or friendship is shared (not merely a professional acquaintance or courtesy) should generally fall outside the purview of government interest and regulation. It is the gray area in between that presents challenges with respect to the government's ability to enforce restrictions on gift-giving while refraining from dictating the boundaries of social interaction.

We believe that as a general rule society ought not regulate the exchange of small tokens of courtesy in business or other social settings. Medicine, however, is different. Limits placed upon pharmaceutical companies' use of marketing wares within this context would not be unfair but rather both appropriate and enforceable. The drug industry is highly regulated, and restrictions on marketing practices are already in place. If the distribution of marketing wares were prohibited, associated expenses would no longer be deductible as a cost of business, and the practices would cease.

The body of evidence reviewed above suggests that guidelines aimed at preserving professional objectivity by limiting the size of gifts physicians receive or companies distribute have thus far been shortsighted. The practice of small gift-giving occurs in an environment where physicians interact heavily with industry sales representatives, have their continuing-education courses funded by industry, receive information from industry-funded studies, are deluged with print advertising, and see patients targeted by direct-to-consumer advertising. In an environment in which industry plays such a prominent role, it might be difficult to determine, even with rigorous research methods, which industry tactics wield the most influence and impossible to say with confidence that if the practice of small gift-giving were to cease, prescribing practices would change.

That said, from a moral and regulatory perspective, policies that determine the acceptability of a gift according to its size are unsound. The power of gift-giving, both large and small, must be acknowledged if appropriate regulatory policies are to be created and enforced. ■

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Physician–Industry Relations. Part 1: Individual Physicians

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This is part 1 of a 2-part paper on ethics and physician–industry relationships. Part 1 offers advice to individual physicians; part 2 gives recommendations to medical education providers and medical professional societies.

Physicians and industry have a shared interest in advancing medical knowledge. Nonetheless, the primary ethic of the physician is to promote the patient's best interests, while the primary ethic of industry is to promote profitability. Although partnerships between physicians and industry can result in impressive medical advances, they also create opportunities for bias and can result in unfavorable public perceptions.

Many physicians and physicians-in-training think they are impervious to commercial influence. However, recent studies show that accepting industry hospitality and gifts, even drug samples, can compromise judgment about medical information and subsequent decisions about patient care. It is up to the physician to judge whether a gift is acceptable. A very general guideline is that it is ethical to accept modest gifts that advance medical practice. It is clearly unethical to accept gifts or services that obligate the physician to reciprocate.

Conflicts of interest can arise from other financial ties between physicians and industry, whether to outside companies or self-owned businesses. Such ties include honorariums for speaking or writing about a company's product, payment for participating in clinic-based research, and referrals to medical resources. All of these relationships have the potential to influence a physician's attitudes and practices. This paper explores the ethical quandaries involved and offers guidelines for ethical business relationships.

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See related article on pp 403-406.

In 1990, the American College of Physicians published a position statement titled "Physicians and the Pharmaceutical Industry" to address ethical issues in relationships between industry and the medical profession (1). The statement, which was prompted in large part by evidence of the drug industry's influence on physician behavior and concern for professional integrity and patient care, examined potential conflicts of interest in relationships with industry and provided ethical advice in certain areas. Since the statement was originally released, evidence of industry's influence on medical practice, research, and education has continued to emerge, and physician–industry relationships have multiplied. Once again, the American College of Physicians–American Society of Internal Medicine reminds physicians and industry to be vigilant about potential conflicts and ethical problems. The College recognizes that while there are no easy answers to many ethical questions, guidance in certain areas can be useful.

This is part 1 of a 2-part paper on ethics and physician–industry relationships. In part 1, the College offers recommendations to individual physicians, mainly clinicians and clinician-researchers, regarding acceptance of gifts and other financial relationships with industry. Part 2 addresses medical education providers and medical professional societies that accept corporate funding for organizational projects or membership events, such as meetings and symposiums (see pp 403-406).

Despite the introduction in the early 1990s of ethical standards for physicians regarding physician–industry relationships, concerns persist and evidence accumulates that commercial rewards can unduly affect clinical judgment (2–9). Industry allocates substantial resources to promote its products to physicians. In 1999, the pharmaceutical industry spent nearly $8.0 billion (U.S.) to send sales representatives to physician offices and to exhibit products at medical conferences and events (10). Such costly corporate overtures raise questions about undue influence and could undermine genuine educational efforts.

In addition to the pharmaceutical industry, physicians are increasingly courted by newly emerging indus-

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tries (biotechnology, pharmacogenetics, e-commerce), and potential conflicts of interest, whether real or perceived, are pervasive. Physicians meet industry representatives at the office and at professional meetings, collaborate in community-based research, and develop or invest in health-related industries. In all of these spheres, partnered activities often offer important opportunities to advance medical knowledge and patient care, but they also create an opportunity for the introduction of bias.

This paper offers two positions to help guide individual physicians in making ethical decisions about interacting with industry. The positions are based on the profession's fundamental principles of responsibility, that is, acting in a patient's best interests (beneficence), protecting the patient from harm (nonmaleficence), having respect for the patient and fostering informed choice (autonomy), and promoting equity in health care (justice). To uphold these principles, the primary purpose of entering relationships with industry should be the enhancement of patient care and medical knowledge. While the ethics of medicine and the ethics of business sometimes diverge, both are legitimate, and a thoughtful collaboration of physicians and industry can result in the best of patient care.

POSITION 1. INDUSTRY GIFTS, HOSPITALITY, SERVICES, AND SUBSIDIES

The acceptance of individual gifts, hospitality, trips, and subsidies of all types from industry by an individual physician is strongly discouraged. Physicians should not accept gifts, hospitality, services, and subsidies from industry if acceptance might diminish, or appear to others to diminish, the objectivity of professional judgment. Helpful questions for gauging whether a gift relationship is ethically appropriate include 1) What would my patients think about this arrangement? What would the public think? How would I feel if the relationship was disclosed through the media? 2) What is the purpose of the industry offer? 3) What would my colleagues think about this arrangement? What would I think if my own physician accepted this offer?

Rationale

Physicians understand that to maintain their professional objectivity they must be mindful of potential biases in medical information (7, 11). In fact, the entire infrastructure of science and much of physician education is built on the fundamental notion of eliminating, or at least controlling for, the many and powerful biases inherent in generating and interpreting scientific data. Ethically and professionally, the objective evaluation of medical information is critical for deciding on best clinical practices (beneficence) and avoiding risks to patient safety (nonmaleficence) (12–14). Thus, physicians have an obligation to themselves, their profession, and society to evaluate, correct for, and eliminate potential bias in medical information from all sources.

Recent studies and reports have examined industry influence on physician objectivity and behavior (15, 16), particularly prescribing practices, formulary choices, and assessment of medical information (3, 7, 17–25). Physicians frequently do not recognize that their decisions have been affected by commercial gifts and services (26) and in fact deny industry's influence (3, 15, 17–22), even when such enticements as all-expenses-paid trips to luxury resorts are provided (23). Research, however, shows a strong correlation between receiving industry benefits and favoring their products (23, 25, 27).

What Would My Patients Think about This Arrangement?

The dictates of professionalism require the physician to decline any industry gift or service that might be *perceived* to bias their judgment, regardless of whether a bias actually materializes. A perception that a physician is dispensing medical advice on the basis of commercial influence is likely to undermine a patient's trust not only in the physician's competence but also in the physician's pledge to put patients' welfare ahead of self-interest. Recent research on patient attitudes shows that patients are more likely than physicians to perceive industry gifts as inappropriate or influential on medical practice (19, 28, 29). More particularly, a significant number of patients believe that industry gifts bias their physicians' prescription practices and ultimately drive up medical costs. Patients make a distinction, however, between acceptable and unacceptable gifts. Most think that inexpensive incentives designed for office use (pens, notepads) and patient care (drug samples, medical texts) do not have a negative effect on health care. They are much more likely, however, to disapprove of items for

personal use (radios, coffeemakers), especially as the gifts become more costly (dinners, trips) (28, 29).

What Is the Purpose of the Industry Offer?

The potential for bias in industry-prepared information becomes especially precarious when such information is accompanied by a gift or free service. Even when the amenity is medically related, a major aspect of the offer involves the establishment of a gift relationship, a phenomenon much studied in social science research. In culture after culture, there has emerged "a vivid sense of the immense pervasiveness of the social obligation" that a gift elicits (30). Social scientists agree that the prevailing purpose of the gift is to establish the identity of the donor in the mind of the recipient and to oblige the recipient to reciprocate (30–32). It is not just lavish amenities that are in question. The acceptance of even small gifts can affect clinical judgment and heighten the perception (as well as the reality) of a conflict of interest (12).

From a certain perspective, drug samples can be characterized as "gifts." Because physicians can distribute such medications to patients at no apparent cost (33), the practice may seem to promote the profession's core principle of equitable access and justice in health care. The practice does allow the patient to try out a new medication before being committed to an expense. However, the sample mainly serves to encourage physicians to prescribe the new product. Research shows that once a patient exhausts a free supply of medication, the physician typically writes a prescription for the same brand (33, 34). Because few samples are for older or less expensive products (35), higher patient costs generally result. Moreover, physicians and their families and staff use approximately one third of the samples (33, 34, 36, 37), which illustrates how the practice fosters access to physicians' offices and encourages a gift relationship.

In addition to drug samples, industry may distribute product literature or "patient care services," such as education aids or disease management software. It is understandable that, in a busy practice, physicians would welcome industry's materials and technologies to keep themselves and their patients current with the latest developments in the medical field. Physicians must keep in mind, however, that industry-supplied medical information, although neutrally packaged, is in fact promotional (4). Physicians should never rely solely on industry-provided information or services as a substitute for an objective review of the literature and understanding of patients' conditions.

What Would My Colleagues Think about This Arrangement?

The issue of industry gifts, hospitality, and subsidies arises as early as medical school and residency programs (18, 20–22, 27, 38–42). Medical students and physicians-in-training often have opportunities to receive instructional materials, medical equipment, or even educational dinner programs. While it is recognized that such arrangements can benefit the medical education experience and that medical students and residents have unique financial and work circumstances, it is also necessary to note that medical training includes instruction on professional ethics, including appropriate relationships with industry. Medical students, physicians-in-training, and practicing physicians should apply the same ethical standards to their interactions with industry (43).

Physicians do not always agree about the appropriateness of gifts. Ideally, physicians should not accept any promotional gifts or amenities, whatever their value or utility, if they have the potential to cloud professional judgment and compromise patient care. As a practical matter, many physicians are comfortable with limiting their acceptance of gifts to items that enhance medical practice or knowledge and that are of modest value. Differences of opinion will undoubtedly arise because of the ways in which an item or service is valued in different practice environments and communities. Nonetheless, such debates are important because they remind physicians of the need to gauge regularly whether a gift relationship is ethically appropriate.

Recommendations

The inherent difficulty in defining what makes a gift appropriate has, to an extent, contributed to lapses in judgment by otherwise ethical persons. It is difficult to set with any precision a monetary value that would render a gift unacceptable. There is no consensus model for determining relative value, and one will not be recommended here. Instead, some specific guidance is offered in the following examples of generally acceptable industry gifts: inexpensive gifts for office use (such as pens and calendars), low-cost gifts of an educational or patient-care nature (such as medical books), and modest

hospitality (such as a reception or other food and drink) that is connected with a legitimate educational program.

Understandably, even these "generally acceptable" examples are subject to interpretation and will frustrate some readers. Together with the fundamental questions listed in Position 1, physicians should use these recommendations as guides in making a good-faith effort to evaluate the potential for influence and to determine what kinds of amenities are ethically appropriate to accept. It is unethical for physicians to accept any industry gift or subsidy that is predicated on recommending a particular product or taking a particular clinical action. The preceding examples cannot and should not be used as a perfunctory substitute for self-appraisal.

POSITION 2. FINANCIAL RELATIONSHIPS BETWEEN PHYSICIANS AND INDUSTRY

Physicians who have financial relationships with industry, whether as researchers, speakers, consultants, investors, owners, partners, employees, or otherwise, must not in any way compromise their objective clinical judgment or the best interests of patients or research subjects. Physicians must disclose their financial interest in any medical facilities or office-based research to which they refer or recruit patients.

Rationale

Like gifts, financial relationships between physicians and industry can jeopardize professional objectivity. While collaborations in pharmaceutical development and biotechnology are often effective spearheads for advancing therapies and patient care, research and investment ties can create dual commitments or conflicts of interest (12) and risk the confidentiality of patient information. Some physicians own, hold stock in, or have other financial stakes in the medical industry and biotechnology; others work for industry as researchers or are university-based researchers who receive industry grants. Increasingly, clinicians are invited to act as industry consultants or to participate in clinical trials of newly developed drugs or devices, often by enrolling their own patients as subjects (12, 44).

Ownership or Other Financial Interest in Medical Resources

Physician ownership or other financial interest in medical equipment, health care facilities, laboratories, and other medically related resources raises ethical and legal concerns that physician self-interest may lead to inappropriate self-referrals or overuse of resources. For example, one study found that physician-owned clinics generated 50% more patient visits than independent clinics, suggesting that self-referral had induced unnecessary demand (45). Because a physician's primary duty is to act in the best interests of patients, physicians cannot allow financial arrangements to influence their judgment about what constitutes an appropriate level of care. It is unethical for physicians to overutilize resources or make unnecessary referrals to goods and services for their own financial benefit. It is also unethical to participate in any arrangement that links income generation explicitly or implicitly to equipment or facility usage or revenues generated by investor-physicians. There are instances, of course, in which self-referrals are acceptable, such as in remote or isolated settings where there is a dearth of alternative medical resources. In any event, if physicians refer patients to resources in which they have a material interest, they need to disclose their financial investments and, to the extent practicable, specify alternative sources of goods and services (12).

Consulting, Speaking, or Writing on Behalf of Industry

Industry may pay clinicians well to act as consultants, speak on behalf of a company, or participate in community-based industry trials. As a rule of thumb, related payments from industry are acceptable for teaching and for research that advances medical and professional knowledge (for example, honorariums for presentations at symposiums), commensurate with the extent of the physician's services and reasonable travel expenses.

Physicians should guard against conflicts of interest when invited to consult or speak for pay on behalf of a company. It is likely that a company will retain only individuals who make statements or recommendations that are favorable to its products, thus compromising the physician's scientific objectivity. Physicians should accept honorariums only for services provided and must disclose any industry sponsorship or affiliation and other potential conflicts of interest to formal lecture audiences and publication editors (31, 46).

Physicians should also be circumspect if asked to deliver educational programming developed by a medi-

cal education and communication company. Such companies, which are largely financed through the pharmaceutical industry, are for-profit developers and vendors of continuing medical education (47). It is important that physicians retained as lecturers in such settings control the content of the educational modules they deliver rather than allow their presentations to be scripted by the company. Lecturers should screen industry-prepared presentation aids (such as slides and reference materials) to ensure their objectivity and should accept, modify, or refuse them on that basis. Presenters using such materials should disclose their source to audience members.

Paid efforts to influence the profession or public opinion about specific medical products are particularly suspect. It is unethical, for example, for physicians to accept commissions for articles, editorials, or medical journal reviews that are actually ghostwritten by industry or public relations firms in an attempt to "manage the press" about certain products or services (48).

Participation in Industry-Sponsored Research

Participation in practice-based research can contribute to our understanding of the benefits and risks of a new product, thereby promoting medicine's underlying principles of beneficence and nonmaleficence. Still, physicians are responsible for ensuring that any clinical research in which they participate is potentially of significant value and is ethically conducted (12, 49). In particular, physicians invited to join "postmarketing studies" that require the prescribing of a company's product need to consider the scientific validity of the research and its potential to enhance medical progress (44, 50, 51). Physicians should not participate in studies that are, in effect, thinly disguised promotional schemes to entice physicians to use new products.

Physicians also have an ethical obligation, based on the principle of patient autonomy and informed choice, to disclose their commercial ties to patients who are prospective study participants (12). Physicians who involve their own patients in office-based trials must also be aware of potential conflicts between what is best for the patient-subject and what is optimal for the conduct of the research. In weighing the two interests, clinicians must consider their role as physician first and as investigator second (12, 52). It is reasonable for the clinician to receive compensation commensurate with time and expenses incurred in study recruitment. However, physicians may not accept compensation simply for referring their patients to an industry study, regardless of whether the physician directly participates in the trial. Known as "finder's fees," such arrangements represent pure profit and create an inherent conflict with the best interests of the patient (12, 49, 53).

Finally, physicians involved in commercial trials must guard against bias in publishing research outcomes. Several studies show that physicians with financial ties to pharmaceutical manufacturers are significantly more likely than independent reviewers to report findings that support the sponsor's drugs; likewise, they are less likely to report unfavorable findings (48, 54–57). To maintain objectivity, it is recommended that physicians secure pre-performance agreements with sponsors ensuring that negative results will not be quashed and that findings will be made publicly accessible. Physicians should also be aware that the International Committee of Medical Journal Editors recently agreed not to publish any studies conducted under conditions in which the sponsor can control the data or prevent publication (58). If a company explicitly or implicitly encourages a physician to suppress particular outcomes, the physician must not participate in the research and should report the incident to the institutional review board overseeing the research, and to the U.S. Food and Drug Administration if the research is a drug trial.

Dealing with Institutional Product Bias

Physicians employed by managed care organizations are obligated to abide by drug formularies and practices of pharmacy benefit management. Formularies specify a list of drugs that are considered most useful and cost-effective, and managed care organizations often limit reimbursement to these drugs. Pharmacy benefit management companies, which increasingly are owned by pharmaceutical manufacturers, act as intermediaries among pharmacies, pharmaceutical companies, physicians, and third-party payers to review prescribing practices and negotiate prescription prices. Pharmacy benefit management companies have access to confidential patient records and may try to influence changes in patients' drug regimens, sometimes to reduce costs and sometimes to favor a manufacturer (59, 60). Current

state and federal policies regarding third-party access are not consistent and can, at times, jeopardize the confidentiality of patient information. Cost savings are certainly encouraged, especially as a matter of justice and equity in health care. However, any agreement to change drugs should be evidence-based, not company-biased. If faced with institutional bias in drug formularies, individual physicians should be prepared to insist on waivers for unlisted drugs when it is in the best interests of their patients.

Electronic Technology

Finally, the development of "e-commerce" has led to ethical issues not envisioned in the 1990 position paper. Since that time, the importance of electronic commerce and Internet technology to the practice of medicine has increased dramatically. Health care systems in the 21st century will undoubtedly take advantage of electronic technology to collect and analyze clinical data, support consumer access to health information, and complement the physician's management of patient care (13).

As valuable as consumer access is, information provided electronically can be biased by its sponsor. To mitigate this potential conflict, physicians who have a material interest in "e-health" businesses or who interact with Internet hosts to publish their own Web sites have an obligation to control the site's medical content and regularly maintain it. Such sites should disclose all sources of industry support and clearly distinguish any commercial advertisements or sponsored content from substantive content, both in form and in placement. Physicians with commercially sponsored Web sites also need to alert users if a sponsor plans to conduct any online tracking.

CONCLUSION

The guidelines offered here identify several examples of financial and other material relationships between physicians and industry, but the list is not exhaustive. As opportunities for commercial ties continue to grow, physicians should be increasingly wary of threats to their professionalism and independent judgment about patient care. Providers of medical education and professional medical societies face similar problems of potential influence. Part 2 of this statement on industry relations will address the ethical risks and responsibilities of professional medical associations and educators.

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Pharmaceutical Marketing Research and the Prescribing Physician

Jeremy A. Greene, MD, PhD

Surveillance of physicians' prescribing patterns and the accumulation and sale of these data for pharmaceutical marketing are currently the subjects of legislation in several states and action by state and national medical associations. Contrary to common perception, the growth of the health care information organization industry has not been limited to the past decade but has been building slowly over the past 50 years, beginning in the 1940s when growth in the prescription drug market fueled industry interest in understanding and influencing prescribing patterns. The development of this surveillance system was not simply imposed on the medical profession by the pharmaceutical industry but was developed through the interactions of pharmaceutical salesmen, pharmaceutical marketers, academic researchers, individual physicians, and physician organizations. Examination of the role of physicians and physician organizations in the development of prescriber profiling is directly relevant to the contemporary policy debate surrounding this issue.

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> Market research in the pharmaceutical industry does not merely require the collection of certain statistical and commercial data. . . . It covers a much broader field, and requires constant observation of the entire medical and pharmaceutical horizon, so that the physicians' prescription habits can be thoroughly studied. For this purpose special personnel should be trained.
>
> —Paul de Haen, 1945 (1)

In recent years, many physicians have become alarmed by the ease and clarity with which the pharmaceutical industry is able to study their prescribing habits (2–4). With a few keystrokes on a handheld personal digital assistant, a sales representative can cross-reference real-time data sets to analyze week-by-week changes in prescribing for a particular drug; compare the data against those of her local and national colleagues; analyze use by diagnosis, specialty, and types of medical practice; and then use those data to fine-tune a sales pitch or allocate marketing resources. Prompted by a growing sense of outrage among physicians, several state legislators, state medical associations, and the American Medical Association (AMA) have put forward a series of proposals to limit the distribution and use of prescriber data (5). In May 2006, the AMA initiated an opt-out program—the Prescribing Data Restriction Program (PDRP)—through which physicians can deny pharmaceutical representatives access to their individual prescribing data (6). The following month, New Hampshire became the first state to prohibit the sale of prescriber information for use in pharmaceutical sales and marketing. A joint suit by health care information organizations (HIOs) to have the law overturned is currently being heard by a federal court (7).

Contrary to common perception, the business of selling prescriber data—the bread and butter of the HIO industry—did not emerge suddenly over the past decade. Private companies that monitor physicians' prescribing practices were founded in the aftermath of World War II, as the growth of the prescription drug market led to increased marketing interest in understanding and influencing prescribing patterns (8). This surveillance has not simply been imposed on the medical profession from the outside. As the PDRP opt-out program suggests, the AMA has played an active but carefully limited role in marketing physician-specific data. This article will provide a brief sketch of how pharmaceutical marketers and other groups gained access to data on physician's prescribing patterns and the role that physicians and physician organizations have played in generating and distributing prescriber information.

Focusing on the Prescription

The system of federal laws mandating prescriptions for the sale of pharmaceutical products was not fully established until 1954, and pharmaceutical salesmen in the first half of the 20th century expended more effort persuading pharmacies to stock their medications than they did persuading physicians to prescribe them (9). In the late 1940s, as a robust pipeline of novel pharmaceutical agents led to an increasing market for brand-name, prescription-only pharmaceuticals, the act of prescribing became a subject of increasing importance for the industry to understand (10). By focusing the key site of consumer decision making to a well-bounded set of professionals, pharmaceutical consumption through prescription enabled the development of more efficient marketing strategies. A single advertisement placed in 4 popular magazines in 1958 would cost more than $80 000 ($500 000 in 2007 dollars) and would reach only a fraction of the consumer market, while the same

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advertisement placed in the 4 leading medical journals would cost less than $3000 (roughly $20 000 in 2007 dollars) and would reach every physician in the United States (11). In addition to medical journals, physicians could be directly accessed through a growing legion of sales representatives. As the drug firms' most direct form of contact with the physician, sales representatives began to serve not merely as mouthpieces for their firms but as sense-organs as well (12).

Pharmaceutical salesmen of the 1940s began using physician caricatures during sales training, such as "Dr. Snob," "Dr. Resistant," and "The Backslapper," to illustrate how different physicians would respond to various sales tactics (13). As the postwar pharmaceutical industry worked to rationalize the activities of its sales force, this grassroots assessment of physician receptivity also began to take on analytic importance for sales management. "To call on every doctor on the block entails a great deal of waste motion at the company's expense," one sales manager noted in 1949, suggesting instead that there were "various methods of selecting the names of physicians who are most likely to prescribe a new product to a large group of patients" (1). One technique advised salesmen to keep logs of their visits in which they rated physicians on 2 axes: the first—coded A, B, C, or D—recorded the size of their practice, and the second—coded X, Y, or Z—recorded their receptivity to salesmen and to novel medications (14). These data, reported back to supervisors, generated a crude map of practice density and marketing receptivity that enabled more strategic deployment of salesmen.

Enterprising salesmen began to use the pharmacy as a site of data collection, asking local pharmacists for monthly lists of prescriptions filled and noting which local physicians were large-volume prescribers. In 1950, pharmacist Raymond Gosselin—inspired by the survey practices recently popularized by Gallup and the increasing ease of tabulating data through IBM punch cards—submitted a master's thesis that represented one of the first systematic, reproducible prescription drug audits (15). Aided by the tabulation team of the Boston University Statistical Laboratory, Gosselin conducted a population-stratified random sample of Massachusetts pharmacies, rummaging through prescription books and coding random samples of scripts. Gosselin subsequently formed a company and began to market the National Prescription Audit (NPA), a subscription database that could segment the prescription drug market by region and give quarterly information on the performance of specific products and therapeutic categories. By 1953, the original panel of 6000 prescriptions had grown to 225 000, and by the end of the decade, industry executives admitted that the NPA sales figures were more reliable than their own (11). The NPA was the leading product of R.A. Gosselin & Co. until the company was sold to IMS Health in 1970. It remains a key plank of pharmaceutical market research today.

The NPA helped marketers visualize prescriptions at the point of purchase—the pharmacy—but its scope did not include the clinic or hospital—a key site of prescription decision making. As one marketing executive noted, prescription audits "do not tell us *how* the drugs are being used . . . we want to go beyond the prescription and learn about the patient for whom it is written" (11). In 1956, Lea Associates—a spinoff group of marketing executives from Smith, Kline, and French—came to market with the National Disease and Therapeutic Index (NDTI), a statistically representative panel of physicians who agreed to use case record diaries to record "basic diagnostic and therapeutic information about all patient contacts made by them during assigned 2-day periods of their practices" (16). The NDTI did for drug prescribing what the Nielsen family did for television watching: It turned a set of real-time consumer decisions into a quantified set of data for market research (17). While the prescription audit showed marketers which prescriptions were being filled in pharmacies, the therapeutic index allowed marketers to tie prescription sales data to specific diagnoses and temporal

Key Summary Points

Prescriber profiling—use of detailed data from pharmacies and clinical practices to target and influence physician prescribing habits—is a widespread pharmaceutical marketing practice whose historical development is relevant to clinicians and policymakers.

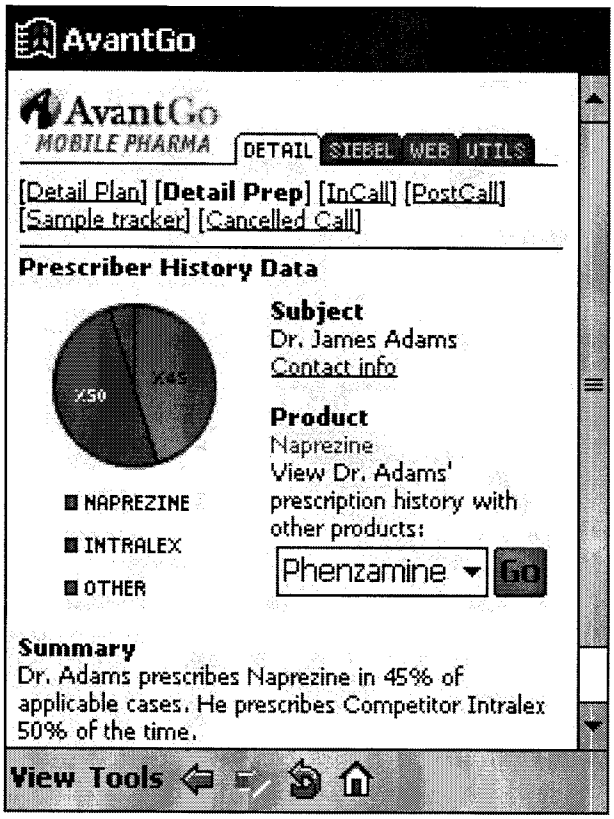
Data products relevant to prescriber profiling are collected and sold by private health care information organizations; these data products have been a central plank of pharmaceutical marketing for the past 50 years and have some secondary use in practice management and public health research.

Historically, prescriber profiling products and services have been sorted into 4 major classes: 1) prescription audits and claims databases, which collect and sort prescriptions sold in pharmacies; 2) physician panels, which enlist physicians to record their own prescribing patterns and clinical experiences on a daily basis; 3) physician databases, which link prescription claims data to detailed information about physician practices; and 4) specialized studies composed by pharmaceutical companies or health care information organizations on an ad hoc basis.

The data systems that enable prescriber profiling were developed through mutual interactions of pharmaceutical marketers and sales representatives, pharmacy chains, individual physicians, and physician organizations.

Current policy responses to prescriber profiling must take into account the historical role of physicians and physician organizations in enabling these practices.

Figure 1. Example of a search results screen on a handheld device.



Handheld software (AvantGo Mobile Pharma, AvantGo, Sybase, Dublin, California) used by contemporary pharmaceutical representatives to trace prescribing habits of individual physicians. (Courtesy of iAnywhere Solutions, Inc.)

changes in therapeutic practice. As this marketing executive explained (11):

> [F]rom the data we can learn how a given drug or class of drugs is being used. We can learn the relative frequency with which our sample of physicians sees or treats a given illness. We can learn how the illness is being treated. We can learn the sex and age distribution of patients. And in most cases we can learn the extent to which the condition is treated by specialists rather than by physicians in general practice. In fact, the possible types of tabulations and crosstabulations are almost limitless.

Similar audits and index panels were established to map hospital purchases and responses to journal advertisements, direct mailings, and sales representatives (18). In addition to database products, early HIOs also ran customized analyses and sold raw data in the form of punch cards for subscribing firms to run on their own IBM machines (19). Electronic data products diversified as the industry consolidated. By 2000, the industry leader, IMS Health (which had absorbed R.A. Gosselin & Co. and Lea Associates, as well as several other HIO firms), reported annual revenue of more than $1 billion from its portfolio of market research databases, providing insight on individual, institutional, national, and global scales with products for mainframe, Web access, and handheld personal digital assistant distribution (**Figure 1**). As the quality and accessibility of prescriber data increased over the decades, pharmaceutical marketers used them to forecast markets and allocate resources, while sales representatives incorporated physician-specific data into their efforts to manipulate the prescribing practices of target physicians.

The Role of Physician Organizations

The AMA provides a unique case for examining the active role of the medical profession in its own market surveillance. In the late 1940s, the AMA created a computerized registry using IBM punch cards of all physicians living in the United States. Along with other clients (such as state licensing boards), this database was actively advertised to the pharmaceutical and medical device industries as a useful tool for market research (**Figure 2**) (20). Marketers could use demographic and practice-related data to weed out retired or nonpracticing physicians and focus marketing efforts on the 125 000 actively prescribing physicians or to further subdivide the profession into relevant segments to promote specific products. Although sales were initially modest, this product evolved over subsequent decades into the product now known as the AMA Physician Masterfile. This database is an important link connecting pharmacy prescription data to individual prescribing physicians via a series of individual identifiers, including state licensing information, medical education information, national provider identifier codes, and U.S. Drug Enforcement Agency numbers for all U.S. physicians. Sales of AMA physician database products in 2005 yielded $44.5 million in revenue, roughly 16% of the organization's total revenue (5).

In the early 1950s, the AMA hired Ben Gaffin and Associates, a Chicago-based opinion research firm, to conduct a series of surveys of AMA members to compare the effectiveness of various means of pharmaceutical marketing on physicians' prescribing habits (21). These studies were then distributed to pharmaceutical and device manufacturers along with promotional pamphlets for advertising in the *Journal of the American Medical Association* (**Figure 3**) (22). They would also play a role in the AMA's decision to end the Seal of Acceptance Program, which had previously limited journal advertising in the *Journal of the American Medical Association* to those products that had passed the AMA's own tests of efficacy. Ben Gaffin and Associates claimed that their market research was directly responsible for the increased advertising revenue that resulted, as noted in a subsequent AMA report stating that "the utilization of

these study findings netted the AMA a return of 3600% in increased pharmaceutical advertising for each dollar spent on research" (23).

As the relationship between Ben Gaffin and Associates and the AMA broadened between 1953 and 1955, the AMA distributed 20 reports to the Pharmaceutical Manufacturers Association and all major pharmaceutical firms discussing the influence of pharmaceutical marketing on the practicing physician. In 1955, Ben Gaffin and Associates was commissioned to generate a total understanding of all influences on prescription habits within a limited geographic test region around Fond du Lac, Wisconsin. A significant budget was allocated to study all actions of pharmacists, physicians, hospitals, and clinics in relation to 5 newly released drugs and all forms of professional, periodical, and promotional information sources regarding their practice. When published, the Fond du Lac Study was distributed directly to the pharmaceutical industry, with the hope "that the industry will be very mindful of AMA publications when setting up advertising media allocations" (23).

In the environment of the late 1950s, the AMA and the Pharmaceutical Manufacturers Association viewed the Fond du Lac Study as an example of free-market industrial–professional cooperation; neither party anticipated that it would carry public relations costs as a symbol of collaboration or collusion. But as the pro-business climate of the Eisenhower era gave way to the more consumer-protectionist policies of the Kennedy years, Senator Estes Kefauver initiated a well-publicized inquiry into the marketing and pricing of prescription drugs. On 5 and 6 July 1961, Hugh Hussey, the chairman of the AMA, was brought before Senator Kefauver's subcommittee and was publicly confronted with the market research reports by Ben Gaffin and Associates as evidence of marketing collusion between the AMA and the pharmaceutical industry. "We are not ashamed of what was found out by these surveys," Hussey maintained under questioning (24). Nonetheless, from the Kefauver hearings onward, a new genre of medical muckraking has attempted to document conflicts of interest between the business offices of the AMA and the pharmaceutical and medical device industries (25).

The AMA has subsequently argued that selling physician-specific data through the AMA Physician Masterfile represents a responsible and necessary relationship between the organized medical profession and the legitimate pharmaceutical industry. Were the AMA to abandon its role in the licensing of physician information, other less responsible parties would market this information instead (American Medical Association. Personal communication). In this context, the launch of the PDRP opt-out program (**Appendix**, available at www.annals.org) can be understood as an attempt by the AMA to temper a long-standing internal conflict between its institutional and pragmatic goals—necessarily dependent on journal advertising and sales of databases for revenue—and an increasing portion of its membership who request that their professional organization insulate them from pharmaceutical marketing.

Figure 2. **Promotional flyer for a computerized physician directory, circa 1953.**

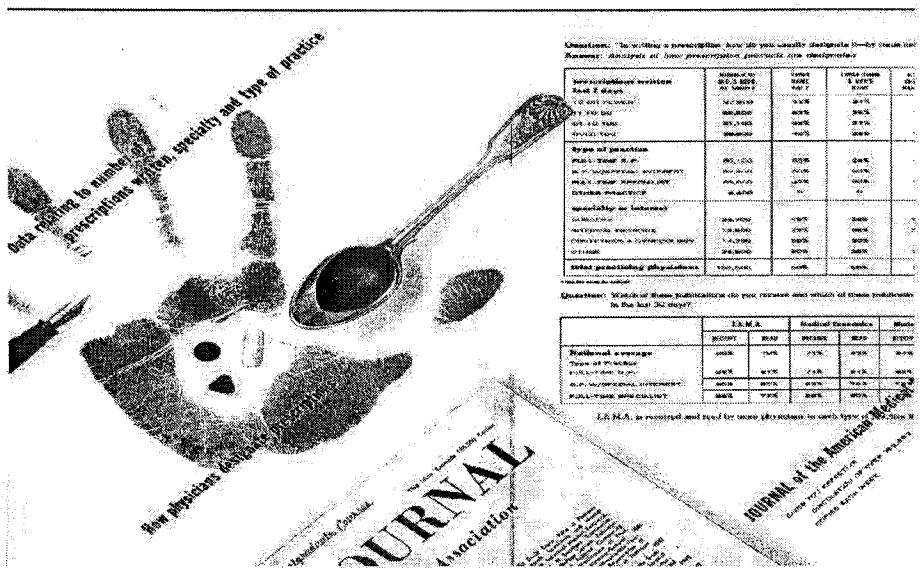
Promotional flyer advertising the computerized American Medical Association physician directory to American pharmaceutical companies. (Courtesy of the American Medical Association Archives [20].)

THE ROLE OF PRACTICING PHYSICIANS

It is difficult to know the extent to which the average physician practicing in the 1950s and 1960s was conscious of the expanding network of prescriber surveillance. Like their counterparts today, most would have been surprised to learn that the industry had developed such interest and data sources pertaining to their clinical practices.

Nonetheless, individual physicians were essential to the development of these surveillance tools. Certainly, physicians participating in panels like the NDTI were consciously aware of and were undisturbed by this practice. By 1960, the NDTI maintained a panel of 1200 quarterly rotating physicians reporting on all private patient contacts occurring in specified 48-hour periods. No physician served for more than a total of 12 months, and every private practitioner in the country had an approximately equal chance of being asked to participate (26). Lea Associates maintained a similarly sized panel for its National Detailing Audit, and rival data companies enrolled physi-

Figure 3. **Promotional report on survey data, circa 1953.**



Promotional report sent from the American Medical Association to American pharmaceutical firms, presenting survey data by Ben Gaffin and Associates on sources influencing physician prescribing. (Courtesy of the American Medical Association Archives [22].)

cian panels for their own data products. Because the medical profession had fewer than 150 000 practitioners at the time, most physicians probably would have been approached at least once to participate in a marketing data panel over the course of the 1950s and 1960s. The subsequent growth of the HIO industry and concurrent advances in medical informatics and electronic data interfaces have increased physician participation in profiling panels; physicians often participate unwittingly through the simple act of using handheld personal digital assistant software to look up the indications or dosage for a drug (27).

Two out of 3 physicians approached in the 1950s agreed to take part in profiling panels, and this trend seems to continue today. Physician participation is directly encouraged through financial award systems, in which collected prescription data is turned in for credits toward "awards," such as washing machines and home theater systems (a sample can be found at www.ims.awardscatalog.com). Physician participation has also been motivated by the appeal of the potential public health and professional benefits of data collection. The head of the National Detailing Audit noted in 1968 that "the principal appeal that leads to cooperation in the panel is the fact that participation helps make possible an annual grant of $25 000 to the American Medical Student Association tuition loan program" (18). Solicitation letters to physicians from the NDTI promised that "[i]n return for the invaluable cooperation of individual reporting doctors, data on morbidity, patient and physician characteristics, and general areas of therapy are made available to the profession" (16). In 1962, Lea Associates began distributing these brief quarterly reports to state, county, and specialty medical associations; medical journals; and medical schools. The reports provided summaries of leading diagnoses covered by physicians and information on the changing reasons for office visits. These reports were distributed free to the medical profession but functioned more as statistical summaries than as research tools (27). To access the data directly, physicians and public health organizations typically have to pay the same prices as pharmaceutical clients.

CONCLUSIONS

If it withstands the current appeal by the HIO industry, the recent action of the New Hampshire legislature will mark the end of one of the most comprehensive market research experiments in U.S. business history. As a well-bounded population of proxy consumers with total representation via the AMA Physician Masterfile, the medical profession has become one of the most easily defined and efficiently studied sectors of consumers in the U.S. economy. While the New Hampshire law would disrupt this complete market surveillance, the AMA's PDRP will continue to allow the sale of prescriber data for marketing purposes. It is possible that prescription data sets would no longer be useful to pharmaceutical sales representatives if a substantial proportion of physicians were to choose to opt out. According to the AMA, however, only 7000 of roughly 650 000 actively prescribing physicians have enrolled in the PDRP to date; only 25% of surveyed physicians are even aware that the program exists (American Medical Association. Personal communication).

In the past year, some physician groups have questioned the ethics of prescriber data collection as an invasion of the physician's privacy. However, these arguments seem tenuous. Physician–patient confidentiality has historically been invoked to protect the privacy of the patient, not the physician, and HIO companies were already maintaining strict anonymity of patient information in all of their data products long before the Health Information Portability and Accountability Act. Unlike the patient, the physician is expected to act as a public figure, whose prescriptions and chart notes are legal documents and whose actions are generally being made more transparent, not less so, by the work of the American health polity, as evidenced by the growing practice of outcomes reporting (28). It is perhaps more fitting to question the ethics of prescribers who participate in market research panels and translate their physician–patient relationships into a market research instrument for an industry with an interest in manipulating prescribing practices.

Prescription audits, such as the NPA and chain store pharmacy databases, can circumvent the physician and record prescriptions because they function downstream from the physician's office. However, the more sensitive tools of prescriber profiling—such as the NDTI and the AMA Physician Masterfile—require participation from both professional associations and practicing physicians. It is important to ask why the medical profession, a group long devoted to maintaining professional autonomy, should willingly reveal these data to an industry with an interest in manipulating prescriber decision making. To a certain extent, financial and pragmatic factors are relevant to the institutional actions of the AMA and may have influenced those practicing physicians who participated in prescription panels. However, many physicians who have participated in pharmaceutical marketing research seem to have done so in the name of broader professional and public health goals with no immediate financial benefit to themselves.

Similar claims of professional and public health benefits have been recently invoked in defense of the practice of prescriber data collection (6). Advocates of prescriber profiling claim that data sets enable development of outcomes studies, clinical guidelines, disease management programs, and evidence-based drug safety studies, as well as evaluation of physician performance and bioterrorism surveillance. While these are insufficient financial motivations to create a database of prescriber data, they are still viable uses for—and thereby a utilitarian justification of—a database created for marketing purposes (29). On historical review, however, these claims of professional and public health benefits to prescriber data collection represent more of a potential space than a true wellspring of benefit. Although it is true that data, once created, are conceptually available for all forms of research, such companies as IMS Health do not have provisions for making their data easily available to public health, pharmacoepidemiology, or policy research personnel without significant expense—indeed, the cost of purchasing data from HIOs is prohibitive for the independent researcher. Moreover, several non-HIO sources of prescription information, such as Medicare and Medicaid claims databases and a growing number of e-prescription databases from health systems with electronic medical records, have been used for pharmacoepidemiology, public health, and practice management research at a fraction of the cost of HIO databases.

The historical perspective presented here is limited by the problems of access common to social studies of the pharmaceutical industry. Although the author reviewed hundreds of articles in the medical, trade, and popular literature and conducted oral histories with retired and active pharmaceutical marketers, limited access to corporate archives and the piecemeal nature of archives preserved in medical and business school libraries provide the historian with only a small part of the complete picture of pharmaceutical marketing research as practiced over the past 50 years.

Nonetheless, 2 firm conclusions can be drawn from this work. First, although controversy over prescriber profiling is fairly recent, the practice itself is not: As early as the late 1950s, a robust network of surveillance technologies allowed pharmaceutical marketers and sales representatives to track prescribing practices and use these data to influence physician prescribing habits. Second, the HIO industry has required the active cooperation of physicans and physician organizations to develop its most robust tools for providing descriptive analysis of prescriber decision making. Any policy to remedy these issues must acknowledge that not only the pharmaceutical industry but also physicians and physician organizations make these practices possible and collectively bear responsibility to ensure their proper utilization.

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Appendix: Prescribing Data Restriction Program

In July 2006, the AMA launched the opt-out program PDRP, enabling American physicians to deny access of their prescribing data to pharmaceutical sales representatives and sales managers. Physicians can enroll in the PDRP via a Web portal (www.ama-assn.org/go/prescribingdata) that serves as a reporting center for any misuse of prescriber data.

The AMA does not directly collect prescribing data on individual physicians, but it does license demographic, educational, professional, and current practice information to HIOs and pharmaceutical clients via the AMA Physician Masterfile. Under the PDRP, HIOs and pharmaceutical companies can only purchase physician data from the AMA if they agree to restrict prescriber profiling by sales representatives to physicians who have not opted out.

Sales-level "restricted data" are defined as "any product-level data regarding the prescription practices of an identifiable physician who has made the PDRP election. This includes measures of prescription volume in absolute and percentage terms, the associated dollar value of a physician's prescribing, any indicators of change in these measures, as well as any means of ranking, benchmarking, or grouping physicians that may reveal prescribing habits for a particular product" (6). Information on physicians who opt out remain available to clients for broader purposes of marketing and research. End user compliance will be assessed by physician complaints to the AMA, and clients with patterns of abuse may lose access to both the AMA Physician Masterfile and HIO data in general.

The restriction must be renewed every 3 years and can be withdrawn. End users are expected to comply with a physician's status change within 90 days. In addition to the PDRP, the AMA offers 2 other privacy options regarding the AMA Physician Masterfile data: do not release status (which prohibits the AMA from releasing any physician information to any AMA database licensee, including state licensing boards and hospitals) and no contact status (which prohibits the use of physician information for marketing by mail, telephone, or fax but permits the use of such information by sales representatives).

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The Constitutionality of State Regulation of Prescription Data Mining

BY SEAN FLYNN

I. Introduction

There is a battle brewing in the federal courts over the rights of states to adopt the same prescription data privacy regulations that now exist in Europe and much of Canada. In those jurisdictions, pharmaceutical companies are not permitted to buy and sell prescription records that identify the prescribing habits of specific health care professionals, but rather can only access aggregate prescription data identified by demographic characteristic or geographic area.[1]

Absent similar regulations in the United States, the multibillion-dollar "health information" industry has been buying prescription records from pharmacies and other intermediaries to compile massive databases on the prescribing habits of nearly every physician and other licensed prescriber in the country. These databases are mined through sophisticated computer programs for information displaying individual prescribing trends and preferences identifying which doctors are more susceptible to various kinds of sales messages, which are more prone to using new drugs or whether a doctor is "brand loyal" to a certain manufacturer and their gift-bearing sales agents.

New Hampshire, in passing its Prescription Confidentiality Act,[2] was the first state in the nation to ban the trade in prescriber-identified prescription data for marketing purposes. On April 30, 2007, a federal district court judge ruled that the New Hampshire law violated the First Amendment rights of pharmaceutical corporations to engage in commercial speech (5 PLIR 457, 5/4/07).[3] Following that decision, Vermont[4] and Maine[5] passed laws that attempted to more narrowly tailor the data restrictions by giving physicians the right to control the subsequent use of prescription records identifying them. These laws have also been challenged in federal court.[6] The New Hampshire decision has been appealed to the Court of Appeals for the First Circuit,[7] setting the stage for an appellate decision with far-reaching repercussions.

This article describes two central legal arguments supporting the rights of states to regulate the use and trade of prescription record data mining in the pharmaceutical industry. First, the collection and sale of complex databases tracking prescribing behaviors of health professionals is conduct subject to regulation by states, not First Amendment protected speech. When a pharmaceutical company uses prescriber data to rank its favored doctors and distribute lavish gifts to reward them

[1] *See, e.g.*, Natalie Dunleavy, *Alberta Delivers New Blow to Prescription Data Mining*, 168 CAN. MED. ASS'N J. 1169 (2003) (reporting that Alberta was the second Canadian province after British Columbia to ban the sale of physician-specific prescribing data); Steve Niles, *No Way to Fill in the Blanks*, 25 EUROMONEY INSTITUTIONAL INVESTOR 1 (May 1, 2006) (noting that "in Europe, Canada, and many other parts of the world" prescription data is available only in a "brick"—"a statistical group put together in such a way that you're not supposed to be able to work out which doctor is writing what").

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[2] N.H. REV. STAT. ANN. § 318:47 f (2006).

[3] IMS Health Inc. v. Ayotte, 490 F. Supp. 2d 163 (D.N.H. 2007).

[4] VT. STAT. ANN tit. 18 § 4631 (2007).

[5] ME. REV. STAT. ANN. tit. 22 § 1711-E (2007).

[6] IMS Health Inc. v. Sorrell, No. 2:07-cv-188 (D. Vt. *filed* Aug. 29, 2007); IMS Health Inc. v. Rowe, 1:07-cv-00127 (D. Me. *filed* Aug. 29, 2007).

[7] IMS Health Inc. v. Ayotte, No. 07-1945 (1st Cir. *appeal docketed* June 20, 2007).

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for their loyalty, the company is engaging in conduct, not speech, to influence drug prescribing. Likewise, a pharmacy or intermediary is engaging in conduct subject to state regulation, not speech, when it sells prescription records under its custody without notice or consent from the patients or prescribers identified in those records.

Second, even if the trade in prescription records was deemed to be speech, there are compelling reasons that justify its regulation by states. An abundance of social science evidence demonstrates that prescriber-identified prescription data trading gives pharmaceutical companies an undue influence over prescribing practices that raises health care costs, promotes irrational drug selection, threatens the professional integrity of the medical profession, compromises patient privacy, and increases the prevalence of harassing and invasive marketing practices. States have an overriding interest in combating these social ills.

II. The Rise of Prescription Data Mining

Direct marketing of drugs to doctors through sales representatives, now called "detailers," has been a staple of pharmaceutical marketing practices since the mid-19th century.[8] But it was not until fairly recently that pharmaceutical firms could systematically track individual prescription writing activity to target and assess the efficacy of such marketing on a micro level.

Starting in the late 1980s and increasing through the 1990s, prescription records went digital to serve the needs of electronic claims processing by insurers and pharmacy benefit managers (PBMs).[9] The technological progression that allowed prescriptions to be electronically transferred to an insurer at the press of the button permitted the same record to be transferred easily to others. A growing industry of "Health Information Organizations" (HIOs) took advantage of this fact, buying up copies of prescription records from pharmacies, insurers, PBMs and others to amass comprehensive databases on the prescribing practices of nearly every physician and other licensed prescriber in the country.[10]

Data purchased from pharmacies, insurers, and PBMs often identifies prescribers only by medical license number or Drug Enforcement Agency tracking number, creating a demand to match these numbers with prescriber identities.[11] For this task, HIOs spend over $40 million a year purchasing access to the American Medical Association's "physician masterfile," which links DEA and other identifying numbers to every physician in the country (including the 60 percent who are not AMA members).[12]

The data-mining companies apply sophisticated computer programs to convert the data into charts and statistical summaries for pharmaceutical marketers. The programs can analyze time series data to "pinpoint prescribers who are switching from one medication to another," display sales trends (e.g. "Increasing Trend, Decreasing Trend, Shift Up, Shift Down, Spike Up, Spike Down") and classify prescribers' brand use (e.g. "Brand Switching, Brand Loyalty").[13] In its 2005 Form 10K, IMS Health Inc., the largest of the prescription data-mining companies, described its ability to generate reports "precisely tailored for each client," documenting "the sales of a client's own products and those of competitors." IMS further described the use of its products to "measure," "forecast," and "target" marketing and sales efforts. It explained:

> Our prescription tracking reporting services are designed to monitor prescription activity and to track the movement of pharmaceutical products out of retail channels. Prescription tracking services are used by pharmaceutical companies to facilitate product marketing at the prescriber level. In the United States, our Xponent® service monitors prescription activity from retail pharmacies, longterm care and mail service pharmacies using a patented statistical methodology to project the prescription activity of nearly 1.4 million individual prescribers on a weekly and monthly basis.[14]

The rise of data mining occurred coincident with pharmaceutical companies' fine-tuning their exertion of influence over prescribing processes with massive outlays of gifts, trips and consultancies to prescribers.[15] Data mining radically increased the influence of marketers by allowing them to specifically observe and reward the most profitable prescribing practices while tailoring switching messages to those not using desired products.[16]

Doctors are generally opposed to the use of prescription records for marketing purposes, although knowl-

[8] *See* Carl Elliott, *The Drug Pushers*, ATLANTIC MONTHLY, April 2006, at 83; Jeremy Greene, *Pharmaceutical Research and the Prescribing Physician*, 146 ANNALS INTERNAL MED. 742 (2007).

[9] *See PricewaterhouseCoopers*, HCFA STUDY OF THE PHARMACEUTICAL BENEFIT MANAGEMENT INDUSTRY, CONTRACT NO. 500-97-0399/0097, at 5 (June 2001) (noting that by the end of the 1990s, PBMs were managing about 95 percent of all drug benefit plans).

[10] *See, e.g., IMS Expands Doctor Marketing Services*, PHARMA MARKETLETTER, Jan. 16, 1992, *available at* Lexis; Steven Pearlstein, *Pipelines Become Paramount: A Revolution in Distribution Fuels Mergers, Creates Rivalries*, WASH. POST, Aug. 22, 1993, at H1 (reporting that the Medco database of physician prescribing habits was an important asset in the Medco–Merck merger); Jeffery Young, *Information, Please*, FORBES, Oct. 25, 1993, at 222-23 (noting that IMS was facing new competitors in the rapidly expanding field of prescription data mining); *Database Identifies Variations in Prescribing Volumes*, BUSINESS WIRE, Dec. 14, 1993; *National Data Corporation Announces Enhancements to Its Pharmaceutical Micromarketing*, PR NEWSWIRE, May 18, 1998, *available at* Lexis.

[11] *See* Sheryl Gay Stolberg and Jeff Gerth, *High Tech Stealth Being Used to Sway Doctor Prescriptions*, N.Y. TIMES, Nov. 16, 2000, at A1.

[12] *Id.*

[13] Paul Kallukaran and Jerry Kagan, *Datamining at IMS Health: How We Turned a Mountain of Data into a Few Information-Rich Molehills*, 24 SAS USERS GROUP INT'L CONF. paper 127 (1999) (on file with author, original removed by SAS at IMS request, source was previously available at www2.sas.com/proceedings/sugi24/Dataware/p127-24.pdf).

[14] IMS Health Inc., Annual Report (Form 10-K), at 23 (Feb. 21, 2006).

[15] *See Advertising, Marketing and Promotional Practices of the Pharmaceutical Industry: Hearing Before the Committee on Labor and Human Resources*, 101st Cong. (1990); EMILY CLAYTON, CALPIRG, 'TIS ALWAYS THE SEASON FOR GIVING: A WHITE PAPER ON THE PRACTICE AND PROBLEMS OF PHARMACEUTICAL DETAILING (2004).

[16] *See* Elliott, *supra* note 8 at 90-91; Liz Kowalczyk, *Drug Companies' Secret Reports*, BOSTON GLOBE, May 25, 2003, at A1.

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edge of the practice remains limited. A survey conducted in 2001 for the Kaiser Family Foundation revealed that 34 percent of physicians in the United States did not believe that "drug company representatives receive information about how often you prescribe certain drugs," and that 74 percent agreed that, if true, such use "bothers me" or is "unacceptable."[17] In 2004, an AMA commissioned poll reported that 25 percent of doctors still did not know that pharmaceutical companies tracked their prescriptions, 66 percent opposed the release of data to pharmaceutical companies, and 77 percent supported the implementation of a mechanism to allow them to "opt out" of data sharing.[18]

III. The New Hampshire Legislation

New Hampshire House Bill 1346 was introduced by state Rep. Cindy Rosenwald, whose husband is a cardiologist who had long known that he was being specifically targeted by drug representatives to switch his prescribing habits. It was not until Rep. Rosenwald came home with a 2003 *Boston Globe* article describing prescriber identity data mining[19] that the two understood how drug reps knew that he was not prescribing their products.[20]

House Bill 1346 proposed "An act requiring certain persons to keep the contents of prescriptions confidential." As passed by overwhelming margins in each house of the legislature and signed into law by the governor in 2006, the act stated:

> Records relative to prescription information containing patient-identifiable and prescriber-identifiable data shall not be licensed, transferred, used, or sold by any pharmacy benefits manager, insurance company, electronic transmission intermediary, retail, mail order, or Internet pharmacy or other similar entity, for any commercial purpose, except for the limited purposes of pharmacy reimbursement; formulary compliance; care management; utilization review by a health care provider, the patient's insurance provider or the agent of either; health care research; or as otherwise provided by law.

The law defined "commercial purpose" as including, but not limited to,

> advertising, marketing, promotion, or any activity that could be used to influence sales or market share of a pharmaceutical product, influence or evaluate the prescribing behavior of an individual health care professional, or evaluate the effectiveness of a professional pharmaceutical detailing sales force.

The act specifically exempted the full range of commercial transfers of prescription data that serve the patient or protect the public health in some way, including for "the dispensing of prescription medications," "transmission of prescription information between an authorized prescriber and a licensed pharmacy," transfers of records "in the event a pharmacy ownership is changed or transferred," "educational communications provided to a patient about the patient's health condition," and in the conduct of clinical trials. As the New Hampshire District Court noted, although the statute defines "commercial purpose" broadly, "it expressly excludes from the statute's scope all conceivable commercial uses of the data except those that are directly associated with advertising and marketing."[21]

In addition, following the examples of several Canadian provinces and the European Union,[22] the law specifically authorized the collection and sale of data in aggregated blocks from which individual physicians cannot be identified.[23]

Rep. Rosenwald, the bill's prime sponsor, described the purposes of the bill as being to protect prescribers' from "unwarranted intrusion" into their professional privacy, as well as to help restrain drug spending. She explained:

> [N]ot only is patient identity inappropriately used for pharmaceutical marketing, but the identity of the prescribers—doctors, nurse practitioners, optometrists and physician assistants—is routinely bought and sold for marketing. Large data mining corporations produce very sophisticated reports that track the individual behavior of our health care professionals. The use of personal identity is both an unwarranted intrusion into professional privacy and, more to the point, it adds to the financial burden of New Hampshire's health care system by increased pharmaceutical costs for the state, our consumers, and our businesses.[24]

A large number of doctors and medical organizations spoke in favor of the bill.[25] In legislative testimony and public advocacy before and during the New Hampshire deliberations, prescribers raised three primary arguments against prescription data mining for marketing purposes. First, prescribers asserted a privacy interest in their prescription records not being used for commercial purposes without their consent. Second, doctors asserted an interest in policing and reinforcing the integrity of the medical profession that is compromised by physicians being rewarded for prescribing particular drugs. Third, doctors rallied against the public health effects of undue marketing influence which can alter medical decisions toward higher cost treatments that

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[17] KAISER FAMILY FOUNDATION, NATIONAL SURVEY OF PHYSICIANS, *Highlights and Chartpack*, chart 3 (2002) (conducted March-November 2001).

[18] American Medical Association, *Reports of Board of Trustees of the American Medical Association, Use of Physician and Patient Prescribing Data in the Pharmaceutical Industry, Resolution 606, I-03*, Interim Meeting of the AMA House of Delegates, Dec. 2004.

[19] *See* Kowalczyk, *supra* note 16.

[20] *See* Jake Whitney, *How Drug Reps Know Which Doctor to Target. Big (Brother) Pharma*, NEW REPUBLIC ONLINE, ¶ 7 (2006), www.tnr.com/doc.mhtml?i=w060828&s=whitney082906.

[21] IMS Health Inc. v. Ayotte, 490 F. Supp. 2d 163, 171 (D.N.H. 2007)

[22] *See* Niles, *supra* note 1.

[23] The law states:

Nothing in this section shall prohibit the collection, use, transfer, or sale of patient and prescriber de-identified data by zip code, geographic region, or medical specialty for commercial purposes.

[24] *Requiring Certain Persons to Keep the Contents of Prescriptions Confidential, Hearing on HB 1346 Before the Senate Committee on Executive Departments and Administration*, 2006 Leg. (N.H. 2006) at 10 (statement of Rep. Cindy Rosenwald).

[25] Supporters of the bill included the New Hampshire Medical Association, the AARP, the National Legislative Association on Prescription Drug Prices, the AFL-CIO, Community Catalyst, and Prescription Policy Choices.

may be clinically no better, or in fact worse, for the patient.[26]

IV. Data-Mining Regulation and the First Amendment

States that have been leaders in taking affirmative efforts to combat excessive pricing and undue influence in the pharmaceutical industry have come to expect the inevitable litigation that follows the passage of every novel and effective law. The New Hampshire law was characteristic in this regard. Soon after passage, IMS challenged its constitutionality based primarily on the argument that the law unduly restricted the company's right to freedom of speech under the First Amendment.

After a bench trial, the New Hampshire District Court sided with IMS and declared the New Hampshire Act unconstitutional. Judge Paul Barbadoro found that (1) the trading of targeted marketing lists compiled from prescription records is a form of commercial speech protected by the Constitution, and (2) banning the trading and use of prescription data did not adequately advance any legitimate interest of the state. The court specifically found that there was insufficient evidence that data mining contributed significantly to harassing sales practices by pharmaceutical markers or that its regulation would advance the state's interest in containing health care costs or promoting evidence-based prescribing practices.[27] This holding is deeply troubling to public health, prescription access, privacy, and states rights advocates and is headed for a vigorous appeal in the First Circuit.[28]

Judge Barbadoro's opinion displays two key errors in constitutional reasoning. First, he ventured into new doctrinal ground by finding that the compilation and sale of identity databases for commercial marketing purposes is "speech" rather than traditional economic conduct. Second, he applied an extraordinarily vigorous version of the lenient scrutiny normally reserved for commercial speech cases, second guessing the nearly unanimous legislature as to whether prescription data mining is harmful to state interests.

A. The bounds of commercial speech

The use of the First Amendment to challenge a law regulating the compilation and sale of marketing databases may at first blush seem odd. Certainly the practice lies far from the core interest of the First Amendment "to ensure that debate on public issues will be uninhibited, robust, and wide open."[29] If every commercial trade of information was subject to First Amendment scrutiny, the regulatory authority of the states and federal government would be incredibly thin.

The District Court extended First Amendment scrutiny to the New Hampshire Act under the so-called commercial speech doctrine.[30] This doctrine emerged in the 1970s when the Supreme Court held, for the first time, that state regulation of commercial advertising was subject to First Amendment scrutiny.[31] The Court reasoned that commercial advertisements may help consumers make fully informed purchasing decisions and form "intelligent opinions as to how [the economic] system ought to be regulated or altered."[32] While recognizing that the legitimate interests of states in regulating commercial advertising is much broader than for other kinds of speech, the Court has struck regulations that completely ban an industry from advertising,[33] restrict the advertisement of prices,[34] and ban certain forms of commercial advertising.[35]

The Supreme Court has never held that every exchange of information between private contracting parties for purely commercial purposes is subject to First Amendment scrutiny. The Court has instructed quite the opposite, noting that such an interpretation would call into question the ability to regulate antitrust, workplace discrimination, corporate fraud, and a large amount of other commercial regulation that necessarily impacts the exchanges of information in corporate life:

> Numerous examples could be cited of communications that are regulated without offending the First Amendment, such as the exchange of information about securities, corporate proxy statements, the exchange of price and production information among competitors, and employers' threats of retaliation for the labor activities of employees. Each of these examples illustrates that the State does not lose its power to regulate commercial activity deemed harmful to the public whenever speech is a component of that activity.[36]

The New Hampshire Act did not restrict corporations from advertising to customers or doctors or otherwise selecting and transmitting sales messages that would fall within any Supreme Court definition of commercial speech. Indeed, the main case cited by the New Hamp-

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[26] *See* David Grande, *Prescriber Profiling: Time to Call it Quits*, 146 ANNALS INTERNAL MED. 751, 751-52 (2007); *see also* JERRY AVORN, POWERFUL MEDICINES 202 (rev. 2003); James D. Capozzi and Rosamond Rhodes, *Ethics in Practice: Prescriber Profiles*, 83-A J. BONE & JOINT SURGERY 115 (2001).

[27] IMS v. Ayotte, 490 F. Supp. 2d 163, 179-80 (D.N.H. 2007).

[28] *See State Appeals Prescription Law Rejection*, UNION LEADER (AP), May 4, 2007, at B5, *available at* Lexis; Joseph Conn, *New Hampshire to Appeal Privacy Decision*, MODERN HEALTHCARE, May 14, 2007, at 32.

[29] New York Times v. Sullivan, 376 U.S. 254, 270 (1964).

[30] *Cf.* Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n, 447 U.S. 557, 589, 591 (1980) (Rehnquist, J., dissenting) (warning against using the commercial speech doctrine "to resurrect the discredited doctrine of cases such as *Lochner*" to strike economic regulations "based on the Court's own notions of the most appropriate means for the State to implement its considered policies").

[31] *See* Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748 (1976).

[32] *Id.* at 765; *see also* 44 Liquormart Inc. v. Rhode Island, 517 U.S. 484, 495-96 (1996) (stating that our economy depends to some extent on the ability of commercial entities to communicate "vital information about the market" to the public through "accurate information about the availability of goods and services.").

[33] *Cf.* Cent. Hudson Gas & Elec. v. Pub. Serv. Comm'n of New York, 447 U.S. 557 (1980) (striking down ban on promotional advertising by electric utilities).

[34] *Cf.* 44 Liquormart, Inc., 517 U.S. at 495-96 (striking down ban on advertisement of liquor prices).

[35] *Cf.* Metromedia Inc. v. City of San Diego, 453 U.S. 490 (1981) (striking down ban on certain outdoor advertising display signs); City of Cincinnati v. Discovery Network, 507 U.S. 410 (1993) (striking down ban of commercial handbills on public property); Edenfield v. Fane, 507 U.S. 761 (1993) (striking down ban on in-person solicitation by certified public accountants). *But see* Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 456 (1978) (upholding ban on in-person solicitation by lawyers).

[36] Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 456 (1978).

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shire court in support of its definition of commercial speech held that the speech in question *could* be regulated by the state. In *Dun & Bradstreet Inc. v. Greenmoss Builders Inc.*, the court ruled that a state could regulate information included in a credit report without meeting the heightened evidentiary standards required in speech cases, because the information at issue was "solely in the individual interest of the speaker and its specific business audience."[37]

The better interpretation of New Hampshire's law, and that of other regulations of data mining, is that it regulates the *conduct* of businesses with regard to prescription records in their possession. "[I]t has never been deemed an abridgment of freedom of speech or press to make a course of conduct illegal merely because the conduct was in part initiated, evidenced, or carried out by means of language, either spoken, written, or printed."[38]

The distinction between speech and conduct using regulated information was emphasized by the Supreme Court in *Bartnicki v. Vopper*.[39] In that case, the Court held that it was unconstitutional to penalize a public disclosure of information from a wiretap on a public affairs radio program, but approved of another section of the law that prohibited "use" of the same information "to prepare strategy for contract negotiations," "to discipline a subordinate," "to create a competing product," and for other commercial purposes.[40] These prohibitions did not implicate the First Amendment, the Court explained, because "the prohibition against the 'use' of the contents of an illegal interception" is "a regulation of conduct."[41]

Data-mining laws restrict the commercial trade in prescription data only for certain commercial marketing purposes, and thus are more similar to the ban on use of information "to prepare strategy," discipline employees, and other uses approved of in *Bartnicki*. Surely if IMS's next venture was to set up a data-mining operation selling information received through wiretaps of doctor offices to guide pharmaceutical marketing it would be subject to prohibition of "uses" of wiretap information left in place by the Supreme Court, not the prohibition of public disclosures that was stuck down. Yet, Judge Barbadoro found just the opposite, holding that the New Hampshire Act regulated "a form of disclosure."[42]

If Judge Barbadoro's reasoning were allowed to stand, a massive amount of legislation at the state and federal level safeguarding consumer and citizen information from commercial marketing uses would be called into question. Federal and state laws contain numerous regulations that prohibit information provided for one purpose from being used for another commercial purpose without consent. Federal law prohibits information furnished to the census from being "used to the detriment of any respondent";[43] prohibits release of individually identifiable health information;[44] prohibits disclosures of "personally identifiable information concerning any consumer" of a video rental establishment[45] or cable operator;[46] requires that Internet service providers "not knowingly divulge" subscriber information and communications except for certain public purposes;[47] and requires states to limit the disclosure of drivers' personal identifying information without their consent.[48]

Similarly, states prohibit divulging, publishing or receiving Social Security numbers in certain forms;[49] regulate the use and disclosure of information "obtained in connection with a motor vehicle record";[50] require that a news-gathering organization "shall not use or distribute" accident reports "for a commercial purpose other than the news- gathering organization's publication or broadcasting of the information";[51] and declare that "prescription records, physician orders and other records related to any patient care or medical condition(s) of a patient that are maintained by a pharmacy ... shall be considered confidential."[52] All of these laws are similar in nature to the New Hampshire Act and have long been considered "unproblematic from a First Amendment perspective."[53] The same should hold for laws that ban the secondary uses of prescription information.

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[37] Dun & Bradstreet, Inc. v. Greenmoss Builders Inc., 472 U.S. 749, 762 (1985) (plurality opinion).

[38] Rumsfeld v. Forum for Academic and Institutional Rights Inc., __ U.S. __, 126 S. Ct. 1297, 1308 (2006) (quoting Giboney v. Empire Storage & Ice Co., 336 U.S. 490, 502 (1949)); United States v. O'Brien, 391 U.S. 367, 376 (1968) ("We cannot accept the view that an apparently limitless variety of conduct can be labeled speech whenever the person engaging in the conduct intends thereby to express an idea.")

[39] 532 U.S. 514 (2001).

[40] *Id.* at 527.

[41] *Id.* at 526-27.

[42] *Id.* at 528 (citation omitted).

[43] 13 U.S.C. § 8(c).

[44] Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104-191, 110 Stat. 1936.

[45] Video Privacy Protection Act, 18 U.S.C. § 2710-2711.

[46] Cable Communications Policy Act, 47 U.S.C. § 551(c)(1).

[47] 18 U.S.C.A. § 2702.

[48] Driver's Privacy Protection Act, 18 U.S.C. §§ 2721-25. *See Reno v. Condon*, 528 U.S. 141 (2000) (upholding Driver's Privacy Protection Act as valid regulation of commerce).

[49] Cal. Civ. Code § 1798.85(a).

[50] Ohio Rev. Code § 4501.27(A).

[51] Ky. Rev. Stat. § 189.635, *see* Amelkin v. McClure, 330 F.3d 822, 827 (6th Cir. 2003) (holding that § 189.635 "does not restrict or even regulate expression").

[52] 20 Mo. Code of State Regulations 2220-2.

[53] Neil M. Richards, *Reconciling Data Privacy and the First Amendment*, 52 UCLA L. REV. 1149, 1190 (2005). *See also* Frederick Schauer, *Commercial Speech and the Architecture of the First Amendment*, 56 U. CIN. L. REV. 1181, 1183-84 (1988) (noting "a vast range" of exchanges of information between companies that do not implicate the First Amendment, including "communications to offerees, stockholders, and investors now regulated by various state and federal securities laws, including the Securities Act of 1933 and the Securities Exchange Act of 1934; numerous communications among business executives about prices and business practices now regulated by the Sherman Antitrust Act; communications about working conditions and the like now regulated by the National Labor Relations Act; representations about products and services now regulated by the Federal Trade Commission and the Food and Drug Administration; representations about products now regulated by various consumer protection laws, by the Uniform Commercial Code, and by the common law of warranty and contract; statements about willingness to enter into a contract now regulated by the common law of contract; and so on and on") (citations omitted); *see also* Robert Post, *The Constitutional Status of Commercial Speech*, 48 UCLA L. REV. 1, 20-25 (2000) (listing examples); Frederick Schauer, *The Boundaries of the First Amendment: A Preliminary Exploration of Constitutional Salience*, 117 HARV. L. REV. 1765, 1777-787 (2004) (same).

B. The legitimate interests for regulating data mining

Even if a data-mining law is held to regulate commercial speech, it is clear that there are sufficient justifications for such regulation. Commercial speech is not afforded the same level of protection as political, philosophical or cultural speech. The Supreme Court has recognized legitimate state interests in regulating—and even banning—commercial speech that is "deceptive or misleading,"[54] exerts an "undue influence,"[55] or that threatens professional standards.[56] States are not limited to regulating speech that is false. The Supreme Court has explained:

> Obviously much commercial speech is not provable false, or even wholly false, but only deceptive or misleading. We foresee no obstacle to a State's dealing effectively with this problem. The First Amendment . . . does not prohibit the State from insuring that the stream of commercial information flows cleanly as well as freely."[57]

There is abundant evidence that the pharmaceutical marketing practices today exert undue influence over prescribing and formulary listing decisions that raise health care costs, promote irrational drug selection, threaten the professional integrity of the medical profession and are increasingly harassing and invasive toward health practitioners. Regulating data mining is one moderate step toward addressing these problems, removing the tool that marketers use to target prescribers for individualized marketing campaigns and gift giving.

1. Protecting against undue influence

There are few more important government roles in our health system than combating the undue influence of pharmaceutical marketing in prescribing decisions.

The Supreme Court has held that states have a substantial interest in regulating commercial solicitation practices that give marketers an "undue influence" through "one-sided" presentations that "may disserve the individual and societal interest . . . in facilitating informed and reliable decisionmaking."[58] This is the clear and primary purpose of data-mining legislation.

Pharmaceutical companies have enormous incentives to use their multi-billion dollar marketing budgets to distort and selectively divulge facts about drug benefits and risks. Access to individualized prescribing data multiplies the influence of this already tilted playing field by permitting marketers to tailor their sales pitches to the specific drugs used by the targeted prescriber. The other side normally has little opportunity to respond because "[t]here is virtually no economic incentive for the manufacturers of generic drugs to send sales representatives."[59] Thus, the practice of detailing is highly biased in favor of the newest and most expensive products, regardless of whether they are best for public health concerns.

Data mining is particularly troubling because of its link to influence peddling through gift giving. Pharmaceutical companies use prescription data to accurately guide their gift giving to compensate the highest or most influential prescribers for the specific uses of marketed products. While 94 percent of all doctors in the country routinely receive gifts of significant value, such as meals, branded office supplies, and free drug samples,[60] prescriber data is used to direct the most lavish gifts and payments to the most loyal and profitable prescribers. High prescribers and thought leaders can receive weekly, even daily, meals for their entire staff, luxury vacations in the guise of educational seminars, and can earn tens and hundreds of thousands of dollars in direct payments each year as speakers, "consultants," and advisory board members.[61] In effect, the prescribers themselves receive pharmaceutical company commissions.

An e-mail from one pharmaceutical company manager to sales representatives released to the *New York Times* described how prescriber data was used to hold doctors "accountable" for all the gifts they received:

> Our goal is 50 or more scripts per week for each territory . . . . If you are not achieving this goal, ask yourself if those doctors that you have such great relationships with are being fair to you. Hold them accountable for all of the time, samples, lunches, dinners, programs and past preceptorships that you have provided or paid for and get the business!! You can do it![62]

The U.S. House of Representatives Committee on Government Reform's investigation of Vioxx revealed that Merck gave sales agents monthly reports showing each prescriber's "market share" of Merck versus competitor product prescriptions. Prescribers were given grades from D to A+ for each product based on how reliably they prescribed a Merck product.[63] Presumably, the high volume A+ prescribers could expect more lavish gifts, consultancies, and speaker bureau invitations.

A former pharmaceutical representative from another company explained:

> Physicians are ranked on a scale from one to ten based on how many prescriptions they write. Reps lav-

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[54] Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748, 771 (1976).

[55] Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 462 (1978).

[56] *See* Edenfield v. Fane, 507 U.S. 761, 767 (1993).

[57] Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, 425 U.S. 748, 772 (1976).

[58] Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 458 (1978) (citations omitted).

[59] *See* Declaration of Avorn and Kesselheim at 6; *See also* Michael Fischer and Jerry Avorn, *Economic Implications of Evidence-Based Prescribing for Hypertension: Could Better Care Cost Less*, 291 JAMA 1850, 1854 (2004) ("There are many possible reasons for this large divergence between routine practice on the one hand and clinical trial data and evidence-based recommendations on the other. Foremost among these is the vigorous marketing of newer, more costly agents compared with virtually no marketing for older, off-patent drugs. Such marketing affects both physician prescribing choices and patient preferences.").

[60] *See* Christopher Lee, *Drugmakers, Doctors Get Cozier*, WASH. POST, April 29, 2007, at A03.

[61] *See* Clayton, *supra* note 15 (describing "five and even six figure checks" given to doctors to induce favorable prescribing); Elliott, *supra* note 8, at 7-8.; Stephanie Saul, *Drug Makers Pay for Lunch as They Pitch, N.Y. Times*, July 28, 2006, at A1; Whitney, *supra* note 20.

[62] *See* Gardiner Harris and Robert Pear, *Drug Maker's Efforts to Compete in Lucrative Insulin Market are Under Scrutiny*, N.Y. TIMES, January 28, 2006, at A14.

[63] *See* Memorandum from Henry Waxman, Ranking Minority Member, Committee on Government Reform, on the Marketing of Vioxx to Physicians, to Democratic Members of the Government Reform Committee (May 5, 2005).

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> ish high prescribers with attention, gifts, and unrestricted "educational" grants. Cardiologists and other specialists write relatively few prescriptions, but are targeted because specialist prescriptions are perpetuated for years by primary care physicians, thus affecting market share.[64]

It is sometimes thought that doctors and other prescribers, being highly educated professionals with training in medical research and scientific analysis, would be relatively immune from unbalanced sales pitches by pharmaceutical companies. Indeed, "the entire infrastructure of science and much of physician education is built on the fundamental notion of eliminating, or at least controlling for, the many and powerful biases inherent in generating and interpreting scientific data."[65]

Most physicians deny that pharmaceutical marketing, including gift-giving, has any effect on their prescribing practices.[66] But studies show that health care providers, despite their extensive training and access to medical literature, generally trust the messages delivered by pharmaceutical representatives,[67] are very poor at detecting false and misleading messages within sales pitches,[68] and are highly susceptible to psychological urges to reciprocate created by the receipt of gifts.[69]

Numerous studies and investigations have documented a significant, measurable, and increasing corrupting influence of pharmaceutical company marketing in convincing doctors to prescribe more expensive medicines that are no better, and often worse, than alternatives.[70] An exhaustive data synthesis from over 500 published studies found conclusive evidence that interactions with pharmaceutical representatives "impact the prescribing practices of residents and physicians in terms of prescribing cost, nonrational prescribing, awareness, preference and rapid prescribing of new drugs, and decreased prescribing of generic drugs."[71] The same study concluded that meetings with pharmaceutical representatives had a direct relationship to physician requests to add drugs to a formulary that had "little or no therapeutic advantage over existing formulary drugs."[72]

Removing the ability of pharmaceutical companies to observe and reward prescribing behavior will not remove all undue influence from the multi-billion dollar effort of pharmaceutical companies to alter prescribing habits toward more profitable products. Indeed, it is one of most moderate measures that can be taken in this area, working to decrease the most abusive marketing practices without regulating the substance of advertising messages or the time, place or manner of sales representative speech.

2. Restraining costs and promoting public health

The general interest of states in reducing undue influence by pharmaceutical marketing is compounded by the enormous costs of such influence to society. These costs are measured not only in dollars, but in the prescribing of drugs that are less effective, and often harmful, to patients.

Nearly a third of the five-fold increase in U.S. spending on drugs over the last decade can be attributed to the increased efficacy of pharmaceutical marketing efforts that shift doctors' prescribing from existing, effective, and lower cost (often generic) therapies to new and more expensive treatments.[73]

One study referenced in the New Hampshire legislative history showed, for example, that marketing branded calcium channel blockers for high blood pressure treatment instead of the less expensive generic therapies that are rated as *more effective* by national treatment guidelines increased U.S. health expenditures by $3 billion in 1996 alone.[74]

In Pennsylvania, a study of Medicare patients on antihypertensive therapy found that 40 percent of patients

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[64] Adriane Fugh Berman and Shahram Ahari, *Following the Script: How Drug Reps Make Friends and Influence Doctors*, 4 PLoS Med. 0621, 0623 (2007).

[65] Susan Coyle, *Physician-Industry Relations, Part 1: Individual Physicians*, Position Paper, 136 ANNALS INTERNAL MED. 396, 397 (March 2002).

[66] *See* Jerry Avorn, et al., *Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians*, 73 AM. J. MED. 4 (1982); S. Suresh Madhavan, et al., *The Gift Relationship Between Pharmaceutical Companies and Physicians: An Exploratory Survey of Physicians*, 22 J. CLIN. PHARM. THER. 207 (1997); Michael Steinman, et al. *Of Principles and Pens: Attitudes and Practices if Medicine Housestaff Towards Pharmaceutical Industry Promotions*, 110 AM. J. MED. 551 (2001) (reporting that 61 percent of medical residents believe that their own prescribing practices are unaffected by pharmaceutical marketing, although 84 percent think that marketing affects the practices of their colleagues).

[67] Ashley Wazana, *Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift?*, 283 JAMA 373 (2000).

[68] Michael Ziegler, et al., *The Accuracy of Drug Information from Pharmaceutical Sales Representatives*, 273 JAMA 1296 (1995) (finding that 11 percent of statements by detailers to doctors were inaccurate, but only 26 percent of doctors who had heard the inaccurate statements could detect them).

[69] *See* David Blumenthal, *Doctors and Drug Companies*, 351 NEW ENG. J. MED. 1885 (2004) (discussing the insidious interplay between the sense of obligation created by even small gifts and the psychological tendency to discount one's own susceptibility to bias).

[70] *See* Jason Dana and George Lowenstein, *A Social Science Perspective on Gifts to Physicians From* Industry, 290 JAMA 252 (2003) (exploring conflict of interest and bias in the context of gifts to physicians); Dana Katz, Arthur Caplan, Jon Merz, *All Gifts Large and Small: Toward an Understanding of the Ethics of Pharmaceutical Industry Gift Giving*, 3 AM. J. BIOETHICS 39 (2003) (summarizing research); Wazana, *supra* note 67 (analyzing 29 studies of the relationship between physicians and the pharmaceutical industry and finding that the there was a marked relationship between interactions with industry and prescribing practices); Nicole Lurie, Eugene Rich, Deborah Simpson, et. al., *Pharmaceutical Representatives in Academic Medical Centers*, 5 J. GEN. INTERN. MED. 240 (1990); Abigail Caplovitz, *Turning Medicine Into Snake Oil: How Pharmaceutical Marketers Put Patients at Risk*, NJPIRG Law and Policy Center, 5 (2006) (reviewing studies); Puneet Manchanda and Elisabeth Honka, *Pharmaceutical Innovation and Cost*, 5 YALE J. HEALTH POL'Y L. & ETHICS 785, 797-808 (2008) (reviewing studies). See, *e.g.* Helen Prosser, et al., *Influences on GPs Decisions to Prescribe New Drugs—the Importance of Who Says What*, 20 FAM. PRAC. 61 (2003).

[71] Wazana, *supra* note 67 at 375.

[72] *Id.*

[73] National Institute for Health Care Management (NIHCM), *Prescription Drug Expenditures in 2001: Another Year of Escalating Costs*, 2-3 (revised May 6, 2002).

[74] Roberto Cardarelli, John Licciardone, and Lockwood Taylor, *A cross-sectional evidence-based review of pharmaceutical promotional marketing brochures and their underlying studies: Is what they tell us important and true?* 7 BMC FAM. PRACT. 13 (2006). *Cf.* Leg. Hist. at 14 (testimony that the least and most expensive calcium channel blocker on the New Hampshire Medicaid formulary is $13.50 versus $87.30 per month respectively).

were on medications other than those recommended by clinical guidelines.[75] This same study of antihypertensive therapy shows that for this class of medications alone, switching to a nonbranded, nonmarketed medication when medically appropriate could save $1.2 billion per year.[76]

A similar effect can be seen in the incredible marketing push and resultant prescription surge for Vioxx, Celebrex, and other COX-2 inhibitors, despite the lack of any conclusive medical evidence that they were more effective pain relievers than older NSAIDs, or that the reduction in gastric side effects were significant for most patients.[77] And in the case of Vioxx, aggressive marketing using prescriber data helped facilitate the widespread adoption of a drug that was far more dangerous to patient health than existing alternatives or than the company's marketing messages admitted.[78]

A significant amount of the increase in irrational prescribing behavior over the last decade is enabled by pharmaceutical marketers knowing that an individual doctor is favoring a less expensive treatment and mounting a campaign in response to convince the doctor to switch treatments.[79] There can be no doubt that states have an overriding interest in responding to these harmful social trends.

3. Maintaining standards in the medical profession

Many physician organizations advocate an end to data mining, along with gift giving and other abusive sales practices, because such practices threaten the ethical standards of the profession and jeopardize their relations with patients.[80]

In *Ohralik*, the Supreme Court explained that "the State bears a special responsibility for maintaining standards among the members of the licensed professions."[81] The Court held that this interest extends to enforcing ethical standards of the profession, including to "avoid situations where the [professional's] exercise of judgment on the behalf of the client will be clouded by his own pecuniary interest."[82]

There can perhaps be no greater affront to the values governing the medical profession than permitting pharmaceutical companies to give pecuniary rewards to doctors based on their prescribing habits. Prescription data mining provides the key tool for pharmaceutical companies to literally pay prescribers—with meals, gifts, vacations and high-value low-work "consultancies," and board appointments—for the use of their products. This incorporation of prescribers into the commission structure of pharmaceutical sales incentives debases the medical profession and, the more the practice becomes public, breaks the chain of trust between doctor and client.[83]

4. Protecting doctors against vexatious sales practices

The Supreme Court has repeatedly held that states have a legitimate interest in regulating marketing that is "pressed with such frequency or vehemence as to intimidate, vex, or harass the recipient."[84] Doctors are pushing many of the reforms in this area in part because a substantial number of them feel harassed by the increasing frequency and aggressiveness of detailing forces fueled by prescription mining.

There are a host of federal and state laws that combat harassing and frequent marketing calls on consumers by limiting marketers' access to identifying information.[85] These laws have been consistently upheld under First Amendment challenge by courts applying extremely deferential standards of review. In 2001, for example, the D.C. Circuit upheld the FTC's rule prohibiting credit reporting agencies from selling targeted marketing lists based on data they collect. There, the D.C. Circuit refused to examine the intricacies of how the rule operated or what other options were available, holding in summary fashion that the lists were "private speech warranting only qualified constitutional protection" and the government interest in protecting consumer privacy and avoiding harassing sales tactics is substantial.[86] In the case of medicines, it is doctors who make the purchasing decisions for the ultimate consumers of the product, and their interests in being protected from harassing sales calls deserves the same level of deference as that afforded to other consumers.

Prescribers may be the most marketed-to class of "consumers" in the world, and access to prescribing data has played a key role in its escalation. In 2004, the industry spent $27 billion on drug marketing, more than any other sector in the United States, on its sales

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[75] *See* Fischer, *supra* note 59.

[76] *Id. See also* AVORN, *supra* note 26, at 338 (describing how new, expensive medicines should be critically evaluated for safety and efficacy compared to existing medicines)

[77] AVORN, *supra* note 26, at 202.

[78] *See* Waxman, *supra* note 63.

[79] *See* Jane Coutts, *Pharmaceutical Group's Head Defends Sale of Medical Data*, GLOBE & MAIL (March 28, 1996) (description of medical expert that "[k]nowing an individual doctor favours thiazide diuretics would enable drug companies to direct a real campaign toward getting him or her to switch to a more expensive even if less effective B drug."

[80] *See* Susan L. Coyle, *Physician-Industry Relations, Part 1: Individual Physicians*, Position Paper, 136 ANNALS INTERNAL MED. 396 (March 2002) (statement of the American College of Physicians); National Physicians Alliance, Issue Brief: The Sale of Physician Prescribing Data Raises Health Care Costs—The National Physicians Alliance Calls for a Ban, http://npalliance.org/images/uploads/IssueBrief-Prescribing_Data_low_res.pdf ("The best way to ensure that physicians retain the trust of patients is to warrant it, by eliminating this commercial intrusion into the doctor-patient relationship. Medical decision-making must remain scientific and objective.").

[81] Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 460 (1978).

[82] *Id.* at 461.

[83] *See* Robert Gibbons, et al., *A Comparison of Physicians' and Patients' Attitudes Toward Pharmaceutical Industry Gifts*, 13 J. GEN. INTERNAL MED. 151, 152 (1998); Dana Katz, et al., *All Gifts Large and Small: Towards an Understanding of the Ethics of Pharmaceutical Gift Giving*, 3 AM. J. BIOETHICS 39, 42 (2003) ("Patients tend to be aware that physicians accept gifts, unaware whether their own physician accepts gifts, and feel that gifts are more influential and less appropriate than do their physicians.").

[84] IMS Health Inc. v. Ayotte, 490 F. Supp. 2d 163, 179 (D.N.H. 2007). (quoting Edenfield v. Fane, 507 U.S. 761, 769 (1993)). *See* Ohralik v. Ohio State Bar Ass'n, 436 U.S. 447, 458 (1978) (State has a legitimate and indeed "compelling" interest in preventing those aspects of solicitation that involve fraud, undue influence, intimidation, overreaching, and other forms of "vexatious conduct").

[85] See, e.g., Fair Credit Reporting Act, 15 U.S.C. Section 1681 et seq. (2000) (credit reporting information); Family Educational Rights and Privacy Act of 1974, 20 U.S.C. Section 1232g (2000 & Supp. III 2003) (educational information).

[86] Trans Union Corp. v. Fed. Trade Comm'n, 267 F.3d 1138, 1140-41 (D.C. Cir. 2001).

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force or media advertising.[87] Over 85 percent of pharmaceutical marketing budgets are targeted at doctors.[88] In the decade after IMS unveiled its flagship prescriber tracking program in 1993, the pharmaceutical industry increased its spending on direct marketing to doctors by over 275 percent,[89] doubled its sales force of detailers,[90] and became the most profitable industry in the world.[91] There were an estimated 101,531 detailers in the United States in 2004; more than one for every five office-based physicians in the United States.[92] Because low prescribers often do not receive sales attention, it has been estimated that the effective ratio of sales representatives to targeted doctors is closer to one for every 2.5 doctors.[93] The average primary care physician in 2004 interacted with a staggering 28 sales representatives each week.[94]

In addition to being harassing by its sheer volume, access to prescriber detailing increases the prevalence of coercive marketing practices in individual sales calls. Database products sold to pharmaceutical companies by IMS and other companies are now so advanced that "[y]ou can literally find out if a rep makes a call at 9:00 am, whether the doctor wrote a script that afternoon."[95] Sales representatives use this data in increasingly obnoxious ways to hold prescribers "accountable" for their marketing messages and gifts, including by telling prescribers that they are being monitored and that the free lunches and gifts will dwindle if they do not meet the marketers' prescribing volume demands.[96] At least part of the increase in the aggressiveness of detailing can be attributed to the availability of prescribing data and its use to not only track prescription writing, but link such writing directly to sales bonuses.[97]

5. Protecting Patient Privacy

While the data-mining companies have not challenged state interests in protecting the privacy of patients in their prescription records, the debate has largely overlooked that this interest cannot be protected by the removal of patient names alone.

Even where patient names are removed, data-mining companies still can, and do, track specific patients' prescriptions through unique numerical identifiers that carry forward through time.[98] With knowledge of who that individual patient is receiving prescriptions from, a pharmaceutical company has all the knowledge they need to monitor patient treatment and mount lobbying campaigns at the prescriber to change to a more profitable course of medications. This insertion of the pharmaceutical company into the monitoring and influence of the patient's treatment is an invasion of privacy of the most odious kind—one that directly affects the treatment course of a patient for the pecuniary interest of another through a breach of confidentiality that is nearly impossible to detect.

V. Conclusion

The weight of authority suggests that state interests in maintaining standards in the medical profession, combating escalating drug prices and avoiding undue influence of one-sided in-person solicitation in a licensed profession may justify completely banning detailing and gift-giving by pharmaceutical sales representatives. New Hampshire's very conservative effort to ban only the marketing-related uses of prescriber identifying prescription records—leaving the companies free to examine geographic and medical specialty sales trends within the same data—is an extremely narrow and eminently justifiable first step to serve a legitimate state interest of the highest order.

States looking to act in this area in the future should strive to create a fuller record documenting their inter-

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[87] Manchanda, *supra* note 70.

[88] KAISER FAMILY FOUNDATION, TRENDS AND INDICATORS IN THE CHANGING HEALTH CARE MARKETPLACE exhibit 1.20, http://www.kff.org/insurance/7031/print sec1.cfm (2005).

[89] *See id.*

[90] *See* Manchanda, *supra* note 70, at 788; Consumer Union, Prescription for Change, *Detailing*, March 2006, http://www.consumersunion.org/pdf/drugreps.pdf (citing Rayna Herman and Ashley Mahoney, *Access Report 2005*, PHARMACEUTICAL REP., July 2005).

[91] Public Citizen Congress Watch, *Drug Industry Profits: Hefty Pharmaceutical Company Margins Dwarf Other Industries* (June 2003) (reporting that 10 largest pharmaceutical companies garner profits equivalent to the other 490 Fortune 500 companies combined).

[92] Rayna Herman and Nick Dabruzzo, *2006 Access Report: The State of the Selling Environment*, PHARMACEUTICAL REPRESENTATIVE, July 2006, *available at* http://www.pharmrep.com/pharmrep/article/articleDetail.jsp?id=353927; Manchanda, *supra*, note 70 at 788; Consumer Union, Prescription for Change, *Detailing*, March 2006, http://www.consumersunion.org/pdf/drugreps.pdf; *see also* Center for Policy Alternatives, *Prescription Drug Marketing*, http://www.stateaction.org/issues.cfm/issue/prescriptiondrugmarketing.xml.

[93] Fugh Berman, supra note 64, at 624.

[94] Consumers Union, *supra* note 90.

[95] *Looking Back. Looking Forward; Interview with Irwin Gerson, Chairman Emeritus of Lowe McAdams Healthcare*, MEDICAL MARKETING & MEDIA, Apr. 1998, 70, available at Lexis.

[96] Gardiner Harris and Robert Pear, *Drug Makers Efforts to Compete in Lucrative Insulin Market are Under Scrutiny*, N.Y. TIMES, Jan. 28, 2006, at A14 (quoting an e-mail message from a pharmaceutical executive encouraging sales reps to "[h]old [doctors] accountable for all the time, samples, lunches, dinners, programs and past preceptorships that you have paid for and get the business!"); *see also* Stephanie Saul, *Doctors Object as Drug Makers Learn Who's Prescribing What* (alternate title, *Doctors Object to Gathering of Drug Data*), N.Y. TIMES, May 4, 2006, at A1 (describing physician anger at aggressive marketing tactics based on knowledge of prescribing habits); Shannon Brownlee and Jeanne Lenzer, *Spin Doctored: How Drug Companies Keep Tabs on Physicians*, SLATE (May 31, 2005), http://www.slate.com/id/2119712/ (same); Elliott, *supra* note 8, at 90-91 (same); Requiring Certain Persons to Keep the Contents of Prescriptions Confidential, Hearing on HB 1346 Before the Senate Committee on Executive Departments and Administration, 2006 Leg.(N.H. 2006) at 33 (Testimony of Ms. Finocchiaro); Sheryl Stolberg and Jeff Gerth, *High Tech Stealth Being Used to Sway Doctor Prescriptions*, N.Y. TIMES, Nov. 16, 2000. at A1 (including statement of outrage[ ] by former president of American College of Physicians); Liz Kowalczyk,
Drug Companies Secret Reports, Boston Globe, May 25, 2003, at A1; Robert Steinbrook, *For Sale: Physicians Prescribing Data*, 354 NEW ENG. J. MED. 2745 (2006).

[97] *See* Elliott, *supra* note 8, at 89 (arguing that with detail prescription data came intensified pressure for pharmaceutical representatives to identify high-prescribing doctors and to relentlessly target those physicians

[98] *See* Jim Carroll and Tanya Foniri, *Infuse Anonymized Patient-Level Information into the Brand Planning Process to Drive Profitable Growth*, IMS, http://www.imshealth.com/vgn/images/portal/cit_40000873/0/78187147Brand%20Planning%20Paper.pdf. (June 1, 2006)

ests to prevent other courts from blindly following Judge Barbadoro's lead.[99] States may consider bolstering an expectation of privacy in prescription records by including statutory findings and inviting testimony that doctors do not and should not expect that their prescription records will be used for purposes other than to fill and process the prescriptions they order.

Vermont and Maine passed statutes requiring prescriber permission before using prescriber data for marketing purposes. Such laws may be considered more narrowly tailored to prescribers' interest in controlling whether or not their data is released to marketers. But opt-out programs do not meet the full range of state interests in banning the trade in prescriber-identified data, including to set standards in the medical profession, advance evidence based prescribing practices, cut the chain of undue influence in data-fueled pharmaceutical marketing, and to protect patient confidentiality. If a state determines that prescription data trading is a corrupting influence, then permitting doctors to engage in it at their own will does not serve the state's goals.

States should assess the efficacy of additional measures as part of a full program to combat the ill effects of undue marketing influence and create a fully rational and evidence-based health system. But the many alternative policies that are available to states to combat undue influence in pharmaceutical marketing and dampen spiraling medicine prices are complements, not substitutes, for the regulation of prescription record trading for marketing purposes.

The most trumpeted alternative to state regulation of data mining is the American Medical Association's Prescribing Data Restriction Program (PDRP). That program allows doctors to flag the identifying data sold by the AMA to data-mining companies to indicate that it should not be used by street level pharmaceutical representatives. However, the AMA continues to include all physician information in the Physician Masterfile that is transferred to data-mining companies, relying on pharmaceutical companies to check an updated "opt out" list and voluntarily keep the prescribing data from their sales representatives. The program does not permit physicians to restrict data access to higher level marketing officials that direct and compensate sales representatives. Thus, the program does not even meet its own narrow interest of protecting physician control over prescribing data.

Gift bans are appropriate programs that aim to lower the undue influence of marketers over prescribers. But most bans in effect or being considered by states include threshold dollar limits (commonly $25) that limit their effectiveness. Evidence shows that even the smallest gift creates a reciprocal relationship that affects prescribing practices, and those impacts are heightened when the gifts are specifically tailored to reward prescribing behavior. And even if all gifts were banned, such a measure would not advance the state's interests in prohibiting the use of prescribing data to target other efforts to influence prescribing behavior to specifically identified practitioners.

Counter detailing programs (a/k/a academic detailing), where the state hires trained individuals to provide objective factual information to prescribers, is another key component of a holistic program to combat undue influence in pharmaceutical marketing. But such programs are not an effective substitute for regulations on prescriber data mining because no state has the resources to battle biased and targeted marketing campaigns of pharmaceutical companies on a dollar for dollar basis. Simply imagine the expenditure of resources it would take to match the 28 visits a week that the average physician receives from a for-profit drug rep. Attempting such a program, without using regulatory authority to correct the flaws in the information market that lead to the most gross abuses, would be foolhardy. For this reason, Dr. Jerry Avorn, professor of medicine at Harvard Medical School and chief of the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital, as well as a primary promoter of counter-detailing programs, supports state restrictions on data mining as well.

Medicaid formularies can help address the high cost of drugs in state programs and promote evidence-based prescribing, but they do not address the problem that formularies themselves are subject to influence by pharmaceutical marketing. Additionally, Medicaid formularies only affect state spending and therefore do not serve the interest that New Hampshire has in the cost and efficacy of prescriptions for all of its residents.

Ultimately, addressing the deeply flawed information markets for prescription drugs that are pushing spiraling prices and distorting evidence-based prescribing practices will require a host of state interventions, one of which should be to curb the use of prescriber-identified prescription data to target marketing campaigns and gift giving. All states have a great interest in ensuring that this latest skirmish over the scope of heightened scrutiny under the leaching "commercial speech" doctrine results in a protection, rather than limitation, of traditional state regulatory authority.

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[99] Judge Barbadoro himself called for such a record, stating: "There is nothing in the record, however, to support a conclusion that the legislature had established expertise in the regulation of prescriber-identifiable data. Moreover, it acted quickly after the bill was introduced, received hearing testimony by numerous individuals who had yet to review proposed amendments, made no express findings either on the record or incorporated into the statute, failed to discuss alternative measures that would not restrict speech, and cited no evidence as to how effective the restriction might prove to be." *IMS v. Ayotte*, 490 F. Supp. 2d 163, 179 (D.N.H. 2007).

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Prescriber Profiling: Time to Call It Quits

Pharmaceutical marketing to physicians recently surpassed $23 billion per year, and the pharmaceutical industry currently employs 1 sales representative for every 5 office-based physicians (1, 2). In this setting, policymakers and patients are understandably concerned about commercial influences on physicians' prescribing decisions.

Real-time, physician-specific data on prescribing habits are a powerful tool that pharmaceutical sales representatives rely on when visiting a physician's office. A representative can quickly access a breakdown of pharmaceuticals prescribed by any physician on a handheld computer, enabling that representative to deliver a tailored marketing pitch to physicians selected for their current prescribing habits. Within weeks, the sales representative can monitor each physician's response to the pitch—as well as to inducements, such as meals, gifts, and drug samples—and can make repeated visits to achieve sales goals.

Given that prescriber profiling is so deeply embedded in pharmaceutical detailing, we have surprisingly little published research about its effect on sales. One recent market research report concluded that profiling improves profit margins by as much as 3 percentage points and the initial uptake of innovative drugs by 30%. Few details of the study are publicly available, and its quality is difficult to evaluate (3). However, other indirect indications of effectiveness exist—for example, the emphasis that pharmaceutical marketing consultants place on the value of prescribing profiles for enhancing sales force effectiveness (4–6).

How do pharmaceutical companies obtain such detailed prescribing data? Currently, retail pharmacies sell deidentified patient prescription records with limited physician identifiers to data intermediaries known as health information organizations (HIOs). By purchasing a comprehensive database of U.S. physicians from the American Medical Association (AMA), HIOs can link individual physicians to prescription records by using identifiers common to the pharmacy databases and the AMA database, such as a physician's U.S. Drug Enforcement Agency and medical license numbers. They also can track a physician's demographic and practice characteristics. The HIOs build prescribing profiles on the basis of these linked databases and sell them to pharmaceutical companies, which use the profiles to identify sales targets and plan detailing visits.

Prescriber profiling is a long-standing practice, not the recent phenomenon one might imagine it was from the attention being paid to it. In this issue, Greene (7) describes the historical origins of the collection and use of physician prescribing and practice profiles for commercial marketing. He finds that pharmaceutical firms were assembling prescriber profiles as early as the 1940s and 1950s. Early alliances between pharmaceutical companies and the AMA were instrumental in the development of the data collection industry, as such collections served the marketing interests of the companies and provided substantial revenue to the AMA. This business relationship between the profession and pharmaceutical manufacturers continues today. In 2005, it contributed to the AMA's $44.5 million in revenue from the sale of database products—16% of the AMA's total revenue for that year (8).

Greene also finds that individual physicians—operating independently of organized medicine—have played a key role in pharmaceutical market research. Physicians have been enrolling in profiling studies conducted by pharmaceutical companies since the 1950s and continue to do so to this day. For 1 such trial, the National Disease and Therapeutic Index, participating physicians maintain detailed practice diaries that they provide to the sponsoring market research firm. Although this market research involves relatively small panels of physicians, the results help marketers to segment the physician market and optimize promotion strategies by providing an in-depth understanding of how physicians make prescribing decisions. Greene reports that two thirds of physicians have agreed to participate when asked and posits that the marketing firms sometimes encourage participation by emphasizing the secondary professional or public health benefits. What physicians believe about the principal purpose of these market research studies and why they participate remain unknown. Are they unaware of the commercial motivation for these profiling studies, do they see assisting in commercial marketing as a valid role for medical professionals, or are they simply attracted by an opportunity to increase revenue?

Many physicians believe that using prescribing profiles in commercial marketing crosses a line of acceptability. A Kaiser Family Foundation survey found that only 60% of physicians were aware that drug companies have access to physician-specific prescribing data. When they were told of the practice, 74% disapproved (9). A physician survey commissioned by the AMA found similar levels of awareness (77%) and disapproval (66%) (10). Anecdotes also confirm the survey findings, with one physician recently commenting, "It makes me feel like a rat in a maze when they put little nibblets in front of me to see if I'll prescribe their drug" (11).

With a substantial majority of physicians opposing the sale of prescribing data and the public and policymakers rightfully concerned about the influence of marketing on prescribing, the key question is what physicians can do to end this practice. In 2006, New Hampshire—with support from the physician community—enacted a ban on the sale of prescribing data. The law allowed use of the data for public health, health care administration, and research purposes (12). Two major HIOs immediately challenged the law on the grounds that it violated their right to commercial free speech (selling information); a ruling from the district court is expected by May 2007 (13). Health infor-

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mation organizations also argue that prescribing data serve important public functions; however, Greene notes that public benefit uses are "more of a potential space than a true wellspring of benefit," given the high cost of purchasing the data (7). The National Physicians Alliance, consumer groups, and several medical societies are working in other states to promote legislation similar to the New Hampshire law (14).

Physician discontent recently led the AMA to launch the Prescribing Data Restriction Program, which enables physicians to "opt out" of having their prescribing data made available to sales representatives (15). While pharmaceutical companies continue to purchase the prescribing data of physicians who opt out, they have agreed not to show the data to individual sales representatives. Providing an opportunity to opt out is a step in the right direction; however, participation in the program thus far is low (<1% of all physicians), as is awareness (25%), which raises concern that the AMA opt-out program is not an effective way to address the concerns of physicians and their patients (7). Moreover, the considerable revenue the AMA is earning from the current system is a conflict of interest—it's not clear to what extent the AMA is willing to develop a remedy that would better serve the public. Physician members of the AMA could introduce a resolution calling for an end to the practice altogether or, at a minimum, to adopt an "opt-in" approach, in which the AMA could release a physician's data only if the physician consented.

Individual-level prescribing data and in-depth physician market research primarily serve to augment the success of pharmaceutical marketing. However, combining pharmaceutical detailing with physician prescribing data allows marketers to influence prescribing in ways that threaten medical professionalism. The Charter on Medical Professionalism identified the primacy of patient welfare as a fundamental principle (16), and a large body of literature already demonstrates the subtle and unconscious influences of gifts on prescribing (17, 18). With profit as the central focus of commercial marketing and market research, professional responsibility requires that physicians make their treatment decisions free from undue influence by marketers.

If physicians want prescriber profiling to end, they must act by urging state legislatures to enact laws similar to those in New Hampshire, lobbying their professional organization to support such laws, and calling on the AMA to place further limits on selling physician data for use in prescriber profiling. Furthermore, physicians should refuse to participate in marketing research that generates prescribing patterns because the primary purpose of this practice is to enhance sales, not patient welfare. The time has come for physicians to roll back the influence of commercial marketing practices on clinical decisions. Ending physician participation in marketing research and the sale of physician prescribing data to marketing firms is the right place to start.

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HEADLINE: Conflicts of Interest at the Doctor's Office

ANCHORS: IRA FLATOW

BODY:

IRA FLATOW, host:

This is TALK OF THE NATION: SCIENCE FRIDAY. I'm Ira Flatow.

How many times have you waited in your doctor's office while your doc waved in some person carrying a heavy briefcase instead? Have you ever wondered where your doctors gets those free samples that you're glad to get because the pills would otherwise cost you ten bucks a piece?

What you've been witnessing and wondering about is the complex and controversial relationship physicians have with the pharmaceutical industry, and you only saw part of it. A force of 90,000 drug reps routinely bring free samples and lunches to doctors' offices. It's not unusual for a drug company to bring in or pay thousands of dollars for lunch for the entire staff, dozens of people. Drug companies frequently pay physicians for speaking at lectures, and they foot much of the bill for continuing medical education in the U.S. They will pay travel expenses to fly people across country to listen to lectures about their products, and practicing physicians aren't alone. Their academic colleagues rely heavily on industry funding for clinical studies.

In their defense, some doctors say interactions with drug companies encourage biomedical research and keep doctors up to date on new treatments. Others claim they aren't influenced by gifts or rewards, but some psychologists say that it's not the size of the gift but the gifting itself that makes a doctor feel indebted to the drug industry. And when these practices came to light some years ago, some organizations began imposing monetary limits on gift-giving.

The Pharmaceutical Manufacturers of America, or PhRMA, issued voluntary guidelines to drug companies and physicians. Many medical organizations, including the AMA, have similar recommendations. And in 2003, the federal government weighed in with guides on gift-giving and drug company-sponsored events. But are these guidelines enough? While expensive gifts are restricted, the drug industry still spends $13 billion a year on direct-to-physician promotion.

This hour we're going to take up the issue of conflict of interests in medicine. Where does your doctor's loyalty lie? Are the conflicts of interest affecting your health? And what does the drug industry actually get for $13 billion a year when it talks to the doctors? Are they getting their money's worth? Maybe they're just paying too much and nothing's really happening.

What do you think? Maybe you've got some issues and things that go on in your doctor's office you'd like to share with us - questions. Our number, 1-800-989-8255, 1-800-989-TALK. And as always, you can surf over to our Web site at sciencefriday.com.

Let me introduce my guest, Ezekiel Emanuel. Dr. Emanuel is a medical oncologist and bioethicist. He's the chair of the Department of Clinical Bioethics at NIH in Bethesda, and he speaks with us today not as a representative of NIH policy but as a doctor and bioethicist. And Dr. Emanuel joins us today from Chicago. Welcome back to the program, Dr. Emanuel.

Dr. EZEKIEL EMANUEL (Medical Oncologist and Bioethicist): Thanks for having me again.

FLATOW: You're welcome. Dr. Sanford Friedman is a cardiologist at Mount Sinai Hospital in New York and an associate clinical professor in medicine and cardiology at Mount Sinai School of Medicine. He's here in our New York studios. Welcome to the program, Dr. Friedman.

Dr. SANFORD FRIEDMAN (Cardiologist, Mount Sinai Hospital): Hi.

FLATOW: Jerome Kassirer is author of On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health, published in 2004 by Oxford University Press. He's a former editor of the New England Journal of Medicine, a distinguished professor at Tufts University School of Medicine in Boston, and he joins us today from Kennebunkport, Maine. Welcome to the program, Dr. Kassirer.

Dr. JEROME KASSIRER (Author, On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health): Thank you.

FLATOW: Thomas Stossel - Dr. Stossel is the co-director of Hematology Division at Brigham and Women's Hospital and the American Cancer Society professor at Harvard Medical Cancer in Boston. He joins me today from Cape Cod. Welcome to the program, Dr. Stossel.

Dr. THOMAS STOSSEL (Co-Director, Hematology Division, Brigham and Women's Hospital): Thank you, Ira.

FLATOW: You're welcome. Dr. Kassirer, I went through some of the problems you see with potential conflicts of interest in the doctor's book at the beginning of the program, but in your book, even in the title of your book, On the Take, you outline many more. What do you think is the worst sin of all of these?

Dr. KASSIRER: Well, I think you did a terrific job outlining some of the gifts, especially the trivial gifts, that drug companies provide for doctors. I think you also made an important point about gifting, and that is that there's a important feeling that when somebody gives you gift, you ought to reciprocate in some fashion for it.

The pocket pens and the coffee cups and even the pizzas and lunches are really a small part of a bigger picture. The most important point that I want to make at the beginning is that, in terms of the research that goes on between industry and physicians, I'm all for it. I'm in favor of that research. I think it's important. I think we need to continue the entrepreneurial spirit that has given us all these major advances in medicine that I've actually seen over the 40-some years of my own clinical experience.

My concern is that other - the kind of spin-offs that drug companies provide for doctors. That is consultations on marketing issues; the development of educational materials by doctors; the involvement of doctors, as you pointed out, as speakers for drug companies.

The kinds of monies that are passed around between drug companies and physicians, I think - and I give many, many examples in the book - are things that tend to increase the chance of, that there will be bias in their recommendations and that that bias can translate to risk to patients, to increase cost of medical care, and to a lot of

hidden agendas that we really don't know about.

The biggest problem is that we have all these conflicts of interest out there, and many, many examples of them - the problem is that we don't have a good fix on how widespread the these conflicts are. We only have some information from medical meetings, such as the American Psychiatric Association meeting where fully a third of the psychiatrists who were giving presentations at that meeting had important conflicts of interests, some of them as many as with 26 companies.

So the problem is that a lot of this is hidden, and we just don't have the kind of transparency we need to understand how widespread the problem is.

FLATOW: Mm-hmm. Dr. Friedman, you're a practicing physician. Do you see these kinds of practices in your daily life?

Dr. FRIEDMAN: Everyday. But Dr. Kassirer makes it sound like that there's a conspiracy, and it's true there's always a chance of bias in just about everything you do in life. But in my practice, I must say, I don't understand the bias.

You see, these folks come by the office. They're often highly educated, attractive women as it turns out, for some reason. And they - they're only allowed to say things which are approved by the FDA. They're not allowed to talk about off-labeled recommendations for these drugs. It's actually quite boring.

FLATOW: Mm-hmm.

Dr. FRIEDMAN: In fact, I don't even know why they come by and say the same old thing over and over again, you know. But the other thing they do, which is in the public interest and their interest as well, is address I think the major scandal in this country, which is things like hypertension are underappreciated, under-treated. I think all the physicians here know it. hyperlipedemia, the same. And so they bring attention to that fact in the hope that the spin-off will be not only better treatment of your patients but eventually the use of their drugs.

The drugs per se, most of us are in HMO practices, and the specific drugs that you use are limited by the deals that the patients make with the HMOs. So there isn't really a whole lot of latitude there.

FLATOW: And the lunches and the paid speeches, the $2,500 to go make a speech...

Dr. FRIEDMAN: Well, I don't - I mean...

FLATOW: ...that doesn't bother you? Those things you don't see as a conflict of interest.

Dr. FRIEDMAN: Well, it's their money. I honestly don't know why they're spending it because, you know, doctors aren't lemmings. There is no quid pro quo. It's - I practice on Park Avenue. I don't practice on K Street.

FLATOW: Uh-huh.

Dr. FRIEDMAN: You know, and...

Dr. EMANUEL: Wait a second.

Dr. FRIEDMAN: OK, fair enough.

Dr. EMANUEL: This is Emanuel. I think...

FLATOW: Yes, Dr. Emanuel, go ahead.

Dr. EMANUEL: I think we need to be a little more careful that - it is very common for people who get money to say, you know, it doesn't influence my view.

Dr. FRIEDMAN: Right.

Dr. EMANUEL: You can hear that from politicians. You know, campaign contributions don't influence how I vote, and most of us as citizens are quite skeptical of that. And one would think that, well, the drug companies are not all-knowing and always prudent, that they wouldn't be spending $13 billion on this if that didn't have some return.

But, on the other hand, I do think that it is important to try to emphasize that a lot of what happens is the drug companies trying to get you to prescribe medications for patients who should be on treatment, but you're not doing it. We do have a lot of data - and again, I agree with the comment that there are lots of conditions that are under-treated in this country. We've got a lot of data to that affect. And part of what they're trying to do is get you to treat people who ought to be treated, and that is a social good even if they benefit at the same time.

And the other part is frequently what they're trying to get you to do is use their drug rather than their competitor's drug. You know, so a Pfizer person wants you to use Lipitor rather than you're prescribing Merck's Zocor for reduction of cholesterol. And, you know, there they do see an interest in market share in that particular niche, and the patient probably doesn't really care, and it probably doesn't hurt them really in those circumstances. But for the drug company, that switch could mean a lot of money, you know.

And I know that many people inside the drug industry think this whole thing is futile because, you know, we have some people who are switching from Merck drugs to Pfizer drugs, and Merck is doing the same thing and switching some people from Pfizer drugs to Merck drugs. And that $13 billion is going out the door, but probably not as much switching is happening as justifies that. But it's a game that everyone plays, so everyone's got to be in it, too.

FLATOW: Mm-hmm. Is there a threshold, Dr. Emanuel, where you can take the pens and coffee cups, but maybe you shouldn't make those - do those $2,000 speeches?

Dr. EMANUEL: Well, I - the rules certainly believe that, and most of the ethical analysis suggests that there is a sort of sliding scale that low things are below what the lawyers and the ethicists call a de minimis, and that, you know, we shouldn't worry - or shouldn't worry a lot about them. But it's the bigger-ticket items that we should worry about.

And I think to some degree that's probably true, but I think, you know, the flip side is why do we make these pens, why do they make the notepads with the company logo on if they had no particular affect?

FLATOW: Yeah, if they weren't there - why spend 13 billion if they're not getting the results they obviously think they are.

Dr. EMANUEL: Yeah, and (unintelligible).

FLATOW: I have to take a break.

Dr. EMANUEL: It's pretty cheap for (unintelligible).

FLATOW: Dr. Emanuel, hang on. Dr. Emanuel, hang on because we're fighting the clock, and we'll never win that battle. So stay with us. We'll take a short break and come right back, more talking about medicine in the doctor's office. I'm Ira Flatow. This is TALK OF THE NATION: SCIENCE FRIDAY from NPR News.

(Soundbite of music)

FLATOW: You're listening to TALK OF THE NATION: SCIENCE FRIDAY. I'm Ira Flatow. We're talking about bioethics in the doctor's office. ethicists and - with doctors and ethicists here on TALK OF THE NATION: SCIENCE

FRIDAY. My guests are Dr. Ezekiel Emanuel, Dr. Sanford Friedman, Dr. Jerome Kassirer, and someone who hasn't had a chance yet, Dr. Thomas Stossel. He is the co-director of the Hematology Division at Brigham and Women's Hospital and the American Cancer Society professor at Harvard Medical Center in Boston.

Dr. Stossel, let me address this to you. You've written that ethics activist have, quote, hijacked the dictionary definition of conflict of interest, and that finding doctors with ties to industry is like, quote, a witch hunt that makes it sound like any relationship a doctor has with a drug company is a conflict of interest.

Dr. STOSSEL: That's absolutely true, Ira. And I would say given the - they can listen to the news, the problems in the world and the challenge in general and the challenges we have with medicine in particular, it's kind of sad that you're wasting an hour discussing conflict of interest.

It's - conflict of interest is a kind of mindset that has set in, in the last 15 or so years, that emphasizes motives over facts. Dr. Kassirer mentioned how much medicine has improved in the last 40 years. That's about as long as I've been in it. When I was a resident, heart attack patients languished on my ward for a month. Imagine what that would cost at today's prices. We did nothing about their risk factors. We did nothing to improve their heart function for all intents and purposes. And it's - while there's lots of room for improvement - medicine is far from perfect - it's nothing short of miraculous what's been accomplished.

And it has not been accomplished because of the high professional standards of physicians or their aversion to commercialism. In fact, it is commercialism. It is only industry has delivered these products to the public. Now a lot of that is at the research end, but getting doctors to appropriately use, understand these products, getting investors to understand and to unleash capital to get more of these products is all to the good. There - the...

Dr. KASSIRER: You know, Ira. It's Jerry(ph) Kassirer again.

FLATOW: Yes.

Dr. KASSIRER: I agree, fundamentally, with everything that Tom said. I think the question of witch hunt is - I mean, I think anybody who's on the defensive often says there's - that there's a witch hunt going on. I think the question is whether patient care or research or the cost of care is influenced by the kind of thing that we're talking about.

It's one thing to be opposed to regulation, opposed to top-down management, and against journals, and in favor of private property and personal freedom and entrepreneurial risk-taking - and there's not doubt that universities and academic medical centers could never produce the kind of products, medical devises, and drugs that an industry does.

But to talk about a waste of time talking about conflict of interest, it really is quite astonishing. I mean, the question is what are the consequences of - the negative consequences of - talking about this? I mean, are we actually inhibiting the implementation of scientific discoveries? Are we discouraging collaboration between university researchers and drug companies? Is there any evidence whatsoever that that's happening because some of us are talking about conflict of interest and being concerned about it? I find no evidence whatsoever.

Dr. EMANUEL: At least at the NIH, that's not true, Dr. Kassirer. The big...

Dr. STOSSEL: (unintelligible)

Dr. EMANUEL: The big congressional investigations have resulted in problems in interacting with industry and problems going to other academic centers.

Dr. KASSIRER: Oh, but...

Dr. EMANUEL: But in general, I agree with you...

Dr. KASSIRER: How many people have left the NIH because of conflict of interest? Maybe a handful.

Dr. EMANUEL: Well, more than that.

Dr. KASSIRER: Yeah, trivial numbers that won't...

Dr. EMANUEL: The NIH...

FLATOW: Hang on, let me get one at a time in here. Dr. Stossel, you wanted to jump in.

Dr. STOSSEL: Yeah, well, I think Jerry is right. We should discuss it. It's good to discuss these things. But I think the key word - he used the word chance - chance of loss of objectivity, chance of negative outcomes.

Dr. Emanuel Ezekiel mentioned, well, does it hurt patients? I would argue that if we're going to take this seriously, let's get evidence. And I think there is evidence that this obsession with conflict of interest has caused a downside. I know of companies that have lost the valuable service of NIH intramural investigators from their advisory boards. That has to hurt product development.

Some of the institutions, like my own, Harvard Medical School, has pretty draconian rules that have prevented technology transfer from taking place. I'm working with the Association of University Technology Managers. We're going to try to get the quantitative data to this point. Certainly it exists anecdotally.

Now, Jerry, you - I think you are in the JAMA where you said that all research support to universities from commercial concerns should go into a pool and be doled out by the academic institutions.

Dr. KASSIRER: No, no, no, no, no, we never said that. We said that educational funds, not research. We never said anything about - that article doesn't talk about research at all.

Dr. STOSSEL: It does talk about research.

Dr. KASSIRER: No, it doesn't.

FLATOW: All right, gentlemen, you'll have to argue this out of court.

(Soundbite of laughter)

Dr. STOSSEL: And I think also it's legitimized the abuse of leading physicians. The press - I don't blame the press. Most of my family is - are journalists. I understand it's hard, but they hear authorities saying this is a serious problem and...

FLATOW: Let me just see if I understand you, Dr. Stossel, correctly. You don't see it as a serious problem, and you don't see how we could see it as a serious problem where doctors are paid thousands and thousands of dollars by drug companies to promote the drugs of the drug companies.

Dr. STOSSEL: I think the question is, are physicians inappropriately prescribing drugs or not?

FLATOW: But that's not the question I'm asking. I mean, that is another question and a legitimate question.

Dr. STOSSEL: (unintelligible)

FLATOW: But you asked how the - why the press doesn't - you can't understand the press seeing this. But when we investigate and we find out how drug companies are paying doctors to take them to conferences, to speak to other doctors, to go to lunches. I had someone who runs a very big office tell me that reps come in and sit in the examination room with a doctor. They're not doctors themselves. And the doctor's paid $2,500 just to let the rep sit in the room there.

Are you familiar with that?

Dr. STOSSEL: I'm not specifically familiar with it.

FLATOW: There are all kinds of things that are going on.

(Soundbite of laughter)

Dr. EMANUEL: Wait, wait, wait, wait.

FLATOW: Yes.

Dr. EMANUEL: Can I - Ira, can...

FLATOW: Yes, please.

Dr. EMANUEL: Let's get a little clear.

FLATOW: OK.

Dr. EMANUEL: That is a problem - the sitting in the room - because it violates the patient's confidentiality.

FLATOW: Well, they ask the patient. They ask the patient do you mind if the doctor - this rep...

Dr. EMANUEL: Well, they asked the patient, but they also don't usually say this is a drug rep.

FLATOW: I agree with you.

Dr. EMANUEL: (Unintelligible) So that - wait a second. That's a violation of confidentiality. I think Tom is raising another question, which is you're concerned about the $2,500 that a doctor is getting to give a talk promoting a drug company's drug, and I - and you say isn't that a problem? Shouldn't we be concerned about that? And I think what Tom is saying, quite appropriately, is let's try to examine and tease out what the harms are.

FLATOW: Mm-hmm.

Dr. EMANUEL: So one harm could be patients are getting inappropriate medications that harm the patients. Another - and the evidence on that is I think very low. Another harm - which Dr. Kassirer mentions, and I agree with this - it leads to use of certain drugs, which could increase costs and expenses by using say, brand-name drugs rather than generics. We have data that that does happen, and that is a problem. So I think it's very important to be careful about what the exact harms of these...

FLATOW: Mm-hmm. Well, can I add another harm?

Dr. EMANUEL: Yeah.

FLATOW: I've heard from doctors' offices, cases where a drug rep will - because he wants you to use his drug instead of the competitor's drug, will tell you - and I heard of this one case in specifics, where the drug was supposed to be given five times, let's say a course of five treatments, and the drug rep said if you use our drug you'd only have to give it three times and you can save money doing that.

And the doctor said, but it says on your insert it has to be given five times, not three times. And he said, well, I'll give you any data you want to back up it be given three times instead of five times. I'll go back. I'll send you anything you want so you can justify just using the three doses.

Do you find that legitimate? Do you find that harmful?

Dr. KASSIRER: Oh, I mean, obviously it's harmful.

FLATOW: Sure. I mean...

Dr. KASSIRER: Also, Ira - this is Jerry again. I think also the free sample bit is something that we ought to at least talk about briefly. You know, it sounds really a terrific idea to give free samples to patients, especially indigent patients.

And I certainly agree that that's a good thing to do. The problem with the free samples, there's several problems. First of all, a lot of those free samples are used by doctors, by nurses, and by office personnel and not by the people who really need them.

And secondly the fact is that you give a patient a free sample of - it always the most expensive drug because it's the newest one. They don't want you to give the generics. So you give the free samples. The patient runs out of them and then has to pay a lot of money to finish the prescription.

And finally, because you're using the free samples and you're used to using the most expensive drugs, you get used to using the most expensive drugs, and of course that drives up the cost of care.

There are some hospitals that have actually given up free samples completely and found that their drug costs have fallen. So it's - the free sample stuff sounds terrific but there are lots of problems with it.

FLATOW: Sandy Friedman's got a pained look on his face here.

Dr. FRIEDMAN: Yes. It's been for a while.

FLATOW: He's been sitting here squirming, literally.

Dr. FRIEDMAN: By the way, just in terms of disclosure, I was a student at Tufts and Jerry was one of our heroes. I happen to be 61...

Dr. KASSIRER: Ah, nice. Nice to hear.

Dr. FRIEDMAN: ...yeah, yeah. The bad news is I'm 61 now, so...

Dr. KASSIRER: Yeah. Well, lots of my students are 61.

FLATOW: That's good.

Dr. FRIEDMAN: Okay. So in any event, moving on the (unintelligible) gestalt of these learned folks who are talking is that they really don't know what life is like on the street. And I'm somewhat mystified by this.

You know, I thought that I had lived a virtuous life. It's true I buy sneakers that may support child labor and I drive a car that may one day inundate Bangladesh. You know, I mean, but I think - I don't think that they're...

FLATOW: In what way?

Dr. FRIEDMAN: Yeah, well, first of all, I think the major thing that drives the cost of medicine is that physicians and hospitals profit from the tests that they order. And this is really the huge dilemma.

On the one hand, because of it there's innovation, and patients, you know, get thorough and expeditious treatment. On the other hand, for obvious reasons it's the major conflict of medicine - conflict of interest in medicine. And it's an incredibly difficult thing to sort through.

As far as my patients are concerned, you know, they say this is expensive. Let's find the cheapest drug. You know, Zocor, Lipitor. It doesn't matter to me as long as they get the target. That's the key. The blood pressure, as long as you get the target.

So you call the druggist and you find out, well, what's the cheapest drug for this person? And as I said before, and the speakers seem to blast over this, the HMO tells you - the HMO makes a contract, they have a drug distribution company, you know, that tells you specifically what anti-hypertensive, what lipid agent to give to this person.

As far as the - it's been said often here that speakers come and they discuss - they praise a particular drug at a conference, at a dinner. That's not what they do.

FLATOW: Mm-hmm.

Dr. FRIEDMAN: If they did do that, at least in New York City, it would be considered extremely tasteless. What they do is talk about the path of physiology of disease. And what usually happens is people talk about interesting cases and, you know, how to handle them.

And there may be some subliminal, you know, influence. I don't know how...

FLATOW: Why would some - why would a drug company pay a doctor all this money to not mention their product?

Dr. FRIEDMAN: You know, they obviously know something I do. I don't fall in love with the concept that everything an industry does necessarily turns into profit. And I'm not in love, you know, particularly with GM and things of that nature, with the concept that they really know what they're doing.

I do know from the receiving end that I don't see this as a doctor/pharmacy conspiracy. But may I make a macro statement about conflict of interest that really...

FLATOW: Sure.

Dr. FRIEDMAN: ...roils me? I think - I don't know what Dr. Emanuel can say, because he's, in a certain way, is a public employee. But look, you have this drug, you have this drug prescription plan. The actuary who lies to Congress about...

FLATOW: I mean, the one that was just passed...

Dr. FRIEDMAN: Right.

FLATOW: ...everybody - Medicare.

Dr. FRIEDMAN: The actuary lies to Congress to the tune of a couple hundred million dollars. Conference committees, reconciliation committees, get together. Democrats are not allowed in. Republicans with proxy members of the drug company, you know, help formulate this bill.

Meanwhile, you have a quarter to a third of America doesn't have access to anti-hypertensives and anti-diabetic medications, etc. And you have hundreds and hundreds of billions of dollars that are being funneled in such a way as to protect the coffers of the drug companies.

And on top of it, the point men in Congress who got all this through quits his job as a congressman and makes millions of dollars a year working for a pharmaceutical company.

You know, talk about conflicts of interest. Never mind your $13 billion.

FLATOW: Mm-hmm. We're talking about...

Dr. EMANUEL: Well...

FLATOW: ...hang on one minute. I have to take care of some business. We're talking about conflict of interest in medicine this hour on TALK OF THE NATION: SCIENCE FRIDAY, from NPR News. I'm Ira Flatow with Thomas Stossel, Jerome Kassirer, Sanford Friedman, and Ezekiel Emanuel.

Who was jumping in there? I'm sorry. Didn't hear...

Dr. EMANUEL: Ezekiel Emanuel.

FLATOW: Yes. Go ahead, Zeke.

Dr. EMANUEL: Well, I'll tell you - Ira, you asked an interesting question there about why would the drug companies pay if they weren't promoting their particular drug.

And I don't want to defend the drug companies on this at all. But I think one of the motivations that they have, even if the speaker isn't promoting their drug above everything else, if you think a lot of people are being under-treated for illnesses, such as high cholesterol, high blood pressure, depression, etc., if you get doctors to treat more - to try to recognize those illnesses and treat those patients more frequently, you know, your sales of your drug are probably going to go up, even if you haven't targeted them with your medicine.

So that may be one motivation.

FLATOW: Which is a good thing. Well, that's...

Dr. EMANUEL: That isn't tied to a particular thing.

FLATOW: Well, but that's sort of...

Dr. EMANUEL: I...

FLATOW: ...I'm sorry. Go ahead.

Dr. EMANUEL: ...well, that's just an explanation for why. You say, why would they, you know, don't they just promote one drug? Frequently they don't.

The second thing I would say in contrast to what you just heard is that there are data, and I do agree here with Jerry Kassirer that, you know, when people go to lectures and hear about a particular brand name drug, they try to get it on the formulary of their hospital, they can frequently try to get it on the formulary of their HMO.

It's not infrequent that you can call an HMO and get override of their formula so that the patient can get this brand name drug if that's what you want to use. And so that is another reason.

Now, typically in those situations the main harm is not necessarily the fact that, again, the person is not getting the drug that they should but they're getting one company's drug over another. And the main harm is cost, driving up cost.

Now, that cost is a big concern because one of the reasons we have 46 million people uninsured is that the costs of the system are too expensive. But we should distinguish high cost from a patient having a problem, a medical problem, because of inappropriate use. I mean...

Dr. KASSIRER: By the way, this is Jerry again. I think that, Zeke, your notion that the pharmaceutical companies are simply helping to educate doctors about treatments that they're not giving is a bit naïve, because...

Dr. EMANUEL: No, no. I didn't say that was the only reason. But I think that is a reason.

Dr. KASSIRER: Well, I - let me finish. And the point is that these companies are pushing drugs for conditions that probably should be treated in other ways. They're pushing it for shyness. They're pushing it for attention deficit disorder, for female sexual dysfunction, and whatever. So they're inventing new...

FLATOW: All right.

Dr. KASSIRER: ...diseases all the time to promote new drugs.

FLATOW: All right. Jerry, hang on there because we have to take a short break. We'll come back and talk lots more about this. And lots of people on the phones, as you can imagine.

So stay with us. We'll be right back after this short break.

I'm Ira Flatow. This is TALK OF THE NATION: SCIENCE FRIDAY from NPR News.

(Soundbite of music)

You're listening to TALK OF THE NATION: SCIENCE FRIDAY. I'm Ira Flatow.

We're talking this hour about potential conflicts of interest in medicine with my guests, Jerome Kassirer, author of the book On the Take: How Medicine's Complicity with Big Business can Endanger Your Health, that's out in 2004; Thomas Stossel, co-director of Hematology Division at Brigham and Women's Hospital and the American Cancer Society Professor at Harvard Medical Center; Ezekiel Emanuel, chair of the Department of Clinical Bioethics at NIH; and also with us is Sanford Friedman, a cardiologist at Mount Sinai and associate clinical professor in medicine and in cardiology at Mount Sinai School of Medicine in New York.

Our number, 1-800-989-8255. Jerome, you were making a point when I rudely interrupted, or finishing one?

Dr. KASSIRER: No, I actually finished the point.

FLATOW: Okay.

Dr. KASSIRER: I did want to make a comment about this issue of speakers, the question of are speakers giving - the speakers who are paid by drug companies, are they actually giving lectures that are in favor of the companies who support them?

Well, they certainly are being paid by the companies. And you can be sure that if they don't continue to stay on the company line, they won't be speakers for long. And we've learned about that, actually, on NPR, from listening to Prakash's report in which she made the point that when the drug - when the Merck speakers were beginning to tell their audiences honestly about the risks of Vioxx, some of them were threatened by a Merck vice president.

And so that people are listening in on these speakers to make sure that they're saying the right things.

FLATOW: Mm-hmm.

Dr. KASSIRER: And it turned out that the Merck people were listening in on the Pfizer speakers.

FLATOW: Mm-hmm.

Dr. KASSIRER: So everybody's listening to everybody else and being very careful that they're sticking to the right points for the company.

FLATOW: Sandy Friedman, do you want to jump in?

Dr. FRIEDMAN: Yeah, I wanted to ask Jerry how many of these lectures he's actually been to.

Dr. KASSIRER: Oh, I've been to many of these lectures. And...

Dr. FRIEDMAN: And what was your experience?

Dr. KASSIRER: ...well, the problem, Sandy, is that I'm not a particular expert in cardiology. So if I go to a cardiology lecture, I can't tell whether the cardiologist is being biased.

But I can tell you that I have a friend at Yale who went to - an expert cardiologist who went to some cardiology lectures and listened in and came - this is lectures at major medical meetings, and came back astonished at how much bias there was in some of these talks.

FLATOW: Let me go to the phones. 1-800-989-8255. Chris in Denver. Hi, Chris. Chris, are you there? Chris, go ahead.

CHRIS (Caller): Hello?

FLATOW: Yes.

CHRIS: Can you hear me?

FLATOW: Yes.

CHRIS: Yeah, I'm sorry. I'm having trouble with this phone. I hit the speakerphone and I can't get it off so I apologize.

FLATOW: It's okay. We hear you just fine. Go ahead.

CHRIS: Anyway, thanks for having me. I love your show. I'm a physician, geriatrician, in Denver. And I used to have drug reps in the office. And I did it monthly because I could have them feed my staff. But - and I'd eat sometimes. I need something for my time.

You're listening to your guests talk about HMOs and the bureaucracy in medicine. A doctor can't, you know, do all this stuff for nothing. There does need to be some kind of remuneration for his time. And I think it's just that. I never thought of, gee, this guy gave me some pizza, I'm going to write for Nevacor vs. Zocor. That never crossed my mind. I'm a physician. I hold myself to a higher ethical standard. And the patient comes first.

And you know, I think that most doctors operate that way. And there isn't a quid pro quo, if you will, that was mentioned earlier. And...

FLATOW: Let me get a reaction.

CHRIS: ...give the doctors the ethical credit.

Dr. EMANUEL: This is Zeke Emanuel. I think, yes, most of us think that we wouldn't be influenced, and I think that may be part of the problem, is that we're not suspicious enough of ourselves, of our own motives. Certainly when we as citizens look at politicians and see them taking checks, even for - you know, pretty much the same amount of money, a thousand or two thousand dollars, as physicians get for a lecture, it doesn't surprise us that there's a correspondence, and of course politicians are the same as doctors and they say, well, you can't buy my vote.

So I do think we need to be a little more suspicious of our motives. That's not to indict any particular individual; it's

to talk about general human tendencies.

And the second thing I would say, Ira, is - I mean it does - you know, one of the things that struck me is when I was a poor house officer, you know, why was I willing to take this pen that probably cost 49 cents, or this meal that, you know, a couple or three or five or even seven dollars. It seems to me that this is chicken feed, frankly, and it's not clear to me why the small stuff we just can't just get out of the system completely, because it really shouldn't be there and shouldn't be something that doctors take and/or offices take.

And I think there ought to be - I mean, we can just get right of that tank, even if it doesn't cause anybody any harm. I just think it's something we ought to get rid of.

Dr. KASSIRER: This is Jerry. Chris makes a very important point. What I think Chris is ignoring is that the drug reps who visit your offices have perfect information about what you prescribe, because the pharmacists are selling that information to the drug reps, and drug reps tell you, and in fact it's already written in books, that they can go into a doctor's office, recommend a certain drug, and the doctor will say yes, I'd be glad to do it, and then when they don't do it, the drug rep knows it, goes back and says, gee, Doctor, you promised to use this particular drug. So the pharmaceutical companies are not about to hire 90,000 people and spend this huge amount of money unless they felt, or have evidence, that this stuff works. Of course...

IRA: Hang on. I want to go to Dr. Stossel first, then I'm going to take a call and go back to Friedman. Go ahead.

Dr. STOSSEL: Yeah, just I want to give Chris a plug here. I think there is way too much not giving folks the benefit of the doubt. The way the game is played is that people ask a doctor, are you influenced by gifts, by pizzas, by whatever, and the answer depends on the way the question is asked. Of course they know - they say no, but I think they know they're influenced. But they're getting many, many influences.

I have family in parts of the country who are getting medical care far removed from academic centers, far from Park Avenue, and they're getting pretty good care because they're getting information from industry. So I just think that this obsession with motivation is a waste of time.

FLATOW: Let me go to the phones. Marcy in Laramie, Wyoming. Hi, Marcy.

MARCY (Caller): Hi there.

FLATOW: Hi there.

MARCY: Can you hear me?

FLATOW: Yes, go ahead.

MARCY: Okay. I was a drug rep for many, many, many years and worked at several companies and sold probably every product for every disease state. And I just wanted to say that $13 billion is way too much, and they're definitely not getting their money's worth out of that promotion. And one of the main reasons why is most of these reps are promoting drugs like, let's take cholesterol products, for example, where there's 12 or 14 already on the market, and they all do the same thing. And so you've got five or six reps from each company going in to see these doctors on a regular basis to sell one drug that already does the same thing that the other 11 drugs do.

FLATOW: So why are they spending all this money, then, Marcy?

MARCY: Because they have the studies that show it works. You know, the TV ads, the direct-to-consumer advertising is hugely successful.

FLATOW: The ask-your-doctor ads.

MARCY: Yeah. They do surveys and they say it works, and then their other thing is share of voice. You know, we need instead of two quality reps going in and providing good representative services, we want to have eight reps going into the same office to sell this drug where there's already five or six or 10 in that class of drug. So I think it's way too much money, and I think there's way too many drug reps, and I agree with what all the speakers are getting at. I mean, it's definitely a problem, and you guys have really hit it on the head here. I'm glad to hear some doctors talking about it.

FLATOW: All right, thanks, Marcy. We're going to have to run. Let me go to Sandy Friedman.

Dr. FRIEDMAN: Well, yeah, I appreciate what Marcy and Chris had to say. Just one minor correction about from what Marcy said. Actually, there are subtle difference amongst these drugs. One of the things I would be afraid of is if I didn't have access to the large panoply of drugs that I have, and my colleagues I think would say the same, because maybe they're all fine for 3/4 of the patients, but for a quarter of the patients, you know, they're not. And if I had to just do one class of drug, if it was dictated, I think that would be a disservice, you know, to my patients.

You know, I'd like to say what I think, and this is presumptuous, what Chris would like to say, and I'm going to say it, okay, what maybe my colleagues are thinking. Look, my practice, it's in New York City. We pay $70,000 for maintenance. Our phone bill is 20,000, our postage is 20,000. My partner and I each see 25 to 30 patients a day. We start work at 7:00, we get home at 9:30, 10:00 o'clock, and we're exhausted. And nobody wants to do this anymore.

I mean the kids are not stupid. They're not lining up to do this, and this represents a major problem in terms of, you know, finding primary cares and doctors and internists, etc., for these people. And so in this context, for cognitive services, which is mostly what we do, even though we profit from, you know, our own tests that we order, but most of what we do is cognitive, talking to patients, caring for them, not processing them. You get 30, 60, $90 for a half hour of work.

Well, you can see the tremendous volume of work. Now, it's true that maybe I would theoretically be even more susceptible to bribery, and it's true what Dr. Emanuel said, that I think all of it, in all situations, not just this narrow situation, should constantly self-examine ourselves in terms of, you know, moral issues. But it's also true when someone wants - my time is valuable, not because I make so much money, but because I have so much to do. And if someone wants 10 minutes of my time, I don't feel the least bit guilty saying, okay, give me a ham sandwich.

Dr. KASSIRER: This is Jerry. I fully agree with what Sandy said. The problem is that general internists and primary care doctors are unbelievably inadequately paid. And that's a source of a serious upcoming shortage of primary care doctors. And the problem is the specialists are overpaid, the primary care doctors are underpaid. And that has nothing much to do with conflict of interest, it has to do with what the national need is. The national need as people get older is to have more and more doctors who can do primary care, and now we have fewer and fewer of them.

FLATOW: We're talking about medicine and conflict of interest this hour on TALK OF THE NATION: SCIENCE FRIDAY from NPR News. So Sandy, what you're saying is that I'm going to take the money because I'm underpaid, my time is worth something, and if these drug companies think that they can influence me, they're a bunch of suckers.

Dr. FRIEDMAN: Yeah, that's pretty much it. I think that, you know, you have to draw the line, and I think that the amount of remuneration does matter. I think this is penny-ante stuff. Maybe in the aggregate it's not, I don't know about national policy.

Dr. EMANUEL: So I have a question for you, all right?

Dr. FRIEDMAN: Yes, sure.

Dr. EMANUEL: We seem to be at least - you know, below probably the $2,000 lecture it does seem to be penny-ante stuff. Why the hell are we doing it? Is the lunch worth it? That's what I can't figure out.

Dr. FRIEDMAN: Well, you know, that's a fair amount. You know, we're reduced to an issue of watching patients pay $10 co-pays, $15 co-pays. You know, you look at that and you say, well, I mean, is that really what a professional is worth these days? My staff doesn't take, you know, like in academic medical centers, my staff doesn't take hour lunches. My staff takes - no, my staff takes 20-minute lunches, and so we pay for the lunch for our staff so that we can keep them up and running. We're right on top of our staff.

We have eight people working, multi-tasking around the clock. They have computer skills. This is what it takes to process thousands of patients. And you help them with all sorts of things that are outside the realm of medicine that we don't have to, you know, go into in detail. So when someone comes and says, you know, we're going to buy you a lunch, and I'm spending $40,000 for one person with computer skills to handle referrals and all sorts of other things, you know, to keep my business going, I'm going to say, you know, let them pay the lunch.

CHRIS: I think what you're saying is very important, because what you're admitting, and I think it's great, is you're in business.

Dr. FRIEDMAN: Yes.

CHRIS: Medicine is a commercial activity. It's not done by objective robots.

Dr. FRIEDMAN: It's a business which is a very bad business model, I might say.

CHRIS: Maybe, but it is a business nevertheless, and we're part of the same economic system as the drug companies and the device companies and the hospitals, and we should work on making it better, not pointing fingers at prurient interests about...

FLATOW: Well, let me ask one question, Sandy. Do you find that when the doctors come to your office...

Dr. FRIEDMAN: Doctors - drug reps.

FLATOW: Do they give you useful information, stuff that you don't have time to study on your own, and do they help your patients with that information?

Dr. FRIEDMAN: Rarely. You see, when they give us lunch, and we actually eat our sandwiches standing, maybe to improve transit time and get on with it.

(Soundbite of laughter)

Dr. FRIEDMAN: Inside joke for doctors. In any event...

FLATOW: Elementary my dear...

Dr. FRIEDMAN: In any event, we want to know, so what are the contraindications, what are the adverse reactions, what are the bad things? Are any of these black-boxed? Is there anything in the PDR that tells us it's an absolute no-no? So also new drugs come to market. Now there's a new drug coming out for smoking cessation - that getting someone off of cigarettes, as you know, is a tough thing to do.

I see that there's an article in the Archives of Internal Medicine. You know, I found it by accident. You know, I have maybe eight journals. You can't expect a physician to instantly have access to all of this stuff, and here's somebody who came to my office and told me about the pill, which I'm now investigating. So I do think that even though it's in self-interest, there is an aspect of public good.

FLATOW: What do you say about that, Jerry?

Dr. KASSIRER: Well, I say that there are plenty of excellent sources of information about drugs that is not influenced by a drug rep who has a special interest in providing that. There are plenty of excellent sites on the Web, there are some computer programs that have drug information in them. There are little handheld things that have information in them. I have a list of such sites which can be useful for doctors. They don't have to rely on drug reps. They can rely on their own sources of information.

Dr. FRIEDMAN: You know, we rely on multiple sources of information.

Dr. KASSIRER: Good. That's the way it ought to be.

Dr. FRIEDMAN: Nothing gives me more pleasure - I beg your pardon?

Dr. KASSIRER: That's the way it ought to be.

Dr. FRIEDMAN: Right, exactly. And nothing gives doctors, most doctors, more pleasure than sitting in an easy chair and reading the New England Journal of Medicine, which Jerry helped make into a terrific document. You know, it's fun to surf the Internet, but nobody has four to five hours at the end of the day to do that kind of research.

FLATOW: All right, and that sums up the state of medicine, I think, in this country. And let me thank my guests for joining us today. Sanford Friedman is a cardiologist at Mount Sinai Hospital and associate clinical professor of medicine and cardiology at Mount Sinai School of Medicine. Ezekiel Emanuel, chair of the Department of Clinical Bioethics at NIH in Bethesda, Maryland. Thomas Stossel, co-director of the hematology division of Brigham and Women's Hospital and the American Cancer Society Professor at Harvard Med Center in Boston. And Jerome Kassirer, author of On the Take: How Medicine's Complicity with Big Business can Endanger Your Health. He's also former editor of the New England Journal of Medicine and distinguished professor at Tufts in Boston. Thank you all for taking time this holiday weekend for joining us. You know what it's like trying to reach a doctor on a holiday weekend, and I thank you all for being with us.

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ETHICS IN PRACTICE

PRESCRIBER PROFILES

Within a two-week period, two sales representatives from competing pharmaceutical companies visited the office of an orthopaedic group practice. One representative was elated that the group had been steadily prescribing his company's new arthritis medication. The physicians assumed that the representative was speaking about the number of sample packs used by their office. Several days later, a competing drug representative visited the office and complained that several physicians in the group were "not thinking of my company's medication first." The physicians were perplexed and asked him how he had come by that information. After multiple attempts at evading the question, the representative explained that pharmaceutical companies pay the drugstores for such data. Although unwilling to disclose the details of the arrangement, he did inform the physicians that the pharmaceutical companies know exactly which physicians are writing which prescriptions. He assured the physicians that patients' names are not disclosed. The physicians spoke to several pharmacists and other pharmaceutical representatives, who confirmed the practice.

This case raises several subtle ethical issues. The orthopaedic surgeon who is surprised to learn that drug-company representatives know his or her prescribing patterns feels violated, as if some private domain has been breached. However, while patients have rights of confidentiality that must be protected, patient-identification information has not been shared with the drug companies and patient confidentiality has not been violated by this practice. The question that arises is: to what extent does this practice of providing physicians' prescribing patterns to pharmaceutical companies infringe upon the doctor-patient relationship?

Traditionally, in ethical discussions regarding the doctor-patient relationship, the focus has been on the patient's right to privacy and confidentiality. In fact, the assurance of privacy and confidentiality is implicit to the trust that patients place in their physicians. But what about the doctor's right to privacy in the rendering of medical care? Does the right to privacy extend to the treating physician as well?

It is true that selling the records of physicians' prescribing patterns to pharmaceutical companies does not disclose patient information—but does the practice have the potential to alter physicians' decisions about their patients' treatment? In the above scenario, the drug-company representatives knew exactly how many prescriptions that each physician had written for each medication. Can that knowledge be used to subject physicians to major coercive influences? A simple illustration may help to clarify this issue.

A well-respected senior physician with an excellent position at a major medical center resisted joining his institution's managed-care plan because he valued his clinical autonomy. However, all around him, his colleagues were discussing the coercive pressures on their medical practices. About a year into the institution's managed-care experience, this physician received his annual summary of the laboratory services that he had ordered. When he compared this summary with similar previous reports, he noticed that the number of laboratory services that he had ordered had decreased by more than one-third even though his patient population had remained the same.

While it could be argued that the change was for the good, the frightening point of this story is that this observant, thoughtful, and scrupulously honest man had not noticed a major change in his own practice pattern. He was not participating in the managed-care plan, he had no concerns about the security of his position, and no pressure was being exerted upon him by administrative bureaucrats. He was moved, so to speak, only by the talk in the air.

If the person who is least vulnerable to psychological coercion can be moved, then those who are more vulnerable to the incentives in the environment can be moved even more easily. And, while everyone feels immune to the effects of the pressures in the medical environment (such as managed care, drug-company advertising, and the attention of the warm, friendly detail representative), no one notices when or how they are affected. The effects are often invisible, but those who deliberately insert the coercive forces into the environment are well aware of their effectiveness and value.

According to a front-page article in *The New York Times* on November 16, 2000, pharmaceutical companies still spend most of their advertising dollars in targeting doctors. Of the 13.9 billion dollars that drug companies spent promoting their products in 1999, 87%, or about $12 billion, was aimed at health-care providers, including physicians, nurse practitioners, and physician assistants. Without question,

these marketing dollars serve an important function in helping to educate doctors about prescribing drugs more appropriately. New drugs become available all of the time, and physicians depend upon marketing information to educate themselves regarding the use of these drugs.

But if medical education is the sole purpose of these marketing dollars, then why is there the need to obtain data on the specific prescribing practices of individual physicians? According to the newspaper article cited above, pharmaceutical marketers admit that they use these reports to help determine which doctors should be offered certain perks. Lawrence Gostin, an expert in health-care privacy at the Georgetown University Law Center, believes that prescribing profiles raise important policy questions about physicians' privacy as well as about the commercial influence on physicians. He considers these profiles to be a fundamental violation of privacy, and he raises the question as to what extent physicians' practices are influenced by commercial concerns.

Because doctors cannot help but behave like ordinary mortals, propelled by the psychological powers of gratitude, friendship, and affection, are they likely to alter their prescribing patterns when targeted by pharmaceutical representatives? It is exceedingly difficult to acknowledge that coercive forces can work on each of us, but studies show that we are indeed susceptible. In a recent article in the *Journal of the American Medical Association,* Ashley Wazana of McGill University reported a definite association between physicians' meeting with pharmaceutical representatives and a rapid change in their awareness about, preference for, and prescription of new drugs over previously prescribed generic drugs. Wazana concluded that, with or without our awareness, we are influenced by these encounters.

So the question remains: is the selling of data on physicians' prescribing patterns to pharmaceutical companies ethical? Certainly, no patient information is exchanged or disclosed in the sale, nor does there appear to be any violation of patient or physician autonomy. Many physicians feel that they are responsible for their own decisions and that profiles and databases have nothing to do with their ethical behavior. The edict of benefit to the patient—the physician acting for the patient's good—does not seem to be violated and, in fact, may even be improved if the physician gains information and insight into a potentially helpful new drug. So what is the ethical issue raised by the practice of selling data on physicians' prescribing patterns?

We believe that the ethical issue that is raised is twofold. The first concern involves the violation of privacy. Why are the data on individual physicians collected without their knowledge or consent? In medicine today, we are surrounded by issues of full disclosure. Every author who is published in *The Journal* must disclose any source of support, funding, gifts, payments, or benefits received. *The Journal's* readership and the public in general are entitled to such information. Why are we then not afforded the same right by the companies buying our prescription profile? If there is no ethical issue, then why are the companies not informing the physicians that they are tracking every prescription that the physicians write?

The second concern raised is one of coercion. With our prescribing profiles in the hands of the pharmaceutical companies, do we as physicians become more vulnerable marketing targets? Can subtle incentives be directed our way in an attempt to alter our prescribing patterns, whether they be in the form of gifts, office lunches, pens and pads, dinner lectures, or weekend courses at resorts? According to psychologists and pharmaceutical marketing representatives, we are indeed influenceable.

As physicians, we are all familiar with pharmaceutical representatives. They are often a tremendous asset in providing us with information regarding new drug products, surgical equipment, and prosthetic implants. However, they can also exert powerful, coercive forces that could potentially alter our medical decisions. And if they have obtained information regarding our practice patterns without our knowledge, we may become even more selective targets for their attention. Although the practice of selling data on physicians' prescribing patterns may be legal, we believe that it raises some important ethical issues and that, at the very least, physicians should be made aware of them.

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'Tis Always the Season for Giving

A white paper on the practice and problems of pharmaceutical detailing

CALPIRG

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A white paper on the practice and problems of pharmaceutical detailing

Desperate to rein in skyrocketing prescription drug costs, lawmakers, healthcare plans and individual consumers are taking a much closer look at the promotional practices of the pharmaceutical industry. One aspect that has come under heavy scrutiny is a marketing technique known as detailing. This white paper examines the mechanics and potential harms of pharmaceutical detailing, describes the steps that have been taken to address those problems, and explores policy options for addressing the issue.

The Process and Problems of Detailing

Pharmaceutical detailing is a marketing method that involves individual pharmaceutical sales representatives (detailers) meeting with doctors to promote specific medications. Detailing is a multi-billion dollar business with closely monitored targets and carefully crafted promotional presentations.

The process begins when drug companies buy – often without the knowledge or prior consent of doctors – the prescribing histories of individual physicians. Purchased from retail pharmacies and then aggregated by data processing companies, this information gives detailers precise information about which classes, forms and dosages of drugs each physician prescribes. Drug companies use this information for direct mail marketing to medical offices and detailers use it to specifically target their sales pitches when they meet with doctors.

Increasing Prevalence

Pharmaceutical detailing is on the rise. Between 1996 and 2000, the number of pharmaceutical sales reps in the U.S. more than doubled from 41,800 to 83,000.[1] Excluding drug samples, pharmaceutical companies spent a total of $4.8 billion in one-on-one promotion in 2000.[2] With samples included, total detailing expenditures topped $12.7 billion in 2000.[3]

As the practice of pharmaceutical detailing becomes more popular, it becomes increasingly competitive. Detailers have a harder time keeping a doctor's attention or even getting through the medical office door. To make a lasting impression, detailers commonly bring gifts and meals along with their promotional information. These gifts and meals can range from pens, notepads and pizza to watches, golf trips and five star dining. A recent New York Times article reports that five and even six figure checks have arrived, unsolicited, in doctor's offices as a means of inducing prescriptions.[4] One former detailer explains the purpose of these gifts: "They buy you time with a doc, time that might change his mind."[5]

Several studies have demonstrated that this gift giving is having its desired effect – increasing the number of prescriptions written for the drugs that are promoted in meetings with detailers. According to research conducted by Dr. Margaret Chren of the University of California, San Francisco, "physicians were more likely to have requested drugs manufactured by specific companies if they had met with pharmaceutical

representatives from those companies or had accepted money from those companies."[6] Another study by J.P. Orlowski and L. Wateska showed that doctors exhibited a "significant increase" in prescribing a company's drugs after attending an all-expenses-paid trip to a drug company symposium.[7]

Increasing Problems

Given the unique doctor-patient relationship and the already extraordinarily high cost of prescription drugs, this gift giving practice is a cause for concern for a number of reasons. The first problem is one of perception. Regardless of any effect that the promotion may have on the prescribing patterns of a given physician, accepting gifts from pharmaceutical salespeople can create the appearance of impropriety. According to an article by Dr. Michael Steinman in the Journal of the American Medical Association (JAMA), "Surveys show that as many as 70% of patients believe these gifts significantly impact prescribing, and as many as two thirds believe they increase the overall cost of medications for the public."[8]

Because physicians are in the unique position of choosing a specific product that someone else must purchase and use, patients must have absolute confidence in the process that leads a doctor to a prescribing conclusion. An editorial in the newspaper of the American Medical Association puts it like this: "The price to be paid for extravagant gifts isn't measured by the size of a drug company's marketing budget, but in the erosion of trust in the medical profession."[9]

The price tag for this promotion is another reason for concern. A recent study estimates that, not including any meals, gifts or drug samples given to a doctor, the average fixed cost of a detailing call is $142 for office-based physicians and $179 for hospital-based physicians.[10] According to the New England Journal of Medicine, when visits from all companies are factored in, this amounts to spending between $6,000 and $11,000 per doctor, per year, on direct promotion.[11] The U.S. total for detailing expenditures, excluding all medicine samples, is nearly $5 billion a year. These costs are eventually passed through to the healthcare system and its consumers.

The fiscal impact of these promotions manifests itself directly in patient prescription costs as well. As indicated by a wide range of studies and the ever-increasing prevalence of the practice, this type of promotion is highly effective at changing the prescriptions that physicians write. According to the Center for Policy Alternatives, "Studies consistently prove that the practice of detailing causes doctors to prescribe the newest drugs, even when overwhelming medical evidence shows that less expensive, tried and true remedies would be much cheaper, just as effective, and often safer."[12]

Because companies focus their promotions on their newest, most expensive medicines, virtually any time that a physician switches to a promoted drug, the price increases. Thus, whenever a physician-oriented promotion is successful, consumers, insurers and government programs pay a higher price for their medications. A recent study in Pennsylvania found that 40% of patients in a state assistance program were given hypertension medicines different than those recommended by medical guidelines. If

doctors had prescribed according to those guidelines, the state could have saved $11.6 million, or nearly 24% of the total money it spent on hypertension medication. The study suggested that pharmaceutical promotion was partly at fault for the variance between the medicines that were recommended versus those that were prescribed.[13]

In addition to the public perception and financial considerations raised by the practice of pharmaceutical detailing, the quality of the information presented by detailers is of significant concern. Numerous academic articles have criticized the incomplete nature of presentations from detailers, and research shows that much of the information presented during these interactions is actually inaccurate. A study published in JAMA found that 11% of all statements made by detailers during monitored presentations were inaccurate and that only 26% of doctors who had seen the presentations were able to recall any false statements.[14] The lack of complete and accurate information from detailers is particularly troublesome because companies promote their drugs most heavily as they first enter the market – a stage when little outside information is available for comparison and doctors are forced to rely more heavily on company sponsored materials and presentations.

Content and Inadequacies of Existing Codes and Guidelines

Content

The problems caused by pharmaceutical detailing have not gone unnoticed by regulators, doctors, consumers and the pharmaceutical industry itself. To address the concerns raised by various stakeholder groups, a number of voluntary guidelines have been developed.

American Medical Association (AMA) Guidelines

On December 4, 1990, in response to growing concern both inside and outside the medical community about the appropriateness of gifts from industry, the American Medical Association adopted a set of guidelines to help doctors determine appropriate limits for gifts and other industry supported programs. Two days later, the Pharmaceutical Manufacturer's Association (PMA), a predecessor of today's Pharmaceutical Research and Manufacturers of America (PhRMA), adopted the same voluntary guidelines.

The document consists of a number of guidelines that physicians should consider before accepting a gift, grant, subsidy or any other inducement from an industry representative. The recommendations advise physicians to avoid accepting any gift that is of substantial value or that does not entail a value for patients. They recommend that doctors only attend meetings and conferences where the primary purpose of the event and incentive for attending is the furtherance of medical knowledge. The guidelines also advise doctors against accepting any gift that is given conditionally.[15]

In 2001, as part of a campaign to remind doctors about the existence of the guidelines and to encourage compliance with them, the AMA published updated recommendations with a number of clarifications.[16]

Pharmaceutical Research and Manufacturers of America (PhRMA) Code

In response to heavy legislative and public scrutiny culminating in an $875 million settlement against TAP pharmaceuticals regarding its marketing practices, PhRMA (an industry trade group and the successor to PMA) adopted a new code of conduct in July 2002. The preamble to the code openly acknowledges the industry's desire to limit the negative public reaction to gift giving. It states that "[w]e are also concerned that our interactions with healthcare professionals not be perceived as inappropriate by patients or the public at large."[17]

The PhRMA "Code on Interactions with Healthcare Professionals" lays out recommendations for many of the same situations addressed in the 1990 AMA guidelines. In addition to outlining advisable conditions for continuing medical education conferences and consulting agreements, the code recommends a few more specific limitations. It suggests that meals be only occasional and of modest value and that meetings no longer take place during entertainment and sporting events. The code advises that gifts only be offered occasionally, that they primarily entail a benefit to the patient and that no single gift exceed $100 in value. It further states that cash and gifts intended for the personal use of a physician should no longer be offered. The code concludes with a number of clarifying questions and answers as well as an admonition that "[e]ach member company is strongly encouraged to adopt procedures to assure adherence to this Code."

Office of Inspector General (OIG) Guidance

In April 2003, to address concerns about abuses in federal healthcare programs, the Office of Inspector General of the U.S. Department of Health and Human Services issued a document entitled "Compliance Program Guidance for Pharmaceutical Manufacturers".[18] The OIG guide gives pharmaceutical manufacturers recommendations for establishing a program to ensure compliance with applicable statutes, regulations, and requirements of federal healthcare programs.

With regard to pharmaceutical marketing and detailing, the OIG report recommends that pharmaceutical companies carefully scrutinize certain types of relationships and promotional practices in order to avoid liability under existing federal law.

The primary law addressed by the guidance is the federal anti-kickback statute (42 USC § 1320a-7b(b))[19]. The anti-kickback statute "is a criminal prohibition against payments (in any form, whether the payments are direct or indirect) made purposefully to induce or reward the referral or generation of federal health care business."[20] The statute and the guidance both deal exclusively protecting with public healthcare programs, including Medicaid and Medicare, from unscrupulous marketing and purchasing behaviors.

Inadequacies

Despite the propagation of these codes and guidelines, there are still significant shortcomings in the regulation of pharmaceutical detailing.

The OIG guidance, while essential to safeguarding the integrity of federal healthcare purchases, is extremely narrow in scope. Neither the guidance nor the anti-kickback statute addresses two key aspects of pharmaceutical detailing. First, the federal statute has no provisions regulating detailer interactions with healthcare providers who have no connection to public health care business. Second, the anti-kickback statute does not address the offer, acceptance or reporting of any gift or other remuneration not intended to solicit or reward government contracts, regardless of the relationship between the recipient and the federal government. Thus, the everyday interactions between most physicians and detailers are not regulated by the OIG guidance or the anti-kickback statute.

The AMA and PhRMA guidelines suffer from both their vagueness and their lack of enforcement mechanisms. While the revised AMA guidelines and the PhRMA code do recommend a few specific numbers ($100 upper limit for gifts), they remain ambiguous in many areas. Suggestions that only "occasional meals" of "modest" value should be offered and that gifts "should not be offered on more than an occasional basis" are largely subjective and open to a tremendous degree of abuse. In an interview with the *Washington Post*, a pharmaceutical company spokesman admitted that the AMA guidelines "are not specific enough to be a practical guide for everyday practice in our industry."[21]

Because the guidelines are discretionary, they are essentially unmonitored recommendations for members of the respective organizations. Violations of the voluntary guidelines have no legally enforceable consequences. The TAP Pharmaceuticals settlement and the fact that PhRMA was forced to issue a new code of conduct in 2002 indicate the failings of this voluntary system. TAP's marketing violations were not prevented by the code and were actionable only because they involved federal healthcare programs. PhRMA's new guidelines, while commendable, are a tacit admission of the failure of the first PMA code and still contain no legally binding enforcement mechanisms.

The voluntary nature of the guidelines can also create a business quandary for manufacturers. If following the guidelines would put a company at a competitive disadvantage with a company that disregards the rules, the first company has little choice but to ignore the guidelines as well. As a former detailer posed the problem, "Here you are, working for a company that wants to abide by the guidelines, and you can't compete with a guy who's giving away tickets."[22] With no punitive mechanism for those who violate the recommendations, gift giving can escalate into an arms race with neither side willing to unilaterally disarm. A more uniform and enforceable standard for appropriate interactions would level the playing field for all companies.

Policy Options

Without binding legislative action, there is no way to guarantee or monitor compliance with any set of guidelines or recommendations. To address the shortcomings of voluntary

self-regulation and to create a level playing field, legislators have considered and undertaken a number different of policy options.

Caps and Bans

In the past year, at least five states have considered either strict monetary limits or outright bans on gifts from pharmaceutical companies to doctors. Minnesota was the first state to set a firm cap on gift value ($50 per gift, with some exceptions) in 1993. A total ban on gifts, while ardently opposed by the pharmaceutical industry, would entirely eliminate any appearance of impropriety in industry-physician relationships. It could also free up a large part of the $4.8 billion a year currently spent on detailing for research or lowering the cost of prescription drugs. A legally mandated cap on either per gift or per capita spending could achieve those same goals to a lesser degree.

Disclosure

In the past two years, Maine and Vermont have enacted, and more than 15 state legislatures have considered, some disclosure requirements for manufacturers or doctors. While some bills would place the reporting requirement on doctors, most would require pharmaceutical companies to report the value, nature, and purpose of any gift or economic incentive over a certain value given to a healthcare provider. Because of the increased possibility for public scrutiny, this type of reporting would require both drug companies and doctors to carefully consider what types of gifts they give and accept. It would also give regulators and the public a clearer picture of the degree to which the voluntary regulations have brought about compliance.

Codification of existing guidelines

Another policy approach that can be taken to regulate pharmaceutical marketing is the legislative codification and enforcement of existing guidelines. Maine is currently considering a bill that would prohibit marketing practices that violate the PhRMA code or induce physicians to breech the AMA code. The California Legislature has passed legislation, Senate Bill 1765 (Sher), that would require pharmaceutical manufacturers to establish a compliance program that encompasses both the OIG guidelines and the tenets of the PhRMA code. That legislation would also require companies to publish firm, per doctor promotional spending caps and to declare each year that the company is in compliance with its own program and caps. Solutions like these take into account the steps that AMA members and PhRMA companies have already taken toward compliance, and simply work to ensure that all companies play by the same rules. While leaving room for individualized approaches to compliance, this policy option will guarantee substantial public scrutiny of industry gift giving.

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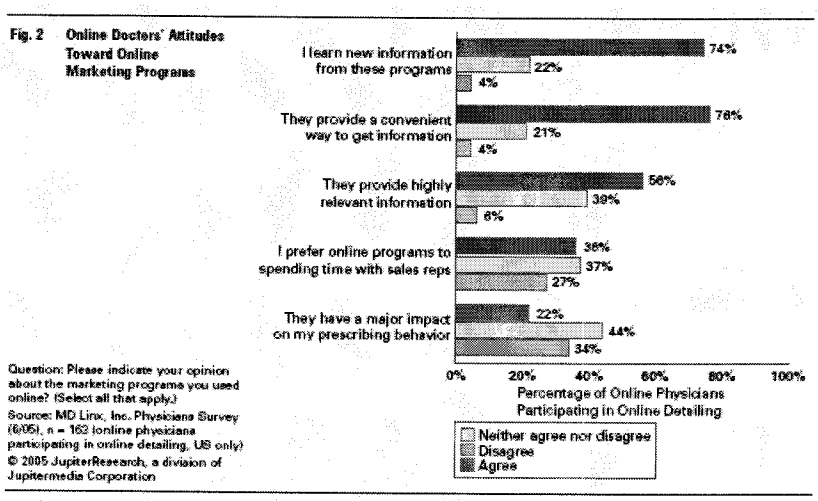
[22] Capaldi, Ralph, as quoted in "Visits from Pharmaceutical Reps," by Elizabeth Ellen. *Psychiatric Times,* Volume XVIII, Issue 1, January 2001. Available at http://www.psychiatrictimes.com/p010121.html.

DETAILING

According to research from Health Strategies Group, "[t]he average primary care physician interacts with 28 sales representatives each week; the average specialist interacts with 14." While this represents a significant amount of time, 2 hours and 13 minutes a week in 2004 per doctor, this is 20% less time than in 1999, where doctors spent 2 hours and 46 minutes a week meeting with sales reps.[c]

DRUG REPS PER PHYSICIAN			
Year	Physicians (P)[a]	Detailers (D)[b]	Ratio D to P
2000	813,869	74,865	1 to 11
2002	853,187	93,612	1 to 9
2003	871,535	94,407	1 to 9
2004	884,974	101,531	1 to 9



For a variety of reasons (e.g. time, professional concerns about information quality, online learning opportunities), 22% of doctors said they see fewer sales reps than in the past.[d] According to the table above, this does not appear to be due to a drop in the number of sales reps. It could be related to online detailing. Sixty-five percent of "online doctors"[e] participated in online detailing in 2005.[f] (See Figure 2)

Another way of looking at influence is to consider professional advertising expenditures per physician. The table at the right uses the cost of sales rep visits (excluding samples) to determine cost of all sales rep visits per physician.

COST OF SALES REP VISITS PER PHYSICIAN			
Year	Physicians[g]	Sales Rep Visit Cost ($)[h]	$ per Dr.
2000	813,869	5,137,000,000	$6311.83
2002	853,187	6,198,000,000	$7264.53
2003	871,535	6,938,000,000	$7960.67
2004	884,974	7,336,000,000	$8289.51

[a] American Medical Association. Available online at: http://www.ama-assn.org/ama/pub/category/12912.html.
[b] Matthew Arnold. "Flexible Forces." *Medical Marketing & Media*. November 2005.
[c] Ashley Mahoney, Rayna Herman. "2005 Access Report: The current state of pharma sales." *Pharmaceutical Representative*. July 1, 2005.
[d] Monique Levy, Jupiter Research. *Online Marketing to Physicians: Evaluating Physicians' Responsiveness to Online Detailing*. September 1, 2005.
[e] Defined as physicians who use the internet for work-related activities. (Jupiter Research).
[f] Monique Levy, Jupiter Research. September 1, 2005.
[g] IMS Health. Total US Professional Promotional Spend by Type, 2004. Available online at: http://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_49695992_75406357,00.html.
[h] Matthew Arnold. November 2005.

A Social Science Perspective on Gifts to Physicians From Industry

Jason Dana, MS

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A CONFLICT OF INTEREST EXISTS WHEN A PRIMARY ETHical or professional interest clashes with financial self-interest, a situation that arises commonly in medical practice. When physicians are remunerated for performing specific tests and procedures, they face a conflict of interest when they also recommend those same tests and procedures. When they are paid for referrals to clinical trials, physicians are in the conflicted position of deciding whether their patients are appropriate for the studies. Performing industry-supported research, physicians face an implicit demand for a positive finding to obtain further financial support. And, when pharmaceutical companies court high-volume prescribers, writing prescriptions becomes an act not only with financial and health consequences for patients, but also with financial consequences for the physician. This last source of conflict of interest is the central focus of this commentary.

In discussions of gifts from industry, whether in medical journals, the media, or in political debates, it is possible to glimpse a common perspective. The biasing effect of accepting gifts is treated as a matter of deliberate choice. The conventional perspective on accepting gifts implies that physicians who are biased by the prospect of personal gains are deciding to do something unethical. Undoubtedly, this perspective contributes to the indignation with which many physicians respond when it is suggested that gifts create bias. Because the bias is seen as intentional, an allegation of bias is an implicit accusation of impropriety.

Many policies dealing with conflict of interest seem premised on this understanding of bias. For example, consider policies on gift size. The recent guidelines for industry put forth by the Pharmaceutical Research and Manufacturers of America[1] and the recommendations of the Office of Inspector General of Health and Human Services[2] define gifts of "more than nominal value" as inappropriate, while small gifts may not be. Surveys reveal that physicians also view small gifts as ethically more acceptable than large gifts,[3,4] and letters to medical journals assert that small gifts do not affect physician judgment toward a product.[5] These policies, surveys, and letters reveal a belief that small gifts are not tempting enough to influence physicians' prescription choices, as if physicians are making a deliberate tradeoff between the cost of bias and the benefit of the reward.

This deliberate choice view is inconsistent with social science research, which shows that even when individuals try to be objective, their judgments are subject to an unconscious and unintentional self-serving bias. When individuals have a stake in reaching a particular conclusion, they weigh arguments in a biased fashion that favors a specific conclusion. Returning to the example of gift size, by subtly affecting the way the receiver evaluates claims made by the gift giver, small gifts may be surprisingly influential. Furthermore, individuals are generally unaware of the bias, so they do not make efforts to correct for it or to avoid conflicts of interest in the first place.

We review basic social science research, which shows how financial motives distort judgment, demonstrate its parallels to medical research on gifts to physicians from industry, and draw out policy implications. A proper policy response to the issue of gifts from pharmaceutical companies critically depends on a realistic understanding of the psychology of conflict of interest. Policies that make sense if bias is interpreted as a matter of deliberate choice (eg, limiting gift size, educational initiatives, and mandatory disclosure of interests) are unlikely to be effective if bias is in fact unintentional and unconscious. We focus on the problem of gift giving from industry because it serves as a convenient example with which to demonstrate our basic points. However, the implications of the social science findings apply more broadly to policies dealing with virtually all conflicts of interest in the medical and health care fields, and to conflicts of interest in areas outside of medicine.

Gifts From Industry: A Problem for Policy Makers

Gifts from the pharmaceutical industry contribute to the rapidly increasing cost of medical care, and more specifically, to the increase in expenditures on prescription drugs. Retail spending on prescriptions has increased rapidly, more than doubling from $64.7 billion to $132 billion in the years 1995-2000.[6] Drug spending increased another 17% to $154.5 billion in 2001, with an estimated one quarter of this in-

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crease resulting from a shift to the prescribing of more expensive drugs. Pharmaceutical companies employ representatives who meet with physicians with apparent success to aggressively promote newer and typically more expensive drugs. A positive correlation has been found between the cost of physicians' treatment choices and their amount of contact with pharmaceutical company representatives.[7,8] Wazana[9] concluded on the basis of a review of 29 empirical articles that physician interactions with pharmaceutical companies led to increased prescription costs and nonrational prescribing. This increase is problematic, given the prevalence of new, expensive drugs of questionable incremental value. From 1989 to 2000, the US Food and Drug Administration judged 76% of all approved new drugs to be no more than moderate innovations over existing treatments, with many being a modification to an older product with the same ingredient.[10] In 2000, the average price of these standard-rated new drugs was nearly twice the average price of existing drugs prescribed for the same indications.[10]

Social Science Research on Conflict of Interest

A line of research with important implications for financial conflict of interest examines the "self-serving bias"[11] in perceptions of fairness: individuals' judgments of what is fair are typically biased in favor of their self-interests. In early experiments by Messick et al,[12] individuals performing a task were given pay for themselves and another individual performing the same task and asked to divide it as they saw fit. They were told that (1) the other individual worked twice as long at the task; (2) completed twice as much work; (3) both; or (4) neither. Individuals kept more than half if they either worked longer or completed more of the task, but felt that an equal division was appropriate when both dimensions were unfavorable to them.

This behavior helps to illuminate the psychological mechanisms underlying financial conflicts of interest. In many situations, there are multiple interpretations of what is considered fair. Actions that do not fall under any of these interpretations are usually considered unfair with little disagreement, but when there are multiple notions of fairness, individuals tend to default to those notions that favor their own interests. In the study by Messick et al,[12] there were 2 competing notions of fairness: equality of payoffs and pay based on effort. When individuals responsible for distributing the pay worked shorter hours and produced less output, they tended to view equality as fair, but when they worked longer or produced more, they viewed pay based on effort as fair and believed that whichever measure of effort favored them was more important.

In a series of experiments that examined the causes and consequences of self-serving bias,[13-16] bargaining experiments were conducted in which individuals were presented with case materials (depositions, police reports, etc) from an actual lawsuit, were randomly assigned to the role of either plaintiff or defendant, and attempted to negotiate a settlement in the form of a payment from defendant to plaintiff. At the outset, the defendant was given a monetary endowment to finance the settlement. Both parties were penalized as a function of how long it took them to reach a settlement, and, if they failed to settle, the defendant's payment to plaintiff was determined by a neutral judge who had been given the same case materials.

Before negotiating, individuals were asked to predict the judge's ruling and were paid for their accuracy. Plaintiffs' predictions of the judge's award amount were substantially higher than those of defendants, despite the fact that they had no bearing on the case, and the larger the discrepancy, the lower was the likelihood of settlement and hence the individuals' payoffs. This suggests that individuals are often unable to avoid bias, even when it is in their best interest to do so.

In subsequent experiments using the same paradigm, individuals were asked to rate the importance of 8 arguments favoring the side they had been assigned (plaintiff or defendant) and 8 arguments favoring the other position, as perceived by a neutral third party.[14] The results showed a strong tendency to view arguments supporting an individual's own position as more convincing than those supporting the other position, further illustrating the difficulty that individuals have in taking a neutral, objective perspective when they have a personal interest in arriving at a specific conclusion. Moreover, when individuals were assigned roles only after reading the transcripts, thus removing any motivation to favor one side when the materials were evaluated, bias was reduced and settlement rates increased markedly. All of these findings suggest that self-interest distorts the way that individuals weigh arguments.

In later studies, the same researchers attempted to reduce bias by educating individuals, describing these behavioral regularities in detail, and testing to make sure they were understood.[17] This intervention was successful insofar as individuals became convinced that their negotiating opponent would be biased, but the individuals themselves believed they would not be. Moreover, when individuals did concede that they might be somewhat biased, they tended to drastically underestimate how strong their bias would be.

These studies help to explain specifically how self-interest affects decision making. First, individuals are unable to remain objective, even when they are motivated to be impartial, demonstrating that self-serving bias is unintentional. Second, individuals deny and succumb to bias even when explicitly instructed about it, which suggests that self-serving bias is unconscious. Third, the studies show that self-interest affects choices indirectly, changing the way individuals seek out and weigh the information on which they later base their choices when they have a stake in the outcomes.

Evidence in Medicine

The medical literature dealing with conflict of interest bears similarities to the social science literature reviewed herein. Like the participants in the studies who did not view them-

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selves as biased, physicians typically report that they are not biased by financial arrangements with pharmaceutical companies, although a large body of research suggests that they are.[18-23] For instance, one retrospective study[24] tracked house staff who attended a grand rounds given by a pharmaceutical company speaker and found them more likely to indicate that company's drug as a treatment than did their colleagues. However, many of the house staff did not recall what company sponsored the grand rounds.

Although most physicians do not perceive themselves as biased, they do admit that conflicts of interest might compromise other physicians' decisions.[25] A recent study of medical residents[26] found that 61% reported that "promotions don't influence my practice," while only 16% believed the same about other physician's practices. Clearly, it cannot both be true that most physicians are unbiased and that most other physicians are biased. Furthermore, medical students recognize gifts as more problematic for other professions than they are for medicine.[27] This finding is analogous to that from the social science research showing that bias is recognizable, but only in others.

Like other self-serving biases, bias in prescription practices appears to be unintentional. Orlowski and Wateska[28] tracked the pharmacy inventory usage reports of 2 drugs after 20 physicians at their institution were sponsored to attend continuing medical education seminars sponsored by the companies producing the drugs. Usage of the drugs described at these seminars increased, both in time series at the institution and compared with the national average during the same period. However, all but one physician denied that the seminars would influence their behavior prior to attending. Being asked about bias should make physicians more aware of the potential of bias entering into the seminar, yet this did not prevent the seminar from apparently having an impact on the physicians' decisions.

Patients, while somewhat more concerned about the possible biasing effects of gifts than physicians, seem to be vicariously self-serving in their perceptions, believing that other individuals' physicians are more likely to be biased by gifts than their own physicians.[29] An implicit embrace of the model of deliberate choice probably colors patients' views of their physicians. Because most patients cannot imagine that their physicians would intentionally put their own monetary interests above those of their patients, they cannot imagine their physicians being biased.

Policy Implications

A research-informed understanding of conflict of interest has important implications for policy. Specifically, the interventions mentioned earlier—limiting gift size, educational initiatives, and mandatory disclosure—are unlikely to eliminate bias because they rest on a faulty model of human behavior. The finding that individuals are not aware of their bias, even when taught about it, suggests that the problem cannot be dealt with effectively through training. For example, even if ethical conduct is clearly illustrated through case studies, few conflict of interest situations that the physician will actually encounter are likely to replicate these cases so closely as to preclude potential mitigating circumstances, thus opening the door for a self-serving interpretation of whether one's own behavior is improper.

The finding that the bias is strong, even in studies with small stakes, suggests that a policy of limiting gift size is unlikely to eliminate bias. Because even small gifts can subtly bias how arguments are evaluated, they can be surprisingly influential. The sheer ubiquity of trinkets given by pharmaceutical companies is evidence of their effectiveness; why else would profit-minded companies continue to provide them? Thus, policies against gifts should not be limited to large gifts.

Finally, the general misconceptions about conflict of interest weigh in against the effectiveness of disclosure as an antidote to bias. Disclosure can only be effective if those informed can rationally update their beliefs—discount the advice they receive from physicians who disclose conflicts of interest—in light of the disclosure. However, most patients would have little idea about, for example, how much to discount their physician's recommendation to participate in a clinical trial if they were informed that their physician would benefit financially from their participation.

In fact, recent social science research involving auditing suggests that disclosure may have perverse effects.[30] Individuals were randomly assigned to the role of estimator or advisor. Estimators made money by accurately estimating the value of a jar of coins they viewed from a distance. Advisors saw the jars close up, and suggested values to the estimators, but they were paid according to how high, rather than how accurate, the estimator's guess was. Half of the advisors were required to disclose their incentives for the estimator to give high estimates. Advisors who disclosed values to the estimators suggested much higher values. The estimators did not discount the advice they received sufficiently and the estimates made with disclosure information were higher than those made by estimators to whom the conflict of interest was not disclosed. As a result, estimators made less money, and advisors more, when advisors disclosed.

Because bias induced by monetary interests is unconscious and unintentional, there is little hope of controlling it when monetary interests exist. The implication for industry gifts is straightforward: they should be prohibited. The American Medical Student Association has already begun an initiative urging physicians to refuse gifts from industry,[31] but one wonders whether such idealism will be maintained in the face of the inducements they are likely to encounter in their professional careers.

Pharmaceutical companies know that gifts influence physicians, which is why many restrict their own employees from accepting even small gifts.[32] Isn't it time for physicians to adopt similar restrictions on gifts to eliminate their vulnerability to unconscious bias?

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Other conflicts of interest for physicians may be more difficult or costly to eliminate. For example, requiring different physicians to recommend and actually perform procedures would help to limit physicians' motivation to recommend unnecessary procedures that they personally benefit from but would limit patient choice and increase costs. Similarly, although many consultancies may serve as a backdoor method of providing incentives for prescribing, barring physicians from serving as paid consultants to pharmaceutical companies would hamper the activities of those who do play essential roles in transmitting important data to drug developers. Perhaps this is why recent guidelines by the Pharmaceutical Research and Manufacturers of America and the Office of Inspector General of Health and Human Services permit pharmaceutical companies to hire physicians as consultants, given the somewhat ambiguous proviso that there is "a legitimate need for the services."[33]

It would be costly, if not impossible, to eliminate all conflicts of interest, but some interventions are relatively obvious and straightforward. Such measures are required if physicians want to retain the widespread public trust that they still enjoy.

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Doctors and Drug Companies

David Blumenthal. **The New England Journal of Medicine**. Boston: Oct 28, 2004. Vol. 351, Iss. 18; pg. 1885, 6 pgs

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Abstract (Document Summary)

In a very thorough review of the literature on the effects of interactions with drug companies on physician behavior, Wazana15 identified 16 relevant studies.

Full Text (4172 words)

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When a great profession and the forces of capitalism interact, drama is likely to result. This has certainly been the case where the profession of medicine and the pharmaceutical industry are concerned. On display in the relationship between doctors and drug companies are the grandeur and weaknesses of the medical profession - its noble aspirations and its continuing inability to fulfill them. Also on display are the power, social contributions, and occasional venality of a very profitable industry whose products contribute in important ways to the health and longevity of the American people but that at times employs methods that are deeply troubling and even criminal. Government also plays a part as it tries with limited success to help the profession stay true to its own tenets and to deter the industry's most egregious excesses. The spectacle is profoundly human and, like most such spectacles, seems never to end or to lose its fascination.

The interaction of doctors and pharmaceutical companies is also extremely consequential for patients, doctors, and the larger society. The drug industry manufactures, distributes, and publicizes powerful chemical and biologic agents that have proven benefits and that physicians sometimes fail to use as often as they should, or in sufficient doses.1 In this sense, industry's efforts to encourage the use of some agents by physicians can be seen as contributing to the public health. At the same time, the marketing by the drug industry of its products to physicians is manifestly aimed also at improving industry profits; in the process, such marketing may contribute to less savory social consequences, including increasing drug costs and the misuse or overuse of medications in ways that may adversely affect patients.2

Several recent developments have focused renewed attention on the relationship between drug companies and doctors. One is the surge in spending on prescription drugs, which totaled $162.4 billion in 2002 after years of double-digit percentage increases.3 A second is the publicity surrounding a number of prominent legal cases in which drug manufacturers have been convicted of crimes related to their marketing of drugs to physicians or have made huge payments in the settlement of civil suits for similar noncriminal violations.4-7 A third is an increasing recognition by both pharmaceutical companies and physicians that, in certain respects, the relationships between drug companies and doctors have become embarrassing to both parties and need to change.8-11

This report reviews the salient aspects of the relationships between physicians and drug companies at the turn of the 21st century. I examine the nature and extent of drug-company interactions with physicians and review what is known about the consequences of those interactions for physicians' clinical decisions, as well as the cost and quality of the care they provide. I then briefly note some recent attempts by private organizations and government agencies to manage or regulate the interactions between physicians and drug companies in an effort to prevent perceived abuses, and I conclude with a discussion of how the relationships are likely to evolve in the future.

THE NATURE AND EXTENT OF THE RELATIONSHIPS

Interactions between drug companies and doctors are pervasive. Relationships begin in medical school, continue during residency training, and persist throughout physicians' careers. The pervasiveness of these interactions results in part from a huge investment by the pharmaceutical industry in marketing. In 2002, the industry expended 33 percent of its revenues on "selling and administration."12 In 2001, one company, Novartis, reported spending 36 percent of its revenues on marketing alone.2 The marketing expenditures of the drug industry have been estimated variously at $12 billion to $15 billion yearly, or $8,000 to $15,000 per physician.7,8,13 In 2001, the industry's sales force of drug detailers, whose job is to meet individually with physidans and promote company products, numbered nearly 90,000 in the United States2,8 - 1 salesperson for every 4.7 office-based physicians.8

Moynihan14 catalogued 16 different ways in which drug companies relate directly or indirectly with doctors. These range from the seemingly trivial (e.g., the ubiquitous dispensing of gifts such as pens and pads with drug names inscribed) to the much more troubling (e.g., the ghostwriting of articles for academic physicians, the payment of large honoraria and consulting fees to prominent physicians who extol the virtues of company products, and the support of lavish trips and entertainment for physicians who commonly prescribe company products).

Surveys of residents indicate that they receive an average of six gifts from pharmaceutical companies annually.15 In a survey of 106 directors of emergency-department programs in 2002, 41 percent responded that their programs allowed residents to be taught by representatives of drug companies, 35 percent reported that residents received free industry samples at work, and 29 percent said that residents' travel to meetings was sometimes dependent on the availability of company support.16 According to another report, residents in a psychiatry program in Toronto attended up to 70 lunches that had been sponsored by drug companies and received 75 promotional items over the course of one year.17

As physicians mature, their relationships with drug companies also change, becoming more likely to involve consulting and honoraria and less likely to involve luncheon seminars. A 2001 survey of a random sample of U.S. physicians by the Henry J. Kaiser Family Foundation found that 92 percent of physicians received free drug samples from companies; 61 percent received meals, tickets to entertainment events, or free travel; 13 percent received "financial or other in-kind benefits"; and 12 percent received financial incentives to participate in clinical trials.18 A 1997 study by Ferguson and colleagues found that 83 percent of internists with the Department of Medicine at the University of Maryland had met with drug-company representatives in the previous year.19 Wazana reports that, on average, practicing physicians meet with drug-company representatives four times a month.15

One of the most common ways in which the pharmaceutical industry now interacts with practicing physicians is through continuing medical education. As of 2003, according to Dr. Murray Kopelow, president of the Accreditation Council for Continuing Medical Education, pharmaceutical companies were providing about $900 million of the $1 billion spent annually on continuing medical education in the United States.20 In fact, new, for-profit companies have arisen, called medical education and communication companies, whose purpose is to provide educational offerings to physicians. These organizations are sometimes subsidiaries of public-relations firms that also conduct advertising for the pharmaceutical industry.2,21

Drug companies do not relate to physicians only as individuals. The pharmaceutical industry also maintains relationships with the organizations to which physicians belong and for which they work.10 Drug companies are frequent financial sponsors of the annual meetings of physician organizations, and they also support special projects by those organizations.2 For example, the American Medical Association has received industry funding, including support to publicize its own guidelines for how physicians should relate to the drug industry.22 As many as 59 percent of the authors of clinical guidelines endorsed by many professional associations have had financial relationships with companies whose drugs might be affected by those guidelines.23

Drug companies also have attempted to influence the pharmaceutical agents that are available for use by physicians who work with and for certain organizations. Some of these practices are widely accepted in the business world both inside and outside of medicine. For example, pharmaceutical companies offer discounts to managed-care organizations and their agents - pharmaceutical-benefit managers - in return for favorable treatment of their products in the formularies used by these organizations. Some pharmaceutical companies, however, have engaged in ethically, and perhaps legally, questionable efforts to affect the drugs that health care organizations allow or encourage their physicians to use. Studdert et al. review several instances of this behavior in another article in this issue of the Journal.24

CONSEQUENCES OF THE RELATIONSHIPS

The relationships between drug companies and doctors would be of little interest if they did not have potential consequences for patients, doctors, and the larger society. Explicitly or implicitly, much of the debate about these relationships revolves around the question of whether drug companies influence physicians' behavior and, if they do, whether the results are, on balance, positive or negative for the quality and cost of health care and for the profession of medicine itself.

Most physicians are quite tolerant of, and even have a positive attitude toward, their interactions with drug companies.15 Many physicians believe that their interactions with drug companies have educational value for themselves and also provide benefits for patients, both because physicians are kept informed about available therapeutic agents and because the free samples they are given can be distributed to patients.25,26 Physicians also tend to be confident that they themselves are invulnerable to any bias inherent in the educational content offered or supported by drug companies. A study of residents found that 61 percent believed that they were not influenced by the marketing efforts of pharmaceutical companies (although only 16 percent were equally confident about their colleagues).25 Brett and colleagues found in a small survey of residents and faculty members at a U.S. medical school that a majority of respondents tended to view a wide variety of interactions between drug companies and doctors as ethically acceptable.26 Examples included the receipt of pencils, pads, and expensive textbooks (valued at $500 apiece), company-funded dinners at which the company's products were favorably mentioned, free drug samples for physicians' offices, free lunches for residents, and the presence of drug representatives during clinic hours and during company-supported "happy hours." Respondents were more likely to view interactions as problematic when the value of the gift or entertainment increased, when it involved recreational as opposed to professional activities, and when information provided to physicians during the interaction was biased or self-serving.26

Despite the confidence of physicians in their ability to resist efforts by drug companies to affect their behavior - especially in ways that may serve company purposes rather than their own or those of their patients - a substantial body of theoretical and empirical literature (as well as physicians' own concern about their colleagues) suggests that many physicians may be mistaken. Some of this literature focuses on what might be called the gift relationship - that is, the manner in which gifts influence human behavior and the role they play in human relationships. According to Katz et al., "When a gift or gesture of any size is bestowed, it imposes on the recipient a sense of indebtedness. The obligation to directly reciprocate, whether or not the recipient is conscious of it, tends to influence behavior. . . . Feelings of obligation are not related to the size of the initial gift or favor."13

The idea that small gifts may be as influential as large gifts seems counterintuitive but is supported by substantial research in social science.13,27 Among the most important influences on behavior are the simplest and most fundamental: food, friendship, and flattery. Indeed, these have constituted the basis of human relationships since the beginning of time.13 Also supported by research is the observation that humans are vulnerable to a powerful, unconscious "self-serving bias"; that is, they have trouble seeing themselves as biased when the bias serves their needs or advances their own perceived interests.27

The social-science literature, therefore, suggests that it would be surprising if doctors were not influenced by the small and large services and tokens of appreciation and interest provided by pharmaceutical companies. Furthermore, if many physicians find the blandishments of drug companies gratifying and rewarding, then physicians in general would be systematically handicapped in detecting any bias in decision making caused by these interactions. To posit otherwise would imply that physicians are different in fundamental ways from their fellow human beings.

A reasonable response might be that the professional training of physicians does differentiate them from others, rendering them resistant or immune to influences that might affect other Homo sapiens and enabling them to appraise their patients' interests objectively and put those interests before all other considerations. However, the evidence suggests that physicians are unable to transcend their humanity in their daily practices.

In a very thorough review of the literature on the effects of interactions with drug companies on physician behavior, Wazana15 identified 16 relevant studies. These studies found that a wide variety of interactions - meetings with company representatives; the receipt of gifts, free drug samples, and free meals; company support for travel to and lodging at educational events; attendance at lectures by representatives of pharmaceutical companies; acceptance of

honoraria; and other relationships - were associated with changes in physicians' use of medications. Involved physicians were more likely to request the inclusion of the company's drugs on hospital or health maintenance organization formularies, more likely to prescribe the company's products, and less likely to prescribe generic medications. The resulting changes in the use of medication were often costly and "nonrational" in that the newly prescribed or requested drugs had no therapeutic advantage over the alternatives. Interestingly, several studies have found that the larger the number of gifts that physicians received, the more likely they were to believe that gifts did not affect their prescribing behavior.15,28 Wazana found no studies that directly measured the effects of relationships between physicians and drug companies on patients' outcomes or on the aggregate costs of health care.15

Interactions between physicians and drug companies may also affect another important consideration: the credibility of the medical profession in the eyes of patients and the public. In rewriting its own guidelines on physician-industry relationships, the American College of Physicians noted, "A perception that a physician is dispensing medical advice on the basis of a commercial influence is likely to undermine a patient's trust not only in the physician's competence but also in the physician's pledge to put patients' welfare ahead of self-interest."10 Obviously, such perceptions among patients, if widespread, could erode the public's collective trust in the profession. The limited research on the attitude of patients toward the receipt by physicians of gifts and other considerations from the pharmaceutical industry suggests that patients are more likely than doctors to believe that gifts may influence prescribing behavior and that patients tend to view gifts that influence prescribing behavior as inappropriate.29

EFFORTS TO MANAGE RELATIONSHIPS

What is clear is that physicians' organizations, drug companies, and the government have become uncomfortable in recent years with the nature, extent, and potential consequences of interactions between physicians and pharmaceutical companies. This discomfort reflects a growing consensus that some drug companies have been offering, and some physicians accepting, financial and other benefits that are ethically and even legally inappropriate.4-6,30,31 In response, professional, industry, and government groups have attempted to clarify standards that differentiate appropriate from inappropriate relationships and thereby to reduce the frequency of suspect interactions.32 The content of several of these new sets of guidelines and regulations is summarized by Studdertand colleagues.24

Taken together, this series of private and public pronouncements seems to embrace the view that relationships between some drug companies and physicians are ethically appropriate, often beneficial, and certainly unavoidable and that the challenge for the medical profession, drug companies, and the government is to contain those relationships within acceptable boundaries and to avoid certain egregious and possibly illegal practices. As such, new and existing policies seem to be generally consistent with the views of most physicians, who have indicated in studies cited here that they view as appropriate the provision by drug companies of modest gifts, free drug samples, support for educational programs (including associated modest meals), and a number of other services for doctors. Physicians are less likely, however, to view as acceptable the receipt of gifts and services that are either very valuable (though there is no consensus on the dollar amount) or unrelated to a professional purpose (e.g., a golf bag or tickets to a sporting event).

A number of critics find the efforts to preserve and manage relationships between drug companies and physicians to be ill conceived and impractical. Two former editors of the Journal, Arnold Relman and Marcia Angell, find the American Medical Association guidelines to be "general and vague."2 Joseph Gerstein, an internist from Massachusetts and a former managed-care executive who first notified federal officials about illegal activities at TAP Pharmaceutical Products,24 believes that it will be difficult for physicians to avoid biases introduced by even modest marketing activities by drug companies. "Maybe there are some physicians who are so morally stout . . . that they can be sure they weren't affected," commented Gerstein in an interview. "I would like to meet that person." He noted further that the Office of the Inspector General (OIG) of the Department of Health and Human Services "has put out some pretty firm guidelines, but there are an awful lot of people working to get around them."

Sidney Wolfe, director of Public Citizen's Health Research Group and a perennial critic of the drug industry, is skeptical that current guidelines will have any meaningful effect on behavior. "The problem," said Wolfe in an interview, "is that there is no detection mechanism and no enforcement mechanism." The only practical approach to dealing with interactions between drug companies and physicians, in the view of many critics, is for physicians not to accept anything of financial value, no matter how trivial, from drug companies. The only professional group to support this viewpoint is the American Medical Student Association, which has called on physicians to sever their relationships with the pharmaceutical industry.33

FUTURE DEVELOPMENTS

It is far too early to assess the ways in which recent efforts to manage physician-industry interactions have influenced the nature, extent, or effects of those relationships. Anecdotal reports attest both to a reduction in some perceived excesses, such as lavish entertaining of physicians at expensive resorts, and to their persistence in the face of new guidelines.34,35 M. Therese Grouse, director of compliance, health care, and marketing at Eli Lilly, asserts that OIG

guidance in particular "absolutely affected the way we are doing business. . . . Entertainment is significantly cut down. . . . [There is] no more golf, no more movie nights." Having just revisited or revised their policies, professional, government, and pharmaceutical groups and agencies seem likely to await the verdict of time before attempting additional interventions.

The one exception may be state governments, which have become much more active on a number of health policy fronts in recent years, including lawsuits against tobacco companies, the regulation of managed care, and, most recently, the scrutiny of behavior by drug companies. As of March 1 of this year, four states - Maine, Vermont, Nevada, and New Mexico - had begun requiring companies to report how much they were spending on the marketing of their products to physicians working in their states.34 Vermont, which requires the disclosure of any marketing expenditures in excess of $25, reported in February of this year that 44 pharmaceutical companies spent $2.47 million in "fees, travel expenses and other direct payments to Vermont physicians, hospitals, universities and others for the purpose of marketing their products" in the year ending June 30, 2003.36

Whether these and other external controls on the interactions between physicians and drug companies will fundamentally change those interactions over the long run, however, remains far from certain. Doctors and leaders of drug companies are mature, consenting parties in relationships that both are highly motivated to maintain - for drug companies because the relationships are vital to selling their products, and for physicians because they value, wisely or not, the information, gifts, and services that companies provide in the course of their marketing activities. From a social standpoint, it is difficult to argue that the relationships are totally without redeeming value, since some of them seek to increase the dispensing of drugs and biologic agents that physicians currently underprescribe, with major adverse consequences for public health. Professional and company attitudes, together with the rationale that marketing by drug companies could in some ways enhance public health, will make it politically impractical for governments to adopt the kind of draconian ban on relationships between doctors and drug companies that their strongest critics favor. And as long as such relationships are legal, the parties involved will face constant temptations to test the limits of professional and industry codes and government regulations. One can predict, therefore, that there will be ongoing cycles of scandal and reform for the foreseeable future.

In many ways, the ultimate arbiter of the nature, extent, and consequences of interactions between drug companies and physicians is the medical profession itself.21 As a for-profit business, the pharmaceutical industry should be expected to market its products aggressively within legal boundaries. It is then up to physicians to decide whether to accept the proffered information and enticements. It is unlikely that professional organizations, as representative bodies, will move far out ahead of their members in making policy on these issues. As its president, Murray Kopelow, notes, the Accreditation Council for Continuing Medical Education "must reflect the values of the profession." So too, in the end, must the interactions between drug companies and physicians.

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Economic Implications of Evidence-Based Prescribing for Hypertension

Can Better Care Cost Less?

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Context Deviation from evidence-based guidelines in hypertension treatment is common, but its economic impact has not been rigorously studied. Suboptimal prescribing patterns contribute to the high cost of medications for elderly patients as well as the difficulty in providing affordable prescription drug benefits for older Americans.

Objective To calculate the potential savings from the perspective of health care payers that would result from increased adherence to evidence-based recommendations for managing hypertension in patients older than 65 years.

Design Comparative analysis of medications prescribed vs potential regimens suggested by evidence-based guidelines tailored to each patient's medical history, with calculation of the costs of both the actual and the evidence-based regimens.

Setting and Patients A total of 133624 patients being treated for hypertension during 2001 who were enrolled in a large state pharmaceutical assistance program that provides prescription drug insurance for elderly persons.

Main Outcome Measure Cost difference between medications actually prescribed and regimens suggested by evidence-based guidelines.

Results The patients studied filled more than 2.05 million prescriptions for antihypertensive medications in 2001, at an annual program cost of $48.5 million ($363 per patient). We identified 815316 prescriptions (40%) for which an alternative regimen appeared more appropriate according to evidence-based recommendations. Such changes would have reduced the costs to payers in 2001 by $11.6 million (nearly a quarter of program spending on antihypertensive medications), as well as being more clinically appropriate overall. Replacement of calcium channel blockers resulted in the largest potential savings. Use of pricing limits similar to those in the Medicaid program would have resulted in even larger potential savings of $20.5 million (42% of program costs).

Conclusions Adherence to evidence-based prescribing guidelines for hypertension could result in substantial savings in prescription costs for elderly patients with hypertension that would amount to savings of about $1.2 billion nationally. Identification of similar areas in which prescribing can be improved will be critical for the affordability of prescription drug benefit programs.

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COSTS OF MEDICATIONS FOR chronic conditions continue to escalate, particularly for the elderly.[1,2] The Congressional Budget Office projected that in 2003, Medicare beneficiaries would spend an average of $2440 per person on prescription drugs.[3] Although some older patients have supplemental insurance to cover the cost of prescription drugs,[1] the proportion without coverage has increased in recent years.[4] Vulnerable older patients may not fill prescriptions because of their lack of insurance coverage.[5,6] Legislation to create a prescription drug benefit for Medicare recipients was recently passed,[7] but substantial copayments will remain for many patients, and the cost of the benefit will likely be much higher than originally anticipated.[8] Identification of areas in which clinical practice can be improved while lowering costs to patients and prescription drug plans will be critical to ensure the affordability of medications for older patients.

More than 60% of Americans aged 65 years and older have hypertension.[9] Estimates of the cost of its treatment have ranged from $7 billion to $15.5 billion per year.[10-13] Therapeutic options have expanded tremendously in the past 2 decades, and guidelines have changed as well.[14] In the recently published Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT),[15] more than 33000 patients with hypertension were randomly assigned to receive amlodipine, lisinopril, or chlorthalidone; the thiazide-type diuretic was shown to be

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most effective in controlling systolic blood pressure as well as in preventing heart failure and stroke; it was also the least costly. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) recommended thiazide-type diuretics as first-line agents for uncomplicated hypertension in most patients.[14] Although some trials offer evidence for angiotensin-converting enzyme (ACE) inhibitors,[16] a comprehensive meta-analysis emphasized strong evidence for thiazides as the preferred agents for the majority of patients with this condition.[17] Specific comorbidities (eg, diabetic nephropathy or coronary artery disease) constitute indications for other agents (ACE inhibitors and β-blockers, respectively), although even in these conditions, guidelines state that thiazide-type diuretics could still be considered first-line therapy.[14]

We investigated the economic impact that would result from better adherence to evidence-based therapeutic guidelines. To do this, we analyzed medication use patterns in more than 130 000 hypertensive patients in a state drug assistance program for elderly patients. We evaluated every antihypertensive regimen in light of the clinical history of each patient and then estimated the potential cost savings to the health care delivery system that could have been realized through adherence to evidence-based recommendations.

METHODS

Sources of Data

Pennsylvania's Pharmaceutical Assistance Contract for the Elderly (PACE) program provides prescription drug coverage for a large population of that state's elderly patients who are not indigent enough to qualify for Medicaid but have annual incomes of less than $14 000 for single persons or $17 200 for married persons.[18] The program covered all drug costs, minus a $6 copayment for each prescription, for 201 000 beneficiaries in 2001. Prior publications have studied medication use in the PACE program.[19,20] Medication claims were available from 1994 through 2001. Data on filled prescriptions were linked to Medicare part A and B files containing additional data on all diagnoses and comorbidities, both outpatient and inpatient, recorded for these patients through the end of 2000. All personal identifiers were transformed to anonymous untraceable coded study numbers to protect patient confidentiality. Institutional review board approval was obtained for review of the claims records. Data analyses were performed using SAS software.[21] Prior research has validated the accuracy of computerized claims data for determining medication exposure.[22-26] The PACE program receives rebates averaging about 16% from drug manufacturers; this was considered in all cost analyses.

Identification of Patients

We identified every patient who filled a prescription for antihypertensive medications during 2001 and who had been an active user of the PACE program for at least 1 year prior to his/her first antihypertensive prescription. To avoid considering antihypertensive drugs prescribed for other indications, we required that study patients have a recorded diagnosis of hypertension.

We recorded data on all other PACE prescriptions filled by these patients since 1994, as well as all diagnoses recorded in all outpatient and inpatient encounters or reflected in medications used (eg, insulin for diabetes) during the period 1994-2001. In this way, we identified the presence of diabetes mellitus, congestive heart failure (CHF), history of myocardial infarction (MI), asthma, chronic obstructive pulmonary disease (COPD), angina, nephropathy, or benign prostatic hypertrophy.

Substitution Analysis

In keeping with current guidelines, we considered thiazides to be appropriate first-line hypertension therapy for patients without specific contraindications or indications for another drug. The JNC VII report includes specific indications for certain classes of antihypertensives,[14] which we incorporated. For patients with CHF or diabetes and nephropathy, we considered ACE inhibitors to be indicated as first-line therapy.[14,27-30] For patients with a history of ischemic heart disease, we considered β-blockers as first-line therapy,[14,31] except in patients with diagnoses of asthma, COPD, or CHF. Angiotensin receptor blockers were considered acceptable first-line agents in patients with diabetes and nephropathy.[32,33] We followed JNC VII in allowing α-blockers as potentially favorable treatment for hypertensive patients with prostatic disease,[14] although some evidence suggests that this may be a problematic strategy.[34,35] For patients with hypertension and angina, we classified calcium channel blockers as an acceptable therapeutic choice based on JNC-VII guidelines,[14] although other recommendations suggest use of β-blockers for most such patients.[36]

For each patient, we considered all comorbid conditions in assigning alternative antihypertensive medications when appropriate. If there were any current or prior prescriptions for a given medication, we assumed that the drug class was currently being used or had been tried previously and was abandoned due to ineffectiveness or adverse effects, and we did not assign it as a substitute. Medications were replaced on a prescription-for-prescription basis, assuming that compliance with the substitute regimen would be the same as compliance with the prescriptions actually filled, in keeping with recent data.[15] The FIGURE summarizes the basic logic used in assigning this replacement therapy. For patients without a significant comorbidity and with no history of thiazide use, we assigned thiazide as replacement therapy; we did the same for additional prescriptions for patients with comorbid conditions. For any patient with a relevant comorbidity who had no history of using the indicated first-line agent, we assigned that agent as a re-

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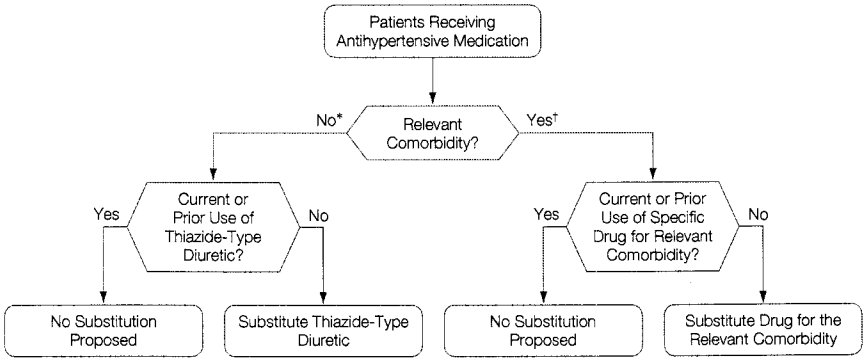
Figure. Substitution Algorithm



*For patients with no relevant comorbidity, guidelines recommend initial treatment with a thiazide-type diuretic.[14]

†For patients with a relevant comorbidity,[14] guidelines recommend initial treatment with a specific drug based on the comorbidity.

No substitution was required of calcium channel blockers in patients with angina, of α-blockers in patients with benign prostatic hypertrophy, or of β-blockers in patients with asthma, chronic obstructive pulmonary disease, or congestive heart failure (CHF). For patients taking angiotensin receptor blockers, no substitution was required if diabetes was present or if CHF was present and angiotensin-converting enzyme (ACE) inhibitors had been prescribed previously. For patients with a history of ischemic heart disease and either diabetes or CHF, ACE inhibitors were used as the primary substitution. If the specific drug group recommended for a relevant comorbidity (see "Methods" section of text) had been used previously, a determination was made of whether a thiazide-type diuretic had also been used in the past. If there was no evidence of thiaizide use, that drug was substituted. If there was no substitution made for a given drug and a second drug was present in the regimen, the algorithm was applied to the second agent as above. Only 1 substitution was made for any individual regimen.

Table 1. Characteristics of Study Population (N = 133 624)

Characteristics	No. (%) of Patients
Age, y*	79.8 (6.8)
Sex	
Female	111 425 (83.4)
Male	22 199 (16.6)
Race/ethnicity	
White	123 394 (92.3)
Black	8702 (6.5)
Other	1528 (1.1)
Comorbidities	
Congestive heart failure	74 284 (55.6)
Ischemic heart disease	61 302 (45.9)
Diabetes	
Total	60 462 (45.3)
With nephropathy	19 054 (14.3)
Angina	59 372 (44.4)
Asthma/COPD	58 027 (43.4)
Benign prostatic hyperplasia	15 387 (11.5)
Year of earliest PACE prescription	
2001	1019 (0.8)
2000	7198 (5.4)
1999	7534 (5.6)
1995-1998	32 322 (24.2)
1994	85 551 (64.0)

Abbreviations: COPD, chronic obstructive pulmonary disease; PACE, Pharmaceutical Assistance Contract for the Elderly.

*Age data are expressed as mean (SD).

placement. For patients receiving combination agents, we used the same logic but continued use of combination drugs. For example, if a patient with CHF was using a calcium channel blocker–ACE inhibitor combination, we assumed replacement with a thiazide–ACE inhibitor combination.

Cost Calculations

We calculated the average per-day cost of each medication class to be substituted, as measured by the average amount PACE paid to pharmacies. The daily cost of thiazides or β-blockers reflected use of generic hydrochlorothiazide or atenolol, respectively. The average cost of ACE inhibitors was that for lisinopril, the least expensive and most often used ACE inhibitor during the study year. For combination agents, we calculated the average per-day cost of the most commonly used combination product in a given category. The cost per day was averaged over all doses of a given medication. We then recalculated the cost of each patient's alternative regimen, using evidence-based substitutions as outlined herein and in the Figure. For both the actual and replacement costs, we subtracted 16% to account for manufacturers' rebates.

To incorporate other health care costs of hypertension treatment, we also included the laboratory costs (calculated from laboratory claims data in the study population) associated with these replacements. For thiazides, we assumed that potassium would be checked twice yearly[37]; for ACE inhibitors, we assumed that both potassium and creatinine would be checked twice yearly.[37] Patients taking thiazide diuretics often need potassium replacement. We calculated the average cost of generic long-acting potassium tablets or capsules based on more than 75 000 prescriptions covered by PACE in 2001. Using findings from the Systolic Hypertension in the Elderly Program (SHEP) trial, we assumed that 30% of patients taking thiazides would require potassium supplements[38,39] and added this cost to the cost of thiazide therapy.

We then calculated the amount paid by the PACE program in the study year for each patient's actual regimen and compared it with the total amount that the evidence-based regimen would have cost the health care system for each patient.

Alternate Cost Calculations

In Medicaid, the prices of generically available drugs are fixed at a lower level by "maximum allowable cost" (MAC) pricing.[18] In secondary analyses, we evaluated the additional impact of using MAC-level pricing for ACE inhibitors. In other analyses, we also varied the percentage of patients taking thiazide diuretics who would require potassium supplements.

RESULTS

Existing Antihypertensive Regimens

Of approximately 201 000 PACE participants, 133 624 (66%) had a diagnosis of hypertension and filled 2 051 281 antihypertensive drug prescriptions during the study year, an average of 15.4 prescriptions per patient. TABLE 1 shows the basic demographic characteristics of this population and the frequency of major comorbid conditions. Table 1 also shows the earliest

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year for which PACE data were available for these patients. Nearly two thirds of patients (n=85 551) had a history in PACE extending to 1994; an additional 32 322 (24.2%) had 3 to 6 years of prior history in PACE. The 2001 program expenditure for antihypertensives (after adjustment for rebates) was $48.5 million, or $363 per patient. For prescriptions costing less than the $6-per-prescription co-payment, the program paid nothing, but data on medication type and quantity were recorded. Including co-payments, total spending for antihypertensive medications by the program and patients was about $60 million.

TABLE 2 summarizes by class the number of prescriptions, amount paid, and average cost across all prescriptions. Calcium channel blockers had the highest average cost ($33.39 per prescription) and the highest total spending ($17 million); ACE inhibitors were the second costliest class ($10.5 million). β-Blockers were the most commonly prescribed antihypertensive drug, but average cost ($15.62) and total spending ($8.0 million) were lower than for ACE inhibitors or calcium channel blockers. Thiazides were among the least expensive medications ($5.33 per prescription) but accounted for only 4.3% of prescriptions.

TABLE 3 presents the numbers of patients in several major clinical categories who were and were not prescribed first-line antihypertensive medications. Among patients with CHF, ischemic heart disease, and diabetes with nephropathy, we found no history of use of a first-line medication for 33% to 38%. Of patients with no major comorbidities, 82% had no history of use of a thiazide-type diuretic.

Table 2. Total Prescriptions and Spending by Drug Class, PACE, 2001

Drug Class	No. of Prescriptions Filled	Mean Cost per Prescription, $*	Total PACE Program Spending, $
Calcium channel blockers	508 991	33.39	16 996 846
Angiotensin-converting enzyme inhibitors	413 590	25.29	10 460 811
β-Blockers	514 810	15.62	8 043 137
All combination products	259 991	21.42	5 569 422
Angiotensin receptor blockers	128 418	33.23	4 266 738
α-Blockers	59 648	25.55	1 524 164
Miscellaneous	40 688	19.80	805 457
Diuretics			
Thiazides	88 032	5.33	469 567
Other	26 804	11.73	314 409
Vasodilators	10 309	3.98	41 074
Total†	**2 051 281**	23.64	**48 491 626**

Abbreviation: PACE, Pharmaceutical Assistance Contract for the Elderly.
*Not including co-payment.
†Data may not sum because of rounding.

Substitution Analysis

For 815 316 prescriptions (40% of total), an evidence-based replacement medication appeared clinically appropriate after review of all of a patient's recorded diagnoses and drug use history. The algorithm identified a lower-cost agent for 631 951 of these prescriptions (31% of total). In 183 365 prescriptions (9% of the total), the replacement (primarily ACE inhibitors) would have cost more than the existing prescription. If all of the substitutions were made, spending on antihypertensive medications and associated laboratory tests would have decreased by $11.6 million in the study year (24% of the program's antihypertensive drug spending), an annual cost reduction of $8.7 million per 100 000 patients treated for hypertension.

TABLE 4 summarizes the projected changes in drug use by drug class. Substitution appeared appropriate for about half of calcium channel blocker prescriptions (244 645 [48%]); the greatest savings came from 140 600 prescriptions that could have been replaced with thiazides, saving $4.32 million. Of existing ACE inhibitor prescriptions, 94 060 (23%) appeared replaceable by thiazides, with associated spending reduction of $2.05 million (20% of spending on ACE inhibitors). In 71 885 β-blocker prescriptions (14%), there was an indication for substitution by an ACE inhibitor, which would have increased spending by $570 000. Most of the $701 622 spending reduction for combination agents was accounted for by calcium channel blocker–ACE inhibitor combinations that could have been replaced with combinations containing thiazides.

Alternative Analyses

Over time, the price of generic ACE inhibitors should continue to fall, so we also considered the potential impact of MAC-level pricing, as used by Medicaid in most states,[18] by recalculating the potential costs if all replacement ACE inhibitors had been priced at the average cost paid by the Pennsylvania Medicaid program for a generic ACE inhibitor. This resulted in a larger reduction in spending of $15.8 million, or 33% of program spending on hypertension. If the MAC price had been used not just for substitution but in place of all brand-name ACE inhibitor prescriptions (analogous to a reference-pricing approach[40]), spending would have declined by another $4.7 million, increasing the total savings to $20.5 million, or a potential reduction of 42% of spending for antihypertensive medications.

If all thiazide users required potassium replacement, the potential savings would have decreased slightly to $10.20 million; if only 20% required potassium replacement, the potential savings would have increased to $11.85 million.

COMMENT

We reviewed the medication choices and costs of antihypertensive regimens in typical elderly patients in a

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large state drug assistance program over a 1-year period and measured the cost implications of evidence-based drug substitution when clinically appropriate in light of their medical histories. A large proportion of existing prescribing for hypertension was outside of published guidelines. Adherence to established guidelines for treating hypertension would have resulted in considerable savings to the health care delivery system ($11.6 million per year, or nearly a quarter of program antihypertensive medication costs). While some controversy persists regarding the precise details of which agents are best for first-line therapy, the broad outline of the approach presented herein would be applicable to most currently proposed evidence-based guidelines with only minor modifications.

There are many possible reasons for this large divergence between routine practice on the one hand and clinical trial data and evidence-based recommendations on the other. Foremost among these is the vigorous marketing of newer, more costly agents compared with virtually no marketing for older, off-patent drugs. Such marketing affects both physician prescribing choices and patient preferences. It is not clear from these analyses to what extent patient vs physician factors cause these findings; this is an important area for future research.

These findings could have considerable national impact. We found potential savings of $87.14 per patient treated for hypertension; the level of per-patient spending on antihypertensive medication in our population is similar to that found in other research.[41] According to the National Center for Health Statistics, in 2000 almost 22 million elderly Americans had hypertension.[42] Survey data indicate that 63% of older hypertensive patients are being treated,[43] translating to more than 13.5 million elderly patients taking antihypertensive medication. Applying our findings to that population corresponds to a decrease in spending for antihypertensive medications of about $1.2 billion per year.

The ALLHAT results[15] indicate that these changes would have been preferred on clinical as well as financial grounds, although some controversy persists about the role of ACE inhibitors vs thiazides in some subgroups.[16,44] As lower-priced ACE inhibitors become more widely available, such evidence-based prescribing would reduce the cost of antihypertensives by at least $2 billion to $3 billion annually.

These data must be viewed in light of several considerations. While we made many conservative assumptions in our estimates of potential therapeutic substitutions, we did not interview or examine the patients, review their primary medical records, or communicate with their physicians. As a result, we were not able to completely

Table 3. Prevalence of Previous or Current First-Line Medication Use by Clinical Category

Condition (First-Line Therapy)	No. of Patients	No. (%) With No Previous or Current Use of First-Line Therapy	No. Receiving First-Line Therapy in 2001	No. Who Received First-Line Therapy Before 2001 but Not in 2001
Congestive heart failure (ACE inhibitor)	74 284	28 233 (38.0)	31 568 (42.5)	14 493 (19.5)
Ischemic heart disease (β-blocker)	61 302	23 031 (37.6)	29 716 (48.5)	8555 (14.0)
Diabetes with nephropathy (ACE inhibitor)	19 054	6288 (33.0)	8246 (43.3)	4520 (23.7)
No major comorbidity (thiazide)	28 442	23 240 (81.7)	3456 (12.2)	1746 (6.1)

Abbreviation: ACE, angiotensin-converting enzyme.

Table 4. Potential Savings by Drug Class

Originally Prescribed Drug Class	No. of Prescriptions	Substitute Drug: More Expensive Than Initial Medication	Substitute Drug: Less Expensive Than Initial Medication	Initial Spending, $	Alternative Spending, $	Potential Reduction (Increase) in Spending, $ (%)	Reduction (Increase), %
Calcium channel blockers	508 991	27 432	217 213	16 996 846	11 357 475	5 639 371	33.2
Angiotensin-converting enzyme inhibitors	413 590	4279	116 123	10 460 811	7 951 446	2 509 365	24.0
β-Blockers	514 810	80 957	111 328	8 043 137	7 097 307	945 830	11.8
All combination products	259 991	2927	43 931	5 569 422	4 867 800	701 622	12.6
Angiotensin receptor blockers	128 418	5584	87 481	4 266 738	2 645 424	1 621 314	38.0
α-Blockers	59 648	7871	22 204	1 524 164	1 102 132	422 032	27.7
Miscellaneous	40 688	12 782	19 998	805 457	502 370	303 087	37.6
Diuretics							
Thiazides	88 032	22 845	1862	469 567	825 492	(355 925)	(75.8)
Other	26 804	11 953	10 799	314 409	372 746	(58 337)	(18.6)
Vasodilators	10 309	6735	1012	41 074	124 934	(83 860)	(204)
Total*	**2 051 281**	**183 365**	**631 951**	**48 491 626**	**36 847 126**	**11 644 500**	24.0

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eliminate the possibility of contraindications for a substitute regimen or hidden indications for the regimens actually prescribed. Diagnoses based on visits, hospitalizations, and filled prescriptions are not as accurate as those measured by review of the primary medical record, but they are a useful way to track whether a given patient ever had a diagnosis of the conditions we studied. We included data on prior prescriptions back to 1994 but could not exclude the possibility that some patients may have taken a first-line agent prior to 1994. We did not define a patient-specific replacement dose when switching a given patient to an evidence-based regimen, and we used the average dose of all prescriptions for each major drug class. Finally, we did not directly address issues of patient adherence[45,46] but assumed that a given patient would comply approximately the same with one regimen as with another. This assumption has been borne out by the results of the ALLHAT study,[15] which even showed a slight adherence advantage for thiazides.

The JNC VII guidelines on which we based this analysis were published in 2003.[14] However, these were quite similar to the recommendations published in JNC VI, which appeared in 1997.[47] The main difference was that JNC VII no longer recommended β-blockers as equivalent to thiazides as first-line treatment for uncomplicated hypertension.[14] While our findings focus on the potential savings from application of the JNC VII recommendations, the results apply equally well if the JNC VI guidelines, which were current at the time of the prescriptions studied, are used as the basis for the analysis.

While we cannot conclude that a given substitution would have been appropriate in any given patient, it is overwhelmingly likely based on extensive clinical trial data that the proposed substitutions would have been clinically reasonable in a large proportion of hypertensive patients. Not all patients will tolerate first-line therapy. In ALLHAT, the 1-year cessation rates were 12.9% for thiazide-type diuretics and 17.6% for ACE inhibitors,[15] and in recent trials of β-blockers, the cessation rate was about 27%.[48,49] Applying these rates to our projections and assuming that the same proportions of patients who switched to these regimens would revert to their previous medications would reduce the potential savings by $1.7 million, to $9.9 million. This amount still represents a 20.5% decrease in program spending for antihypertensive medications.

These estimates of potential savings are conservative in several ways. Since many thiaizides cost less than 8¢ per tablet, patients filling these prescriptions would pay less than the $6 co-payment required for costlier prescriptions. Thus, for many of the 430 514 prescriptions for which thiazide replacement was suggested, patients would also have paid less out of pocket, in addition to the program savings described.

We were also conservative in making exceptions for recommended therapy. We excluded patients from substitution if they had filled even 1 previous thiazide prescription. Many of these patients likely did not have intolerable adverse effects and may well have been able to use thiazides instead of more expensive antihypertensives, resulting in greater savings, but we did not consider this possibility. Similarly, we followed the JNC VII guidelines and considered any diagnosis of angina as an acceptable indication for maintaining calcium channel blocker treatment,[45] even though other guidelines prefer β-blockers as in such patients.[36,45] Likewise, patients with a diagnosis of benign prostatic hypertrophy may have prostatic enlargement without urinary symptoms or may have already had surgical correction of the condition. Nevertheless, we used the JNC VII guidelines, which considered α-blockers an acceptable therapeutic choice in such patients, although evidence from ALLHAT would suggest replacing many of these α-blocker prescriptions with thiazides.[34,35]

Bringing medication use closer to established practice guidelines would require some initial costs for physician education as well as some additional office visits at first as patients' prescriptions are converted to new antihypertensive medications. Recent research addressed this problem directly in examining the effect of a reference-pricing system and found that the costs of additional physician visits associated with switching patients' antihypertensive therapy were very small in relation to the savings achieved.[40] Although additional costs might be incurred when patients switch drug classes, the savings from these changes would continue over years of subsequent drug use, offsetting these modest initial implementation and transition costs.

Overall drug spending for Medicare beneficiaries in 2002 was projected at $87 billion,[3] and addition of a Medicare prescription drug benefit will add substantially to this cost; estimates of the eventual cost of this program have already increased dramatically from $400 billion over 10 years to more than $530 billion.[8] Initiatives to improve prescribing could result not only in better clinical outcomes but also in lower spending on medications for hypertension and, potentially, for other conditions as well. Such rationalization of prescribing could make the difference between programs that are fiscally viable and those that are not.[50]

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Study concept and design: Fischer, Avorn.
Acquisition of data: Avorn.
Analysis and interpretation of data: Fischer, Avorn.
Drafting of the manuscript: Fischer.
Critical revision of the manuscript for important intellectual content: Avorn.
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Feature

What have we learnt from Vioxx?

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In October UK patients who had cardiovascular events while taking rofecoxib lost the right to fight Merck in the US for compensation. But researchers and journals can still benefit from this case if they learn from the mistakes, write ***Harlan Krumholz and colleagues***

Rofecoxib (Vioxx) was introduced by Merck in 1999 as an effective, safer alternative to non-steroidal anti-inflammatory drugs for the treatment of pain associated with osteoarthritis. It was subsequently found to increase the risk of cardiovascular disease and withdrawn from the worldwide market. Merck now faces legal claims from nearly 30 000 people who had cardiovascular events while taking the drug.[1] The company has stated that it will fight each case, denying liability.[2] Our recent participation in litigation at the request of plaintiffs provided a unique opportunity to thoroughly examine and reflect on much of the accumulated court documents, research, and other evidence. This story offers important lessons about how best to promote constructive collaboration between academic medicine and industry.

Early suspicion of cardiovascular risk

Since the early development of rofecoxib, some scientists at Merck were concerned that the drug might adversely affect the cardiovascular system by altering the ratio of prostacyclin to thromboxane, which act in opposition, balancing blood flow and clotting.[w1] A study sponsored by Merck during 1996-7 reported that rofecoxib reduced urinary metabolites of prostacyclin in healthy volunteers by about half.[w2] In internal emails made public through litigation,[3] Merck officials sought to soften the academic authors' interpretation that cyclo-oxygenase-2 (COX 2) inhibition within the vascular endothelium may increase the propensity for thrombus formation, the basis of what became known as the FitzGerald hypothesis.[w3] The academic authors changed the manuscript at Merck's request—for example, they changed "systemic biosynthesis of prostacyclin ... was decreased by [rofecoxib]" to "Cox-2 may play a role in the systematic biosynthesis of prostacyclin."[3 w2] To the authors' credit, they continued to investigate the effects of COX 2 inhibition and ultimately provided much of the basic science knowledge that clarified the pathways by which rofecoxib probably leads to cardiovascular events.[w4-w7]

However, despite Merck's knowledge that rofecoxib might increase thrombus formation, none of the intervention studies that constituted its new drug application to the Food and Drug Administration in 1998 were designed to evaluate cardiovascular risk. The nine studies were generally small, had short treatment periods, enrolled patients at low risk of cardiovascular disease, and did not have a standardised procedure to collect and adjudicate cardiovascular outcomes.[4] Moreover, Merck seemingly pooled data from these studies and others for analysis of cardiovascular risks, despite FDA concern,[5] and disseminated the results to promote the drug's cardiovascular safety to doctors in its "cardiovascular card,"[6 7] a marketing device cited by US Congressman Henry Waxman for falsely minimising cardiovascular risks[8] and never approved by the FDA.

The VIGOR study

In January 1999, Merck launched its largest study yet of rofecoxib, the Vioxx gastrointestinal outcomes research (VIGOR) study. The study was intended to expand the drug's approved indications by showing that it would have fewer gastrointestinal side effects than naproxen for the treatment of rheumatoid arthritis. The study of over 8000 patients was initiated without a standard operating procedure for collecting information on cardiovascular events and without a cardiologist on the data safety monitoring board. Data safety monitoring boards are independent committees whose purpose is to monitor the results of an ongoing trial to ensure the safety of trial participants.[w8] The study was designed to continue until a predetermined number of confirmed uncomplicated or complicated gastric perforations, ulcers, or bleeds had occurred.

The first non-endpoint safety analysis was presented to the safety board in November 1999, at which time a 79% greater risk of death or serious cardiovascular event was found in one treatment group compared with the other (P=0.007).[9] The board allowed the study to continue and planned to review subgroup analyses in December, at which time the analyses again showed higher cardiovascular risk in one group. On this basis the board recommended that an analysis plan be developed to examine serious cardiovascular events and that the study continue until it reached its gastrointestinal endpoint target (expected March 2000).

Matters were complicated by the existence of conflicts of interest among board members. According to Merck policies, the board is supposed to be independent, without financial or emotional stake in the trial being monitored.[10] Yet, the head of the VIGOR board was awarded a two year consulting contract two weeks before the trial ended and as the trial was concluding disclosed family ownership interest in Merck shares worth $70 000 (£37 000; € 55 000).[11 12] Although it is not possible to tell whether this financial relationship made any difference, the conflict of interest was not a matter of public record at the time the trial was conducted or published and of itself calls into question the independence of the safety board.

The VIGOR study had enormous financial implications for Merck. If it showed rofecoxib to have better gastrointestinal safety than naproxen, it could be used to petition the FDA for a new indication. However, if the study raised concerns about cardiovascular harm, the billion dollar drug franchise would be threatened. The study showed that rofecoxib was not more effective in relieving symptoms of rheumatoid arthritis but did halve the risk of gastrointestinal events. However, there was also evidence of an increased risk of myocardial infarction (relative risk 5.00, 95% confidence interval 1.68 to 20.13). When this result was circulated internally at Merck, Edward Scolnick, the company's chief scientist, wrote in an email to colleagues about the cardiovascular risk: "It is a shame but it is a low incidence and it is mechanism based as we worried it was. [Merck employees/consultants] were right about the metabolite meanings, ie, urine [prostacyclin] data."[13] This indicates that, at the least, there were grounds for suspicion within Merck before the VIGOR study was published that Vioxx was associated with cardiovascular risk.

Obscuring the risk

Despite the concern articulated by Dr Scolnick, the published VIGOR study obscured the cardiovascular risk associated with rofecoxib in several ways. The report contained data from an interim analysis that had different termination dates for cardiovascular and gastrointestinal events (gastrointestinal events were counted for one month longer than the cardiovascular events). This highly irregular procedure was not described in the publication and had the effect of favouring the drug's effect on gastrointestinal events while understating the risk of cardiovascular events.[w9] The published cardiovascular risk was not accurate because three additional myocardial infarctions occurred in the rofecoxib group in the month after the researchers stopped counting cardiovascular events (none had occurred in the naproxen group). The potential harm was further minimised by a post hoc subgroup analysis based on "indication for aspirin prophylaxis"; had Merck included the three cases, the subgroup analysis would have shown an increased cardiovascular risk in both groups.[w10]

The publication concealed the cardiovascular risk even further by presenting the hazard of myocardial infarction as if naproxen was the intervention group (relative risk 0.2, 0.1 to 0.7) and without reporting the absolute number of cardiovascular events, even though all other results were presented appropriately with rofecoxib as the intervention group.[w11] Finally, the authors proposed a naproxen hypothesis, suggesting that rofecoxib had not been harmful but that naproxen had been protective, despite there being no accepted evidence that naproxen had a strong cardioprotective effect.

Merck strongly promoted the VIGOR study, purchasing nearly 1 million reprints to circulate to doctors and other health professionals. The *New England Journal of Medicine* reported problems with the study in an "expression of concern" published in 2006,[w10] and the editor in chief has said that the authors "withheld critical data on the cardiovascular toxicity of Merck's drug Vioxx."[14] Nevertheless, none of the authors has publicly conceded error or taken responsibility for the biased presentation of the study results. In fact, two VIGOR authors and the head of the VIGOR board continue to collaborate on high profile research with Merck.[15]

Except for a 2001 study published in *JAMA* that raised questions about the safety of rofecoxib and the validity of the naproxen hypothesis,[w12] few academic researchers publicly questioned the company before its voluntary withdrawal of the drug. Moreover, Merck selectively targeted doctors who raised questions about the drug, going so far as pressurising some of them through department chairs.[16]

Short and long term use

For several years, Merck continued to investigate other indications for rofecoxib and conducted additional trials. The increased cardiovascular risk compared with placebo was reported in a 2004 analysis of the adenomatous polyp prevention on Vioxx (APPROVe) study,[w13] which led to the drug's withdrawal. The financial implications were immense not only because of loss of revenue but also because of expected litigation. The key question was when the risk became manifest. If short term use was not associated with increased cardiovascular risk, Merck's liability would potentially be drastically reduced.

The APPROVe authors, five of whom were Merck employees and the remainder of whom received consulting fees from Merck, asserted that the increased risk became apparent only after 18 months of use.[w13] This conclusion was based on an analysis that was not prespecified and a flawed methodological approach. Merck subsequently admitted that it had incorrectly described the statistical approach, and the *New England Journal of Medicine* issued a correction indicating that statements regarding an increase in risk after 18 months should be removed from the article.[w14] Again, mistakes that favoured the company, with colossal economic implications, made it through the journal peer review process to the profession and the public.

Medical journals

The *New England Journal of Medicine* has had a prominent role in the story. It published the VIGOR and APPROVe studies, responding to their inaccuracies with "an expression of concern"[w9 w10] and a correction[w14] and publishing a methodological paper[w15] and other related comments and editorials.[w16-w24] But other academic medical journals also played important parts. In 2001, *Circulation* published a pooled analysis of 23 phase IIb-V studies examining the association between rofecoxib and cardiovascular risk. The paper had no editorial commentary or critique,[w25] even though the study was coordinated internally at Merck, the results highly favoured the safety of rofecoxib, and five of the seven authors were Merck employees (the two academic authors acknowledged being paid consultants to Merck). Moreover, in internal emails made public through litigation, even an executive scientist at Merck criticised the analysis, stating: "The data appears to have been interpreted to support a preconceived hypothesis rather than critically reviewing the data to generate hypotheses."[17]

The *Annals of Internal Medicine* published the assessment of differences between Vioxx and naproxen to ascertain gastrointestinal tolerability and effectiveness (ADVANTAGE) study.[w26] It later learnt that article was written by Merck without accreditation,[w27 w28] contained errors in the presentation of cardiovascular events with rofecoxib (minimising cardiovascular risk), and was conducted for marketing purposes, a so called seeding trial. The journal was quick to condemn ghostwriting[w29] and a full correction of the errors was published recently[w30] after Merck scientists provided an initial, but incorrect explanation.[w31] Many other journals have published articles with results favourable to rofecoxib that court documents have shown to be ghostwritten by scientific writing companies hired by Merck.[w32-w36]

Promoting constructive collaboration

The rofecoxib case is bad news for industry, academics, journals, and the public. Merck was once one of the US's most publicly admired companies,[w37] and its behaviour may not be different from that of others in the pharmaceutical or biotechnology industry. Journalists have questioned the ethics of industry and academic researchers.[18 19 20] And yet, there is hardly a sense of outrage in the profession about the events that transpired.

Defenders of Merck may say that we do not know how rofecoxib's cardiovascular risk compares with that of other COX 2 inhibitors or traditional non-steroidal anti-inflammatory drugs. But the proper place of these drugs in the medical armamentarium is beside the point. With billions of dollars at stake, Merck conducted the trials, stored and analysed the data internally, paid academic researchers as consultants to the investigative teams and the safety monitoring boards, and maintained heavy involvement in the writing and presentation of findings. The journals published the studies, and the academic community accepted the findings without expressing much concern. Nearly 107 million prescriptions for rofecoxib were dispensed in the US between 1999 and September 2004,[21] when the drug was withdrawn from the market, and none of the people picking up those prescriptions had the opportunity to consider the true balance of its risks and benefits.

What should we do going forward? Academic medicine, industry, medical journals, and government agencies need to come together to define a set of principles by which we can restore faith in collaborations on new treatments that can improve patient care. We might consider adopting some new approaches. Academics engaged in industry designed and sponsored studies should insist that the data are stored on an academic site, analysed by non-company investigators, and eventually made accessible to the public for scrutiny. Several early, large clinical trials of rofecoxib were not published in the academic literature for years after Merck made them available to the FDA,[22] preventing independent investigators from accurately determining its cardiovascular risk using meta-analysis. In addition, independent audits should be conducted to ensure that companies follow a standardised, prespecified protocol.

Independent data and safety monitoring boards should be mandated and their governance should not be under the control of the company. Industry should not be allowed to select who serves on these boards or allowed to compensate members after their service.

In considering articles for publications, journals should understand that studies with immense financial implications require a higher level of scrutiny than others, especially when the study is conducted by the company with the financial stake. Journals should be prepared to go beyond the usual high quality review, paying particular attention to the possibility of bias. Articles should be accompanied by editorials by people without financial conflicts of interest. Moreover, ghostwriting constitutes a false statement of authorship or a false attribution of authorship, and academic researchers who sign off or "edit" original publications or reviews written by industry should be penalised unless there is full disclosure of the authorship, such as: "Representatives from *XYZ* drafted the manuscript; the authors were responsible for critical revisions of the manuscript for important intellectual content."

Even the best oversight cannot always detect mistakes. When journals discover that information has been withheld or that results are incorrect, they need to rapidly disseminate that information and ensure that any web search that identifies the errant manuscript also identifies the correction. Authors should sign agreements that they will notify journals if such information becomes available or face being blacklisted by the journal.

Our system depends on putting patients' interests first. Collaborations between academics, practising doctors, industry, and journals are essential in advancing knowledge and improving the care of patients. Trust is a necessary element of this partnership, but the recent events have made it necessary to institute proper systems that protect the interests of patients. A renewed commitment by all those involved and the institution of these systems are the only way to extract something positive from this unfortunate affair.

Summary points

Merck faces legal claims from nearly 30 000 people who had an adverse cardiovascular event while taking rofecoxib (Merck denies liability)

Published studies of the drug obscured the risk

Merck had influence over all aspects, including data analysis, safety monitoring, and reporting

Academic medicine, industry, medical journals, and government agencies need to define a set of principles to restore trust in collaborations on drug development

References w1-w37 are on bmj.com

Contributors and sources: HMK's research is focused on determining optimal clinical strategies and identifying opportunities for improvement in the prevention, treatment, and outcome of cardiovascular disease with emphasis on older populations. He was responsible for the concept and writing of this article and is its guarantor. JSR has studied and reported on conflict of interest in medicine. He participated in the concept and design of this article and revised it for critical content. AHP has research interests in the history of public health and law, including pharmaceutical research and marketing. He consults on this topic at the request of plaintiffs in the Vioxx litigation. He contributed document research and interpretation to this article and participated in its revision. DSE has studied and reported corporate corruption of science. He contributed to the development of this article and revised the work for critical content. This article arose from access to Merck documents as a result of tort litigation.

Competing interests: HMK has research contracts with the American College of Cardiology and the Colorado Foundation for Medical Care; serves on the advisory boards of Amgen, Alere, and UnitedHealthcare; is a subject expert for VHA; and is editor in chief of *Journal Watch Cardiology*. All authors have been consultants at the request of plaintiffs for recent suits against Merck related to rofecoxib.

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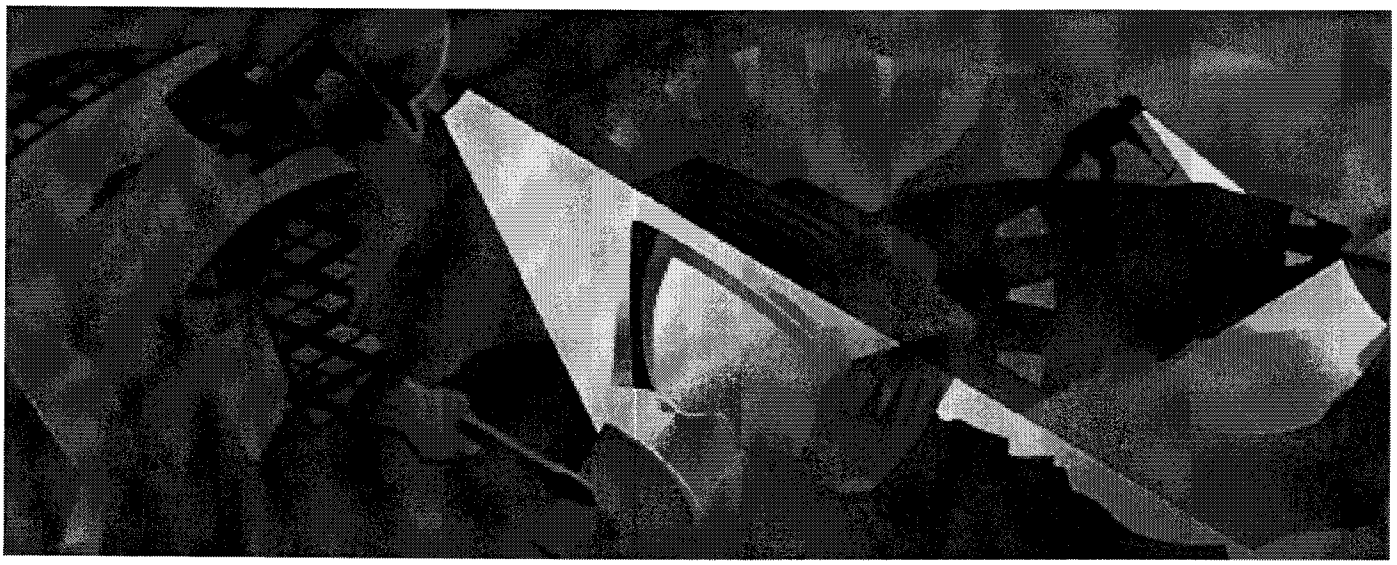

USING DATA MINING TO GET BRAND SWITCHING

by Susan Neyhart

This is an actual case history from the files of IMS America. The names of the products and companies involved have been changed to protect the client's privacy in a competitive market. Otherwise, the data associated with the products and the market are accurate.

The company with the insight and resources to quickly capitalize on marketing opportunities has a true competitive edge. A major prescription pharmaceutical company, which we will call Maxwell Pharmaceuticals, found a news-breaking opportunity and capitalized on it. The company's product, which we'll call Statwell, faced competition by a new product, which we'll call Taracet. Statwell was losing ground. Then, a prominent medical journal published a clinical study citing side effects linked to Taracet. The impact on the market was greater than expected by competitors — including Maxwell.

Maxwell knew that it needed to address this news event immediately. It had to ensure that there was no negative spill-over effect on its brand. It had to position both Statwell and a new line extension squarely and positively against Taracet — in short, it had to respond to the marketing opportunity.

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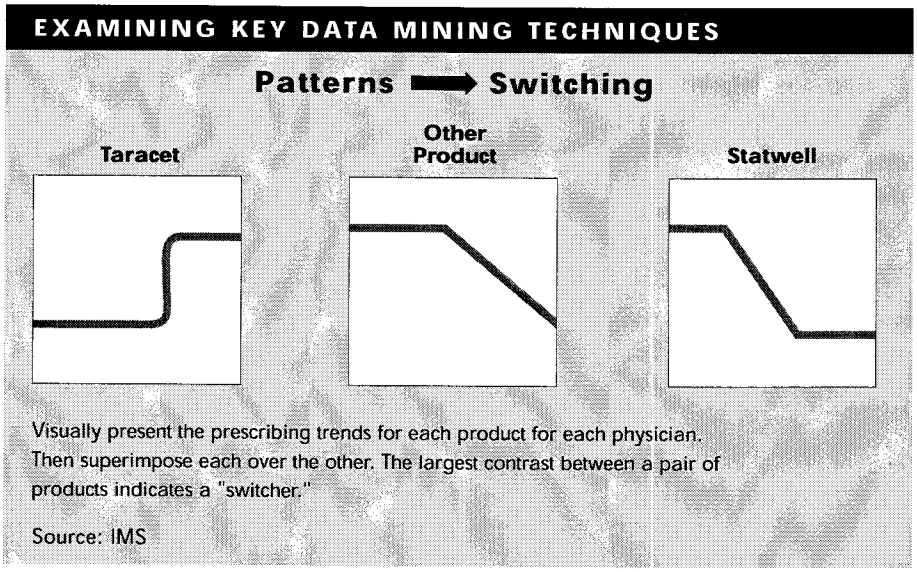
EXECUTIVE SUMMARY:

Negative press for a competing product created an opportunity for brand switching. Here's how one company used sophisticated "data mining" techniques to address the situation and achieve effective results.

Some market background

Maxwell Pharmaceuticals is fortunate to have a product competing in a $1.5-billion chronic-care market. This market has considerable upside potential, with sales dollar growth of more than 20 percent each year. This consistent yearly increase is due to

FIGURE 1



incredible growth rates of the disease being treated. In the U.S. alone, five to seven percent of the population has the disease. In addition to its rapid growth, the market has seen two recent developments. First, the National Institutes of Health's (NIH) recommendation on stepwise therapy of the disease had changed. And second, the new product — Taracet — entered the market.

The NIH change had an immediate impact on Maxwell's product, Statwell, as well as on their competitors. The NIH reclassified these products from third-line to second-line therapy, used for moderate forms of the condition. Taracet is the only new product in this therapeutic area in the last 12 years.

Statwell was introduced several years ago, it holds a respectable 25-percent market share, and is the number-three product in its class. Six months after the launch of Taracet, Maxwell introduced a line extension of Statwell in an effort to expand its share of the market — resulting in only minor gains.

The launch of Taracet was backed by a $2 to $2.5 million per month detailing and journal advertising campaign — receiving the average share of voice for a new product. The campaign performed very well, particularly among key specialty groups. Awareness was reported at 95 percent and use at 75 percent after only four months on the market. As expected, Taracet most often displaced the top-three products in the class, including Statwell.

After 10 months on the market, Taracet had a share of about 15 percent with close to $70 million in total sales. However, the medical journal article concerning the side effects of Taracet created an adverse impact. The company marketing Taracet acted immediately, trying to lessen the effects of negative publicity.

Acting fast on breaking news

Maxwell examined how it could capitalize on the negative publicity, while preventing spill-over to its drug from the bad news. Designing and delivering custom messages was the essential part of its chosen strategy. While messages were to be delivered to selected prescribers by sales representatives, by "Dear Doctor" letters, journal advertising, and redesigned sample packaging — the central issue was what messages to what doctors?

The first step in developing a successful micro-marketing effort was to segment the market. It was determined that the best segmentation would be based on the recent switching behavior of target prescribers. The selected prescriber segments were:

1. Switched to Taracet
2. Switched to Statwell
3. Switched to another product in the market
4. Not switching and using Taracet
5. Not switching and not using Taracet

Hidden patterns reveal switching behavior

Maxwell used data mining and predictive software to develop the optimal audience for a successful micro-marketing campaign. The computerized approach and extensive database allowed identification of physicians who exhibited patterns of brand switching among the competing products. The company used data mining techniques to determine the pattern of switching and maximize the campaign's impact and results.

Maxwell turned to IMS America for use of a service called the Prescriber Brand Switching Application (PBSA) — allowing the company to know which physicians switched to and from Taracet (see Figure 1, above). PBSA is a software tool that finds predictive information hidden in large databases, typical of those in the information-rich pharmaceutical industry. Switching is identified by a prescriber's writing activity for selected products. In this particular application switching occurs between two brands, Taracet and Statwell. To identify switching behavior, a prescriber's Rx trend for one product is superimposed over his or her Rx trend for another product. The two trends are then compared.

The "degree of switch" is calculated using a mathematical formula — a switch index of 100 indicating a complete switch from one product to another — and 0

showing no switching at all. To spot these kinds of trend patterns, PBSA uses a common data mining technique called a "neural network," which resembles biologic neural networks in structure. Other data mining techniques include tree induction, genetic algorithms, nearest neighbor method, and clustering.

The tree induction technique uses "if-then" rules, based on statistical significance to distinguish between elements in a data set. It is especially useful in identifying characteristics that distinguish groups of prescribers who behave differently. One practical application would be to predict a prescriber's reaction to a promotional event, such as a dinner meeting or sales call.

Genetic algorithms are used to optimize allocation of promotional resources directed toward physicians. The technique determines the combination of promotions to "apply" to a set of prescribers that will maximize impact. The familiar technique of clustering divides a data set into mutually exclusive groups. Once groups are defined, unique marketing programs are directed toward each.

Rapid action, effective results

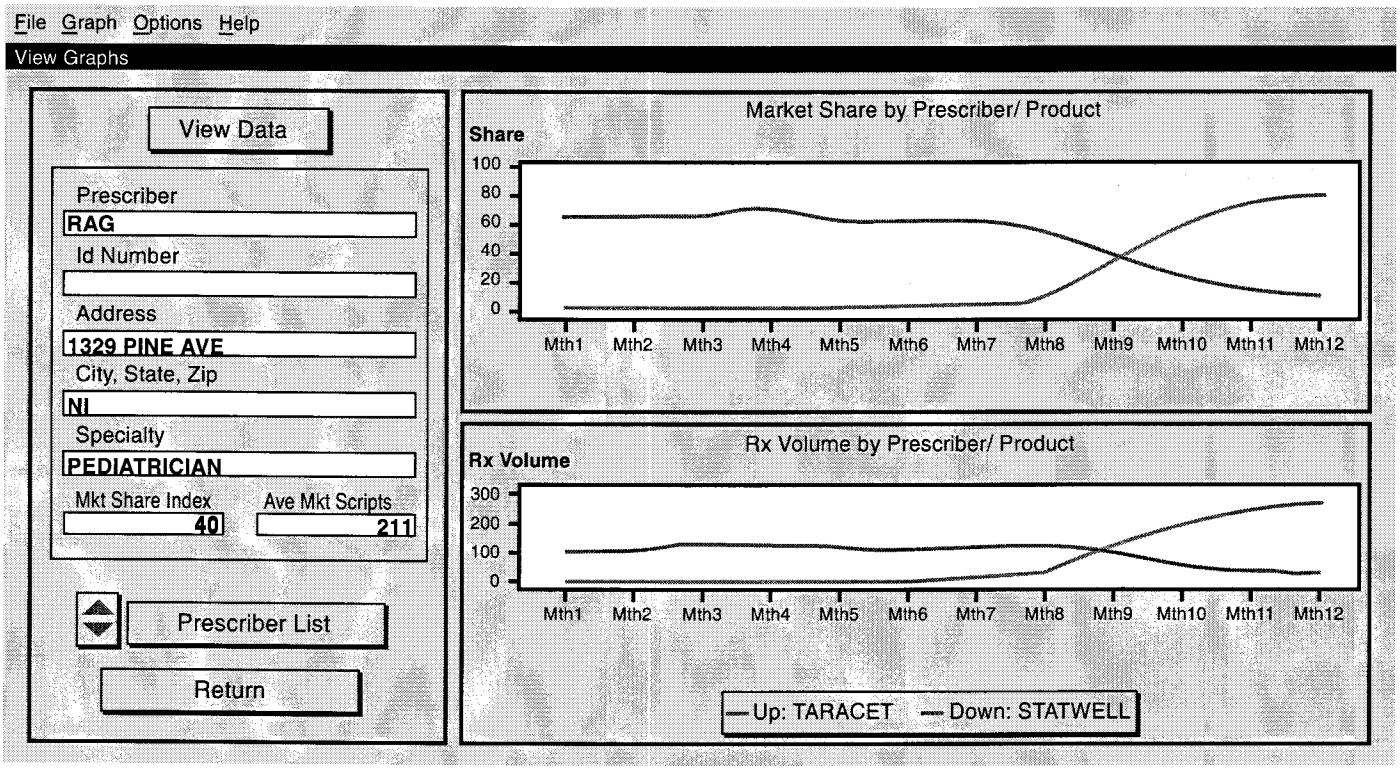
Maxwell Pharmaceutical acted fast. It set the market definition, established the time periods, and generated target lists — all within a week (see Figure 2, above). Maxwell then established appropriate message strategies for each of the five physician segments. When the lists were sent out to the field, implementing the strategy focused on delivering the customized message to each segment.

Feedback from field sales representatives was very positive. The customized messages produced results. The Taracet market share, which had reached over 19-share points prior to publication of the negative journal article, fell to 15.6 percent — the year's low. The share fall was aided by a 17-percent decrease in dollar volume over the average monthly sales of the previous quarter. A 13-percent decrease for the market as a whole also contributed to the decline.

With its targeted promotional "intervention," despite the overall market decline, Statwell maintained its market position at a strong 19-percent. That 19-percent share was up from a low of less than 18 percent four months earlier.

Rx trends of the targeted prescribers who received the custom messages awaits comprehensive analysis. It is clear, however, that data mining, analysis, and appropriate application of information can be effective in many marketing situations that require precise target lists. The result can be cost-effective promotion and improved market position for the product. □

FIGURE 2



Example of the graphic display of the prescribing activity for a "switcher."

NGP
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Same Market, New Opportunities

Moving Beyond "Share-Shift" Battles

BY LISA MORRIS, IMS HEALTH

There's an old story about a man who persisted in searching for his lost keys under the lamppost because "that's where the light was best." In the same way, pharmaceutical companies have searched for new business by concentrating on those market opportunities illuminated by traditional information sources (e.g., measures of total and new prescription share and volume, primary market research, etc.). Consequently, they have all too often had to compete for the same turf "under the lamppost."

By providing rich, quantifiable details on the diagnosis, testing, medical procedures, and pharmaceutical therapy for millions of de-identified patients,APLD familiarizes marketers with patient types and treatment practices, and allows them to evaluate the market from a number of different angles.This capability is critical in today's complex market, where making a sale involves
understanding and addressing the simultaneous interests of patients, payors, and prescribers. APLD provides pharmaceutical companies with a more precise, quantifiable view of the interactions between these key stakeholders.While dispensed prescription data will always be the gold standard for measuring market performance, and primary market research data will
Anonymized patient-level data (APLD), which provide a longitudinally-linked record of patients' medical and pharmaceutical care, provide detailed information on patient, payor, and provider dynamics, and represent a searchlight that can illuminate previously darkened areas of the market — areas that can hold the key to growth.

Lisa Morris leads development of IMS' APLD products and services, helping clients uncover new growth opportunities and
improve the efficacy of their sales and marketing programs. She can be reached at
lmorris@us.imshealth.com. always play a role in measuring attitudes and perceptions, APLD provides

added visibility that can allow companies to capitalize on opportunities that may go undetected by the competition, and move beyond "share-shift" battles.

Given the richness and precision afforded by its insights, APLD can and should be used to inform the full spectrum of a company's marketing activities, starting with the brand team's need to assess market size and performance, segment patients and physicians, make pricing and market access decisions, and develop and deliver key promotional messages. One of the unique benefits of this type of information is that it can not only be used by marketing teams to enhance their understanding of complex market dynamics, but it can also be used by sales organizations to better segment and reach physicians, better monitor product performance, and more effectively align sales compensation metrics with more granular marketing objectives. In this
manner, APLD allows marketing teams to develop measurable strategies and tactics based on a more robust understanding of their market that can be translated into actionable sales strategies and tactics that can be evaluated on an ongoing basis. It has the ability to unify companies' commercial activities by bridging the gap between primary market research (which is known for
providing rich insights, but does not lend itself to timely tracking and trending) and dispensed prescription data (which provides timely tracking and trending insights, but less richness around specific treatment behaviors).

Therefore, using APLD, pharmaceutical companies are better able to address the simultaneous interests of patients, payors and prescribers with a cohesive approach to the market. In this article we will explore how APLD can be used by companies to optimize their marketing activities. Specifically we will examine how APLD can be used to enhance two key marketing activities: assessment of market and competitive dynamics to identify new brand opportunities, and segmentation of patients to
inform/refine product positioning and messaging.

THE LIGHT DAWNS: A BIOLOGICS MANUFACTURER REVISES ITS COMPETITIVE SET

Sometimes, after observing how products are actually used in the real world, companies may rethink certain aspects of their marketing strategy. Let's examine how one large manufacturer used a better understanding of actual treatment patterns to reassess its competition, identify new opportunities to drive share, and ultimately refine its positioning and messaging.
A large biologics manufacturer was interested in understanding treatment patterns for moderate to severe psoriasis patients in order to validate its product positioning and overall marketing strategy.

Pre-launch primary market research with physicians seemed to suggest that physicians would consider using the product — which was indicated for those patients who were candidates for treatment with phototherapy or other systemics — as an alternative to phototherapy.The company was planning on positioning its product as a more efficacious alternative to phototherapy, a treatment that, like the company's biologic, was administered in doctors' offices.

To study real-world use, the company turned to APLD, the only source that tracks treatment across all ambulatory sites of care, as well as both drug and nondrug treatments (traditional prescription databases cannot accurately measure usage of biologics, which may be infused in clinical settings, or phototherapy, which is a non-drug treatment). APLD is also unique in its ability to show drug utilization by indication, an important level of detail for biologics, which are oftentimes used for
multiple indications.

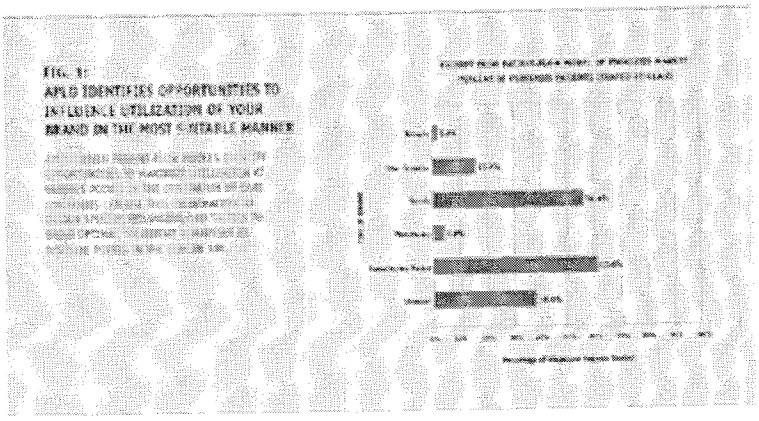
The company relied on a patient-flow model to better understand treatment patterns in this market. Patient-

flow models have become a standard modeling application for identifying where patients enter the healthcare system, and how treatment progresses within a disease area. Such models are useful in identifying opportunities to maximize product utilization by, for instance, disclosing a large untreated population, uncovering diagnostic hurdles, or revealing the need for a combination therapy.The company populated the patient flow model with APLD, mapping out the journey that psoriasis patients take through the healthcare system, and paying particular attention to the treatment choices that physicians were making (see Fig. 1).

Through this analysis, the company realized that very few patients (3.9 percent) were actually being treated with phototherapy, which was significantly less than they had assumed based on the thought leadership interviews and physician survey data they had gathered.The company realized that this segment of patients, which had originally driven the focus of their positioning and messaging, was actually quite small, and didn't represent as large of an opportunity as it had originally thought. In contrast, other systemics accounted for 16 percent of the market and represented a significant opportunity. Given this evidence and insight, the company revised its original marketing strategy to include the segment of patients who were on other systemics in order to drive greater uptake of the product, and refined product positioning and messaging accordingly.

The sales force could carry out this strategy by identifying the physician segments that treat patients with phototherapy and systemics respectively, and delivering tailored messages about the benefits of the biologic over the respective therapy. Both marketing and sales could then track the effectiveness of their programs by monitoring share of new patients and share of patients that switch to their brand from each of the competitor therapies.

This evidence-based assessment of physician treatment behaviors caused the brand team to reshape its competitive set and revealed an opportunity to increase product utilization. Given its coverage of biologics and non-pharmacologic therapies as well as its reporting by indication,APLD was the only source that could reveal treatment patterns.Without the benefit of APLD, the company may have missed this critical treatment dynamic and continued to pursue a much smaller market. Additionally, this information may have provided a significant advantage over competitors who were potentially unaware of this market dynamic.



APLD SPOTLIGHTS A KEY PATIENT SEGMENT IN THE PPI MARKET

For years, marketers have had to segment their patient populations with limited insight into real-world, evidence-based clinical information.They primarily had to rely on primary market research (which was

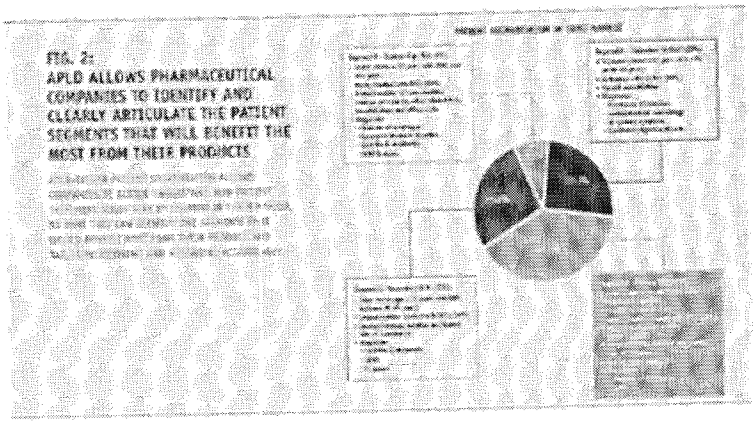
sometimes limited by small sample sizes and inaccuracies related to physician and patient recall), in combination with dispensed prescription data to understand how product utilization varied by patient segment.

Today,APLD, which combines patient demographics with actual treatment statistics on millions of de-identified patients, present no such limitations. Companies can use APLD to identify distinct patient segments based on their disease attributes, treatment specifics and/or key demographics, and take their patient segmentations to a more sophisticated and comprehensive level.They can use this deep understanding of patients to market their product to the groups who would benefit the most from them — with messaging appropriate to each segment.

In the following example, a major player in the proton pump inhibitor (PPI) class used an APLD-driven patient segmentation approach to improve its performance in the gastroesophageal reflux disease (GERD) market.

The company's brand team had observed that all products in the class were experiencing a high volume of patient switches (i.e., patients switching to and from their brand) and restarts (i.e., patients restarting their brand after quitting).They hypothesized that utilization varied significantly based on patients' clinical profiles. If this theory was borne out, the company intended to identify and concentrate its efforts on those segments that represented the highest current and potential value to its brand.The manufacturer leveraged APLD to segment the market and analyze actual utilization patterns within each segment.

The segmentation revealed four distinct patient segments characterized by different demographics, clinical factors and therapy usage. (See Fig. 2.) Segments B and D had the largest percent of patients treated with PPIs, and their PATIENT SEGMENTATION OF GERD MARKET clinical characteristics indicated a good potential "fit" with the company's product. Patients in Segment B, which represented 40 percent of the market, tended to be older, male and suffering from the fewest number of comorbidities. Most (68 percent) were treated with PPI's, and this group registered the longest duration of therapy with the greatest rate of compliance.This segment, therefore, presented the greatest potential value of the brand.



Interestingly, the company learned that each brand in the PPI class had a relatively similar share of each segment. For example, if a brand had a six percent share of Segment A, it likely had a similar share of Segments B, C, and D.This suggested a lack of product differentiation between the available brands in the minds of physicians.The analysis of market shares across the

segments also seemed to confirm that none of the company's competitors had singled out Segment B as a high priority population, as no brand had a particularly dominant share.

The company was able to capitalize on its newfound knowledge of patients in Segment B by developing very tailored messaging for physicians. Rather than simply recommending that physicians use the brand for patients who suffer from GERD, the brand team designed physician messaging that described the specific clinical profile of the patients who would benefit most from the therapy (i.e., older patients, males, patients diagnosed with diseases of the esophagus, etc.).

As a subsequent step, the sales force could then use APLD to identify the segments of physicians who were treating patients in Segment B, and deliver these tailored messages to ensure that the right patients are receiving the right treatments at the right time.Then, both marketing and sales could monitor the success of the company's revised strategy by measuring changes in
product uptake among key segments of physicians.

APLD was the only information source that could provide the real-world, evidence-based clinical insights needed to identify and articulate the patient segments that would benefit most from the brand. Using APLD, the company was in a position to differentiate its brand in a relatively undifferentiated market, leading to a potential advantage over competitors who were
communicating a broad, general message. By enabling the brand team to take a more granular and sophisticated look at the market, APLD gave the company a significant marketing edge.

LIGHTING THE WAY TO COMPETITIVE ADVANTAGE

Because APLD sheds light on previously hidden aspects of the market, it offers new possibilities for companies to see opportunities more clearly and potentially seize a competitive advantage — and go beyond simply trying to steal share from competitors. Market assessments and competitive analyses can now include evidence-based details on the continuum of patient care—information that can be used to identify and fill unmet needs and competitive gaps. And marketers can now operate with
a deeper understanding of the patients their products are meant to treat, enabling them to segment and communicate to them more effectively. Furthermore, APLD can be translated directly into sales strategies and tactics, ensuring a more cohesive, comprehensive, and effective approach to the market.

For more information about anonymized patient-level data offerings from IMS, call us today at 800.783.6362, x484 or e-mail
us at apld@us.imshealth.com.

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IMS Announces Integration of Anonymized Patient-Level Data Across Global Portfolio of Offerings

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New Disease and Treatment Insights Critical to Identifying Unmet Treatment Needs, Understanding Pharmaceutical Effectiveness and Value

FAIRFIELD, CT, November 28, 2006 – IMS Health (NYSE: RX) today announced that it has successfully integrated anonymized patient-level data (APLD) across its global portfolio of information, analytics and consulting offerings. As a global leader in protecting individual patient privacy, IMS uses de-identified healthcare data to deliver critical, real-world disease and treatment insights. These insights help medical researchers, government agencies, and healthcare and pharmaceutical companies identify unmet treatment needs and understand the effectiveness and value of pharmaceutical products in improving overall health outcomes.

IMS is the only company that combines the industry's most trusted and widely used sources of prescription information – **IMS National Prescription Audit (NPA)**TM and **IMS Xponent**® – with robust longitudinal prescription and medical claims information to deliver an integrated view of treatment practices, as well as physician and payer dynamics.

Today, dozens of pharmaceutical companies are already leveraging IMS's patient-centric insights to better anticipate and address evolving market and treatment needs. In one recent competitive win, a Top 10 global pharmaceutical company switched to IMS for all of its APLD services in the U.S., citing the company's comprehensive portfolio, seamless tie to industry-standard metrics and long-term strategy to address evolving market dynamics locally and globally.

"IMS is uniquely qualified to help the industry apply APLD to drive innovative pharmaceutical brand and portfolio strategies, and ensure that the right patients receive the right therapies at the right time," said William Nelligan, president, IMS Americas.

Complete View of Patient, Physician and Payer Dynamics
IMS's APLD portfolio reveals in greater detail than ever the interplay of factors

such as disease and treatment patterns, compliance and persistence, physician practices, payer impact and the cost of care – over time. By integrating these insights across an array of industry-standard information, analytics and consulting services, clients gain a complete, globally consistent view of the market.

INFORMATION: Part of IMS's ***New Models, New Metrics***TM program of next-generation market measures, APLD information offerings deliver key early indicators of brand performance, as well as insights into particular therapeutic areas. For example, **IMS NPA Market Dynamics**TM combines source-of-business metrics – such as switching, add-on therapies and prescription restarts – with industry-standard prescription measures to help clients better plan, forecast and measure brand performance. **IMS NPA New to Brand**TM improves understanding of new prescription volume growth generated from first-time patients on a brand, filtering out continued or restarted prescriptions. **IMS Disease Analyzer**TM incorporates the most comprehensive longitudinal anonymized patient-level data in Europe, enabling single- and multi-country analysis of treatment dynamics over time. Widely used by leading companies and regulatory authorities worldwide, Disease Analyzer information is fully integrated with IMS medical claims information, allowing for regional and global treatment analysis. And **IMS Xponent Prescribing Dynamics**TM combines comprehensive treatment insights with the power and reliability of IMS Xponent to help researchers and clients better understand treatment patterns at a territory level, driving fast response to market events and more effective physician-level messaging.

ANALYTICS: Advanced, proprietary analytics are central to IMS's APLD portfolio. For example, the **IMS Patient Flow Model**TM uses APLD to characterize treatment experiences and gauge how treatment progresses in a disease area. An understanding of patient treatment over time is critically important in building accurate forecasts and developing clinically relevant education and value-based messaging for unique patient segments. Another analytic, **IMS Dynamic Capture Rate**TM, measures the share of physicians' active therapy decisions, taking into account the volume of new business impacted by switching. This measure can detect trend shifts an average of eight weeks earlier than traditional total prescription measures. IMS also offers a range of customized performance management dashboards and analytics to help pharmaceutical companies track the performance of their brands.

CONSULTING: IMS has conducted and delivered hundreds of custom studies that leverage the company's rich disease and treatment insights, across all major therapeutic areas and multiple geographies. IMS consultants tap into the company's global breadth of information and analytics to address critical client issues in areas such as forecasting, health economics and outcomes research (HEOR), medical education, pricing and market access, promotional optimization, sales force effectiveness and therapy area studies.

"Patient-centric insights are helping the industry move away from measuring consumption alone to measuring market potential and product value," said Nelligan. "IMS will continue to make significant investments in our global APLD portfolio to ensure that our clients optimize the value of these new insights to advance evidence-based healthcare."

For more information about IMS's comprehensive portfolio of APLD offerings, contact Lisa Morris, IMS global director, APLD, at 610.834.5210.

About IMS

Operating in more than 100 countries, IMS Health is the world's leading provider of market intelligence to the pharmaceutical and healthcare industries. With $1.8 billion in 2005 revenue and more than 50 years of industry experience, IMS offers leading-edge business intelligence products and services that are integral to clients' day-to-day operations, including portfolio optimization capabilities; launch and brand management solutions; sales force effectiveness innovations; managed care and over-the-counter offerings; and consulting and services solutions that improve ROI and the delivery of quality healthcare worldwide. Additional information is available at http://www.imshealth.com.

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Infuse Anonymized Patient-Level Information into the Brand-Planning Process to Drive Profitable Growth

By Jim Carroll and Taryn Foniri

Pharmaceuticals at a Crossroads

With income growth falling to single-digit levels, the pharmaceutical industry is rapidly reaching a crossroads. To be successful, pharmaceutical companies will need to do a better job of finding and exploiting revenue opportunities while optimizing resources. Doing this requires a solid understanding of both the customer and consumer and the underlying drivers of behavior within the competitive context. Compared to other, more consumer-oriented industries, however, the pharmaceutical industry lags behind when it comes to understanding the dynamics between its customers (physicians and payors) and its consumers (the patients they treat). While much is known about the pharmaceutical brands that physicians prescribe, little is known about the patient treatment context that drives physicians to initiate treatment and to actively manage it. A better, more balanced understanding of the overall context in which these brands are used, the ways in which patients are actually treated, the underlying drivers of physician behavior, and the resulting positive implications on patient outcomes, has the potential to greatly enhance companies' prospects for growth.

APLD = New Opportunities for Growth

Much has been written about anonymized patient-level data (APLD) and its ability to help companies understand, at both a national and physician level, the behaviors of treated patients using source of business metrics. While significantly more valuable than dispensed prescription data alone, these metrics represent only the tip of the iceberg when it comes to the applications of this rich source. APLD allows brand teams to understand the key characteristics and behaviors of physicians and the patients they treat with a greater degree of insight than ever before. Through an improved understanding of the customer/consumer dynamic within healthcare, a new realm of opportunities is uncovered to fuel growth demands. When used to its full potential, APLD can enhance companies' abilities to:

- Segment the market in new ways that can lead to competitive advantage
- Identify novel opportunities for growth
- Seamlessly link marketing and sales strategies to ensure that the right messages are reaching the right stakeholders at the right time
- Measure performance using key indicators that allow companies to align performance with strategic objectives, identify mid-course opportunities and threats, and improve marketing and sales effectiveness

APLD allows pharmaceutical companies to identify new opportunities, allocate resources more efficiently to pursue these opportunities, and drive more profitable growth in today's complex environment.

In order to fully realize these benefits, it is a strategic imperative for companies to use APLD-driven insights to inform their key commercialization activities – starting with the annual brand-planning process. But how?

Infusing APLD into the Brand-Planning Process

The annual brand-planning process consists of several key phases: the situational assessment, the development of objectives, strategies and tactics, the execution, and the ongoing evaluation of performance.

To drive profitable growth, APLD should be applied to the following three phases of the annual-brand planning process:

I. The situational assessment
II. The development of marketing objectives and strategies
III. The ongoing evaluation of performance

The following examples illustrate how brand managers and market researchers can successfully leverage APLD during these important phases of the brand-planning process to identify and pursue opportunities to drive profitable brand growth.

I. Uncovering New Opportunities as Part of the Situational Assessment

During the situational assessment, a pivotal phase of the annual planning exercise, brand teams evaluate the current status of their brands by subjecting them to a thorough business review. Brand teams use this information to inform their SWOT (Strengths, Weaknesses, Opportunities, Threats) analysis, which then serves as a critical building block for the strategic plan for the coming year. During the situational assessment, brand teams assess a number of different macro- and micro-environmental factors that have the potential to impact brand performance, including the political / legal environment, competitive dynamics, and customer/ consumer interactions. APLD has the potential to add more clarity to the assessment than traditional intelligence sources, specifically as it pertains to the following key areas:

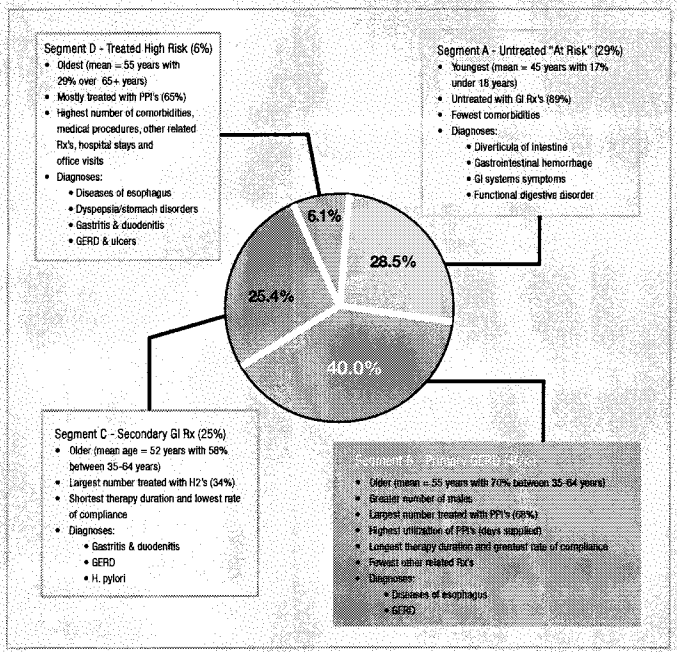
- Market sizing
- Patient segmentation
- Treatment dynamics / patient-flow
- Patient adherence
- Cost of care
- Competitive dynamics

As the following two examples will illustrate, the novel perspectives introduced through the use of this source can lead to the identification of opportunities that may not have been visible using traditional market intelligence.

Example 1: APLD-Driven Patient Segmentation

A significant player in the proton pump inhibitor (PPI) class used patient segmentation to better understand the Gastroesophageal Reflux Disease (GERD) market. The company had a hypothesis that utilization in this market (which is characterized by a high volume of patient switches and re-starts) varied significantly based on the clinical profile of patients, and was interested in segmenting the market along clinical and demographic characteristics to identify those segments that represented the highest current and potential value to the brand. APLD became a critical input to this process, since it was the only comprehensive source of healthcare utilization information available that would allow them to calculate a given segment's value to the brand based on actual, segment-specific utilization patterns.

FIG. 1: APLD-DRIVEN PATIENT SEGMENTATION
SEGMENT B REPRESENTED GREATEST POTENTIAL VALUE TO BRAND ON ACCOUNT OF ITS SIZE AND UTILIZATION OF PPI'S.



Source: PharMetrics Market Profiler

The increased precision afforded by APLD-driven segmentation allows brand teams to focus their attention and resources on the portions of the market that matter most to their brands – leading to better resource allocation and better brand performance.

The assessment revealed four key patient segments, with Segment B representing the greatest current and potential value to the brand (Fig. 1). Segment B patients, which represented 40% of the entire market, were more likely to have a primary diagnosis of GERD and be treated with a PPI. This segment utilized more pills over longer periods of time than any other segment, making it the greatest per-patient source of revenue for the brand.

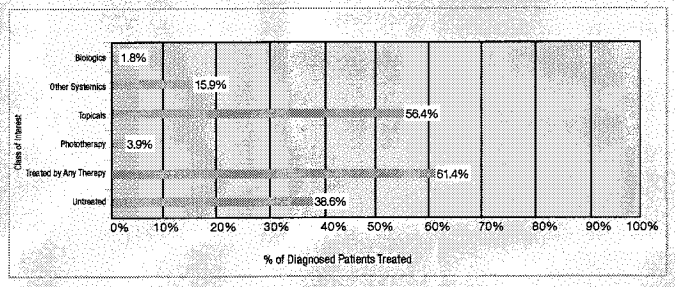
Based on this information, the company was equipped to re-align its positioning, targeting and messaging strategies with the most appropriate tactical investments to increase their share of Segment B patients and ultimately maximize their brand's performance. APLD enabled the company to segment their market with a greater degree of precision than what would have been available using traditional market intelligence, and allowed them to identify opportunities to maximize their brand's performance that would have otherwise gone unnoticed.

Example 2: Treatment Dynamics/Patient Flow

A large biologics manufacturer had launched a product that was indicated for the treatment of moderate to severe psoriasis, and was interested in understanding how actual use of its product aligned with their labeling (the product was indicated for use in patients who were candidates for phototherapy, a non-pharmacologic treatment, and other systemics). APLD was critical to this process as it was the only source available that allowed them to accurately track usage of their biologic product, and assess usage of non-pharmacologic therapies, such as phototherapy. Interestingly, the analysis revealed that few patients were actually progressing to phototherapy – indicating that the brand's key competition was primarily coming from other systemics (Fig. 2) – a treatment dynamic that had not been readily apparent based on the traditional market intelligence they had been using. By highlighting how the brand fit into the current treatment algorithm, the brand team had the necessary insights required to develop more appropriate and compelling messages for physicians, as well as a potential advantage over competitors who were unaware of this critical treatment dynamic.

FIG. 2: PERCENT OF PATIENTS TREATED BY CLASSES OF INTEREST

FEW PATIENTS PROGRESS TO PHOTOTHERAPY IN THE PSORIASIS MARKET.



Source: PharMetrics Market Profiler

APLD provides an understanding of actual, real-world treatment dynamics, and allows brand teams to design more compelling, targeted messages as well as tactics.

II. Developing Meaningful Objectives, Strategies and Tactics

Once the situational assessment has been completed and distilled into the SWOT framework, brand teams will then prioritize the most promising opportunities and the most significant threats and use this prioritized list to drive the development of objectives and strategies for the next implementation cycle. The insights generated during the situational assessment are used to not only populate the SWOT framework but also to inform a number of other strategic-level activities that are found in the annual brand plan, including:

- Forecasts, both near-term and long-term
- Investment planning, including clinical and promotional programs
- Positioning, targeting and messaging

The increased market insight that APLD provides ensures that the right clinically-driven message is getting to the right audience at the right time in the flow of patient care to drive desired behaviors and increase utilization.

III. Optimizing Performance Evaluation

Having articulated the marketing objectives, strategies, positioning, investment plan and tactics in the annual brand plan, brand teams must then identify a meaningful set of metrics that they can use to evaluate performance during

the implementation cycle. These metrics will serve to establish measurement parameters so that the brand team can keep performance on track and course correct as necessary. One of the unique benefits of APLD is that the increased granularity it provides enables a tighter link between the marketing objectives called out in the brand plan and the metrics that are used to evaluate performance. This tighter link improves the likelihood of actually achieving the marketing objectives that have been set for the brand.

For example, during the situational assessment, a brand team may use APLD to identify a set of specific patient and physician behaviors that it would like to influence to promote maximum brand utilization, and use these insights to develop a set of strategies and tactics to achieve this objective. Using APLD, the team can then evaluate how specific behaviors were influenced, and course correct as necessary to ensure that objectives are achieved – something they previously could not have accomplished using TRx and NRx metrics alone. In fact, using APLD, brand teams are better able to identify and diagnose potential issues and opportunities and respond with a targeted series of actions faster and more effectively, which significantly improves their chances of success.

To optimize performance evaluation, APLD is best for monitoring three key areas:

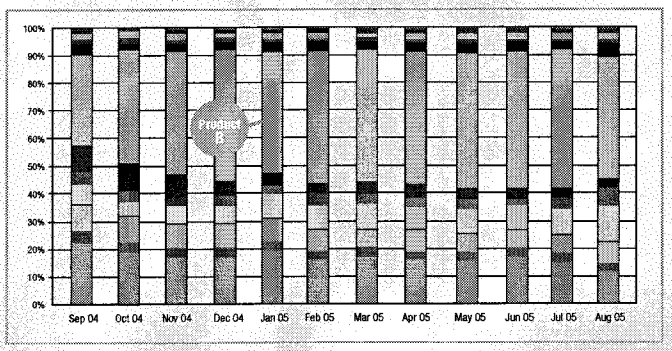
- Evaluation against marketing objectives
- Identification of mid-course opportunities and threats
- Evaluation of marketing and sales effectiveness

The following two examples illustrate how APLD can enhance the ongoing performance evaluation process.

Example 3: Evaluation Against Marketing Objectives

A manufacturer had recently introduced a line extension for a product that would soon be going off patent. The manufacturer's marketing objective was to transition a high percentage of patients from the legacy product to the newer formulation as a means of retaining patients. Using APLD, the company was able to translate this marketing objective into a performance metric that allowed them to track the volume of patients switching from the old brand (Product A) to the new brand (Product B) – something they would have been unable to do using the more traditional NRx and TRx metrics (Fig. 3). This new, APLD-driven performance metric allowed them to evaluate their success in meeting their strategic objective, and gave them the ability to quickly identify deviations in performance so that they could quickly refine their tactics as necessary and ensure that they were able to deliver on this expectation.

FIG. 3: PRODUCT A SWITCH FROM DISTRIBUTION (%)
THE BULK OF SWITCHING FROM PRODUCT A IS TO PRODUCT B.



Source: IMS NPA Market Dynamics™

Visibility to performance metrics that are tied to strategic objectives improves the brand team's ability to manage and deliver on expectations, as they are better able to evaluate performance and refine tactics throughout the year to ensure optimal performance.

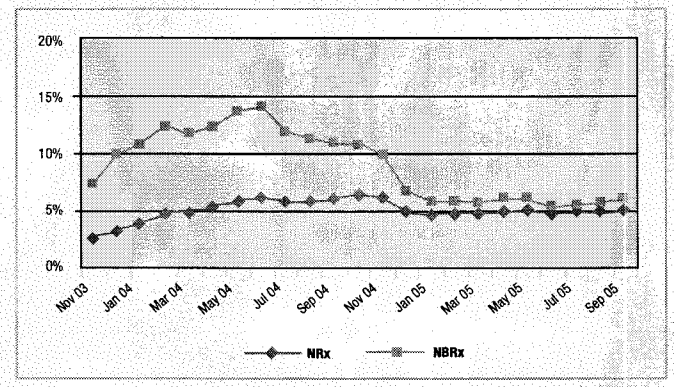
Example 4: Identification of Mid-Course Opportunities and Threats

APLD-driven performance metrics can also provide an earlier warning of mid-course opportunities and threats, which allows teams to respond earlier-on to keep performance on track.

In this example, it was critical for the brand team to understand how much actual new business they were attracting at any point in time, as this metric often acts as a leading indicator of future product performance since it reflects the most current physician prescribing decisions (as opposed to the more traditional NRx metric which measures the number of new 'pieces of paper', and can be skewed towards more historical physician prescribing decisions). In Figure 4 the product's new to brand (NBRx) share is compared to the more traditional new prescription share metric (NRx). This particular product was competing in a market where a competitive product had recently been launched. Using NRx-only, it would have been difficult for the brand team to gauge the effect of the launch on their brand's performance.

However, by looking at the new to brand metric, the brand team was able to see that physicians were writing fewer prescriptions for their brand for truly new patients, which ultimately had a negative effect on the product's future performance. In this case, the NBRx share decline from July 2004 to January 2005 was a precursor to the product's flat NRx share. Therefore, by using the new to brand metric, the brand team was in a position to take corrective action sooner and potentially prevent a slow down in the brand's growth.

FIG. 4: NRX AND NBRX SHARE TRENDS
THE NBRX SHARE DECLINE FROM JULY 2004 TO JANUARY 2005 WAS A PRECURSOR TO THE PRODUCT'S FLAT NRX SHARE IN 2005.



Source: IMS NPA New to Brand℠

APLD = Key to Success

In order to be successful in today's complex environment, pharmaceutical companies need to better understand the dynamics between the key customers (physicians and payors) and consumers (patients) they serve. APLD represents the best source for understanding these dynamics. By infusing APLD into their annual brand-planning process, pharmaceutical companies will be better equipped to identify new opportunities for growth, more appropriately invest resources to pursue those opportunities, and optimally align marketing and sales activities to drive profitable growth.

Jim Carroll
Director of Product Management
PharMetrics, a unit of IMS

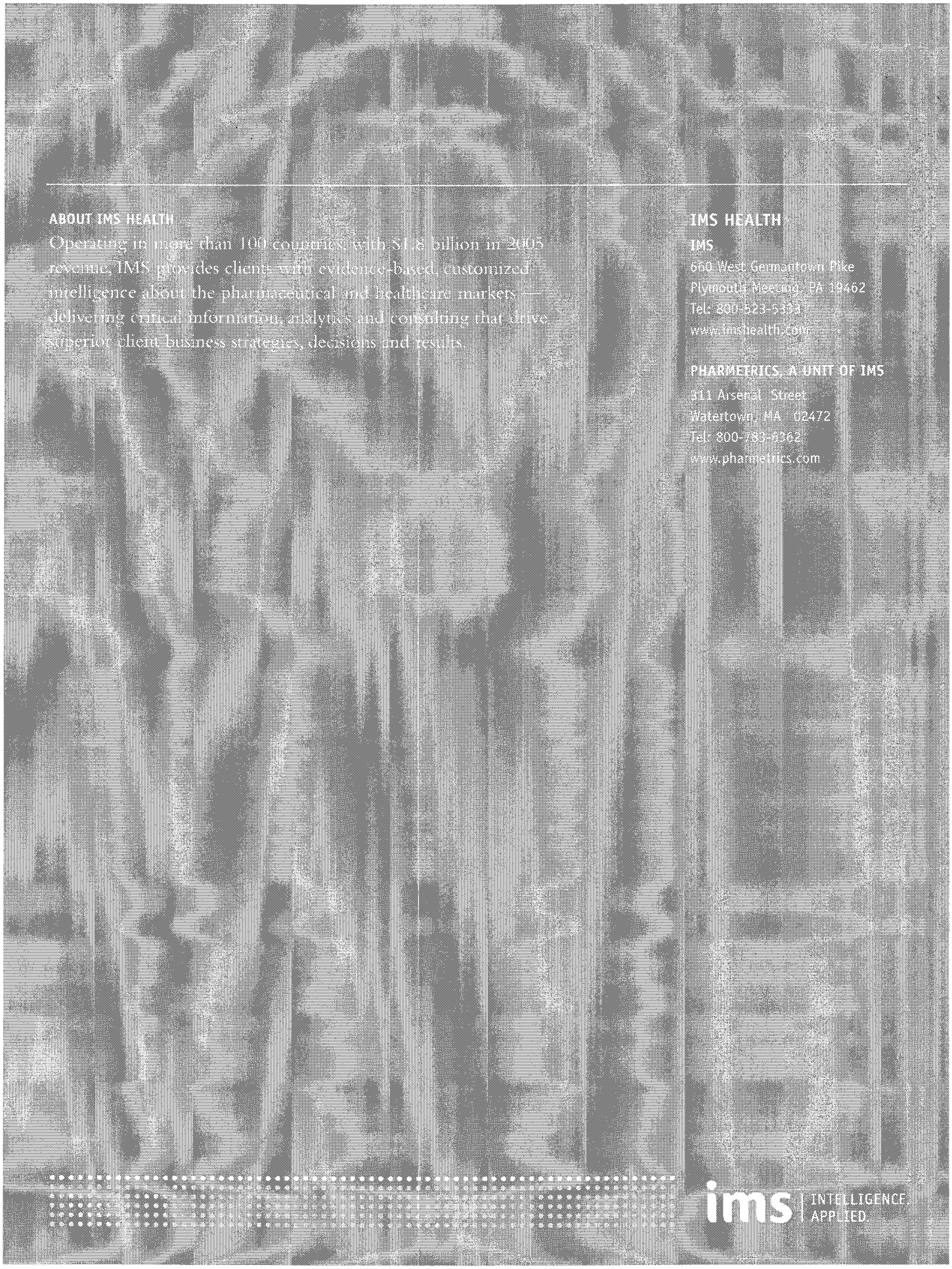
Jim Carroll is responsible for the design, creation and management of APLD-driven intelligence solutions, including the Profiler Series, which enables brand teams to make better strategic decisions and improve their performance.

Carroll's background includes over fifteen years in the healthcare industry, with extensive experience in pharmaceutical marketing and new product development. Carroll has spoken at many industry conferences on improving brand performance through the use of APLD. He is based in Watertown, MA and can be reached at jcarroll@pharmetrics.com

Taryn Foniri
Product Marketing Manager
PharMetrics, a unit of IMS

Taryn Foniri has responsibility for the development of product marketing strategy and oversees related marketing activities for the portfolio of offerings at PharMetrics, a unit of IMS.

Foniri's background includes several years of experience as a marketing strategy consultant for the Monitor Group, a management-consulting firm that focuses on the top management issues most critical to pharmaceutical and biotech industries. Foniri has written several articles on the applications of APLD to brand strategy. She is based in Watertown, MA and can be reached at tfoniri@pharmetrics.com



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2009 Session

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The original is on file at the Montana Historical Society and may be viewed there.

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Scanning by: Susie Hamilton

Additional Document

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DATE 2-9-09
HB 394

Meredith Jacob

Documents for Record

HB 0394 (McAlpin)