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Determinants of Drug Utilization

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Outline

- ▶ Marketing and promotion
- ▶ Emerging evidence
- ▶ Regulation
- ▶ Coverage and reimbursement

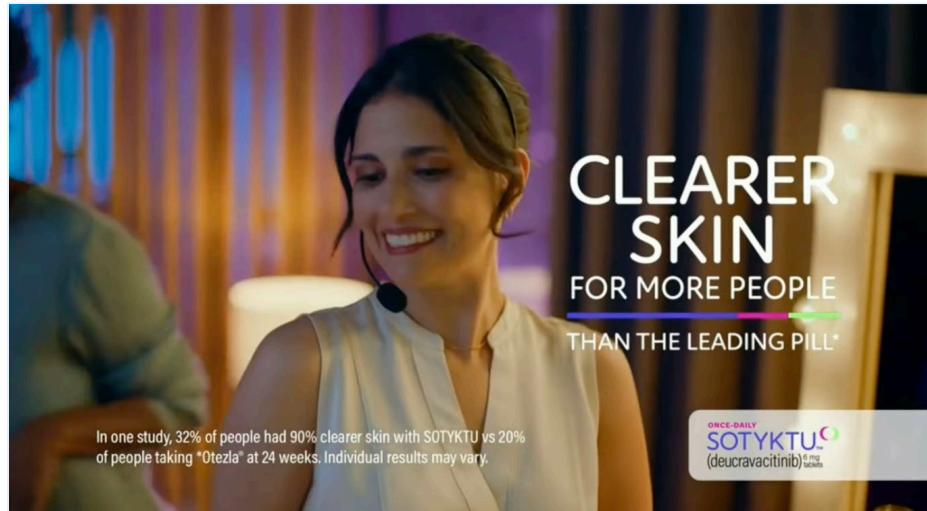


Marketing and Promotion

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What Do We Mean by “Marketing and Promotion”?

- ▶ Promotion to providers
 - ▶ Office-based promotion
 - ▶ Hospital-based promotion
 - ▶ Journal advertising
 - ▶ Free samples
 - ▶ E-promotion
 - ▶ Conferences and meetings
- ▶ Promotion to patients
 - ▶ Television
 - ▶ Print
 - ▶ Internet
 - ▶ Radio
 - ▶ Outdoors



An Example

FREEDOM FROM PAIN!

**Extra strength pain relief
free of extra prescribing
restrictions.**

- Telephone prescribing in most states
- Up to five refills in 6 months
- No triplicate Rx required

Excellent patient acceptance.
In 12 years of clinical experience, nausea, sedation and constipation have rarely been reported.¹

	COMPARATIVE PHARMACOLOGY OF TWO ANALGESICS				
	Constipation	Habitual Dependence	Irritation	Emesis	Physical Dependence
HYDROCODONE	X			X	
OXYCODONE	XX	XX	XX	XX	XX

Blank space indicates that no such activity has been reported. Table adapted from Facts and Comparisons 1992, 23-24 and the usual approach to management of pain caused by cancer. Soren, Uloch-Hansen, M. 1992 and Rother, J.R., et al.: The chronic pain syndrome: epidemiology and management. *Annu. Rev. Med.* 1992; 53-92.

The heritage of VICODIN,[®] over a billion doses prescribed.²

- VICODIN ES provides greater central and peripheral action than other hydrocodone/acetaminophen combinations.
- Four to six hours of extra strength pain relief from a single dose
- The 14th most frequently prescribed medication in America³

vicodin ES[®]
(hydrocodone bitartrate 5 mg [Warning: May be habit forming] and acetaminophen 500mg)

Tablet for tablet, the most potent analgesic you can phone in.

An advertisement for Vicodin ES. The top half features a prescription bottle with a torn label that reads 'Rx Specify Do not substitute'. The bottle is surrounded by numerous silver nails scattered across a light blue background, symbolizing the potential dangers of prescription drug abuse. The bottom half contains the product name 'vicodin ES' in large red and blue letters, followed by '(hydrocodone bitartrate 7.5mg (Warning: May be habit forming) and acetaminophen 750mg)' in smaller text. Below this, a large headline reads 'It's your prescription – not a suggestion.'

Image source: Vicodin ES advertisement [Still image]. (1992). University of Wisconsin--Madison. Ebling Library for the Health Sciences. Retrieved November 21, 2024, from <https://search.library.wisc.edu/digital/A2BBNINIOHLOXA82>

Enduring Controversies

- ▶ One of most profitable industries in US
- ▶ Several features may justify profitability and aggressive marketing and promotion
 - ▶ Large failure rate—exceeding 90%
 - ▶ High value of many medicines
 - ▶ Costs of bringing a new therapy to market—\$0.3 to \$2.8 billion
- ▶ Variety of criticisms leveled at industry as well
 - ▶ Drug development costs grossly inflated
 - ▶ Cost-related medication burden plagues many
 - ▶ Costs of drugs in the US are 50% or more than in other countries
 - ▶ Excessive profits, government funds much of new research

Competing Perspectives

EDITORIAL

Finding Out Who Pays Your Doctor

Published: February 18, 2013

The Obama administration issued a new rule this month that requires the makers of prescription drugs and other medical products to disclose what they pay doctors for various purposes, like consulting or speaking on behalf of the manufacturer. This overdue rule adds much-needed weight to previous, more limited disclosure requirements.

Related

[U.S. to Force Drug Firms to Report Money Paid to Doctors](#) (January 17, 2012)

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 **Opinion**

The goal is to let the public know about payments that might lead doctors to prescribe treatments that benefit them financially without necessarily benefiting patients.

This information will allow patients and their families to check whether their own doctors are receiving payments and to see if those financial connections affect a doctor's recommendation for a particular treatment or device.

The rules may require 1,000 or more makers of drugs, medical devices and other medical products to report payments, gifts, consulting fees, research support among other types of compensation made to physicians and teaching hospitals. The federal government will post the payment data on a public Web site that will be easily searchable starting late next year.

The rules don't flatly forbid any payments, but even disclosure alone is an important first step. The data collected will provide the most comprehensive evidence yet of how common various types of payment are, and will allow researchers to document more fully whether these payments influence medical judgments in ways that actually harm patients.

If it turns out that they do, there will be a strong basis for banning such payments completely.

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LETTER

Payments to Doctors

Published: March 3, 2013

To the Editor:

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For Op-Ed, follow @nytopinion and to hear from the editorial page editor, Andrew Rosenthal, follow @andyNYT.

 **Opinion**

Re "Finding Out Who Pays Your Doctor" (editorial, Feb. 19), about the Physician Payments Sunshine Act:

Patients benefit significantly from interactions between physicians and pharmaceutical companies, and these relationships are critical to ensuring the high standard of care patients receive.

Working together in a variety of academic, institutional and other settings, industry and physician research collaborations are critical to the discovery of new and improved medicines. Physicians also share their firsthand knowledge with pharmaceutical professionals so that they capture important patient experiences with medicines related to drug efficacy and compliance.

We fully embrace transparency. With it comes more understanding of how these collaborations are advancing patient care.

JOHN J. CASTELLANI
RAY E. STOWERS
Washington, Feb. 26, 2013

Mr. Castellani is president and chief executive of the Pharmaceutical Manufacturers Association, and Dr. Stowers is president of the American Osteopathic Association.

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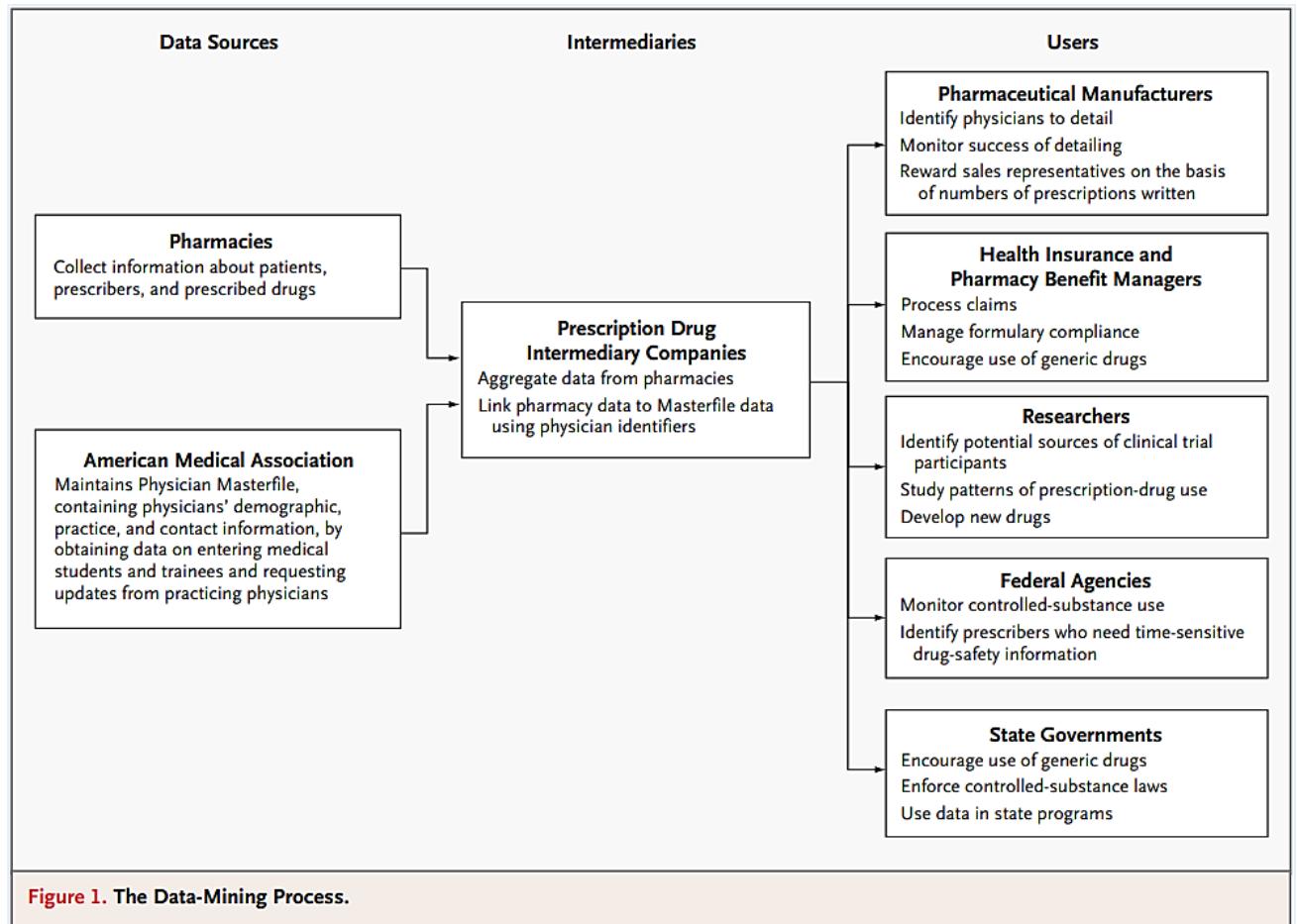
STOKER
NOW PLAYING

Billions Are Spent Each Year on US Medical Marketing

- ▶ From 1997–2016, annual spending on medical marketing in the United States increased from \$17.7 to \$29.9 billion (drugs, disease awareness campaigns, health services, laboratory tests)
- ▶ Marketing to health care professionals accounted for most promotional spending, accounting for \$20.3 billion (2016), including \$5.6 billion for detailing, \$13.5 billion for free samples, ~\$1 billion for direct physician payments (e.g., meals), and \$60 million for disease education
- ▶ Direct-to-consumer advertising (DTCA) represented one-third of spending in 2016 (\$9.6 billion), most of which was DTCA for prescription drugs
 - ▶ Over 400 direct-to-consumer awareness campaigns in 2016, with the most intensive including chronic dry eyes (\$40 million), opioid-induced constipation (\$37 million), exocrine pancreatic insufficiency (\$36 million), hepatitis C (\$35 million), and diabetic neuropathy (\$28 million)



Marketing Is Powered by Data



Source: Mello, M. M., & Messing, N. A. (2011). Restrictions on the use of prescribing data for drug promotion. *The New England Journal of Medicine*, 365(13), 1248–1254. <https://doi.org/10.1056/NEJMhle1107678>

Physicians and the Pharmaceutical Industry: Is a Gift Ever Just a Gift?

- ▶ Reviewed 538 studies, selected 29 for inclusion
- ▶ Focused on extent of and attitudes towards relationship between physicians and industry, and industry impact on knowledge, attitudes, and behavior
- ▶ Interactions with industry associated with breadth of outcomes, including requests for additions to hospital formulary, residents and attending prescribing, and perceived benefits of industry interactions
- ▶ Conclusion of review: “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”

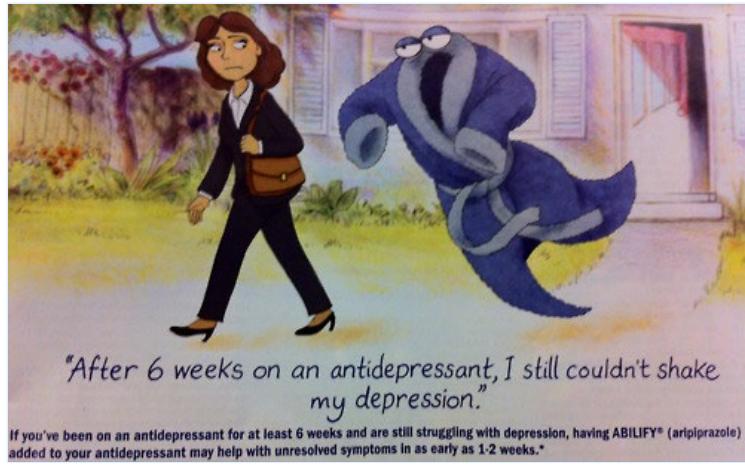
Three Other Systematic Reviews

- ▶ Spurling et al. (2010)
 - ▶ “With rare exceptions, studies of exposure to information provided directly by pharmaceutical companies have found associations with higher prescribing frequency, higher costs, or lower prescribing quality or have not found significant associations”
- ▶ Brax et al. (2017)
 - ▶ “Out of the 19 studies, 15 found a consistent association between interactions promoting a medication, and inappropriately increased prescribing rates, lower prescribing quality, and/or increased prescription costs”
- ▶ Fickweiler et al. (2017)
 - ▶ “Physician–pharmaceutical industry and its sales representative’s interactions and acceptance of gifts from the company’s PSRs have been found to affect physicians’ prescribing behavior and are likely to contribute to irrational prescribing of the company’s drug”

Sources: Spurling, G. K., et al. (2010). Information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing: a systematic review. *PLoS Medicine*, 7(10), e1000352. <https://doi.org/10.1371/journal.pmed.1000352>; Brax, H., et al. (2017). Association between physicians' interaction with pharmaceutical companies and their clinical practices: A systematic review and meta-analysis. *PLoS One*, 12(4), e0175493. <https://doi.org/10.1371/journal.pone.0175493>; Fickweiler, F., Fickweiler, W., & Urbach, E. (2017). Interactions between physicians and the pharmaceutical industry generally and sales representatives specifically and their association with physicians' attitudes and prescribing habits: a systematic review. *BMJ Open*, 7(9), e016408. <https://doi.org/10.1136/bmjopen-2017-016408>

Direct-to-Consumer Advertising

- ▶ Only a small number of products are heavily advertised directly to consumers
- ▶ In 2010, about two-thirds of all DTCA was accounted for by 25 products alone, including statins, PDE-5 inhibitors, atypical antipsychotics, and TNF-alpha inhibitors
- ▶ Products heavily advertised DTCA may also be heavily detailed and distributed as free samples, complicating efforts to isolate DTCA impact
- ▶ Systematic reviews: evidence is thin, increases prescribing volume and patient demand, shifts prescribing to less cost-effective treatments, no evidence of improved treatment quality or earlier provision of care
(Gilbody et al., 2005; Mintzes 2012)



Sources: Gilbody, S., Wilson, P., & Watt, I. (2005). Benefits and harms of direct to consumer advertising: a systematic review. *Quality & Safety in Health Care*, 14(4), 246–250. <https://doi.org/10.1136/qshc.2004.012781>; Mintzes B. (2012). Advertising of prescription-only medicines to the public: does evidence of benefit counterbalance harm?. *Annual Review of Public Health*, 33, 259–277. <https://doi.org/10.1146/annurev-publhealth-031811-124540>; Otsuka America Pharmaceutical, Inc. (2011, October 31). [Print advertisement for Abilify]. In *Time Magazine*, 178(17), p. 61. Retrieved November 22, 2024, from <https://archive.org/details/time-2011-11-28/Time%202011-10-31/page/n1/mode/2up>

What Happens When Patients Request a Medicine?

Table 2. Regression Analysis (Mixed-Effects Model) Predicting Antidepressant Prescribing Among SPs Portraying Major Depression and Adjustment Disorder

	Major Depression		Adjustment Disorder	
	Adjusted OR (95% CI)*	P Value	Adjusted OR (95% CI)*	P Value
Request type†				
Brand-specific request	2.72 (1.09-6.80)	.03	13.3 (4.20-42.10)	<.001
General request	7.99 (2.96-21.6)	<.001	6.34 (1.99-20.10)	.002
City‡				
Sacramento	0.76 (0.29-1.99)	.58	0.42 (0.15-1.18)	.10
San Francisco	0.38 (0.14-1.05)	.06	0.69 (0.25-1.91)	.47
Physician specialty: general internal medicine (vs family medicine)	1.10 (0.49-2.47)	.82	1.42 (0.57-3.57)	.45
Male physician (vs female)	1.77 (0.80-3.95)	.16	0.83 (0.35-1.94)	.66
Visit order: first (vs second)§	0.53 (0.24-1.17)	.12	0.58 (0.25-1.32)	.19
Suspicious for SP visit (vs unsuspected)	0.82 (0.28-2.39)	.71	0.33 (0.08-1.34)	.12

Abbreviations: CI, confidence interval; OR, odds ratio; SP, standardized patient.

*Values are adjusted for all other independent variables listed in the Table.

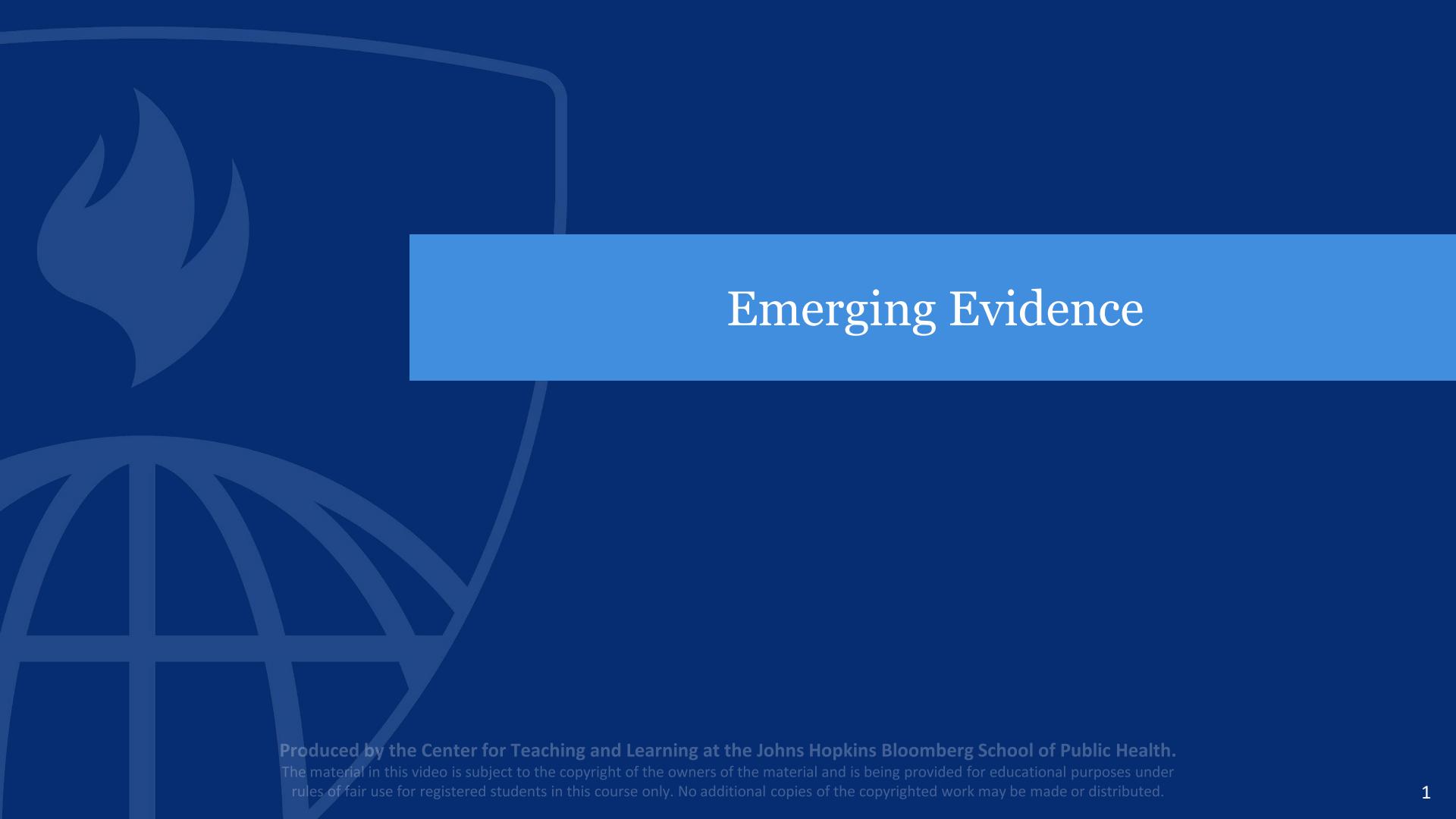
†No request is the reference category.

‡Rochester is the reference category.

§Reflects whether the visit was the physician's first or second study encounter.

Relevance to Drug Utilization

- ▶ Perennial interest in understanding effect of marketing/promotion on utilization (and value)
 - ▶ Free samples
 - ▶ Manufacturer coupons
 - ▶ Other copayment offsets (e.g., GoodRx model)
 - ▶ Patient assistance programs
 - ▶ Promotion by non-manufacturers (e.g., telehealth platforms)
- ▶ The effect of these—and other—promotional activities may vary based on frequency and intensity and across products, diseases and patient populations
- ▶ Promotion and marketing may also be an important confounder or co-intervention
 - ▶ How should we understand the effect of emerging evidence on use?
 - ▶ What is association between patient requests and clinician prescribing?
 - ▶ What is effect of a regulatory advisory about the risks of a given therapeutic class?



Emerging Evidence

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Products Are Used in a Highly Dynamic Landscape of Evidence—1

Heart Attack Risk Seen in Drug for Diabetes

 Share full article  



The Food and Drug Administration is trying to estimate the number of heart attacks that may be linked to GlaxoSmithKline's Avandia.

JB Reed/Bloomberg News

By Stephanie Saul

May 22, 2007

An article in a leading medical journal yesterday raised serious safety questions about the widely used diabetes pill Avandia and renewed skepticism about the vigilance of federal drug regulators.

Source: Saul, S. (2007). *Heart attack risk seen in drug for diabetes*. The New York Times. Retrieved November 22, 2024, from <https://www.nytimes.com/2007/05/22/business/22drug.html>

Products Are Used in a Highly Dynamic Landscape of Evidence—2

Long-term use of acid reflux medications linked to higher dementia risk

People who take proton pump inhibitors for about 4½ years or more have a 33 percent higher risk of developing dementia, study shows

4 min 155



(iStock)



By [Lindsey Bever](#)

August 10, 2023 at 6:40 p.m. EDT

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1 Lead f cinnar Consu

2 It's neve concuss injured.

3 Column gastroenter the surp gluten.

4 Guest co

Source: Bever, L. (2023). *Long-term use of acid reflux medications linked to higher dementia risk*. The Washington Post. Retrieved November 22, 2024, from <https://www.washingtonpost.com/wellness/2023/08/10/acid-reflux-heartburn-medication-dementia/>

Products Are Used in a Highly Dynamic Landscape of Evidence—3



THE WALL STREET JOURNAL.

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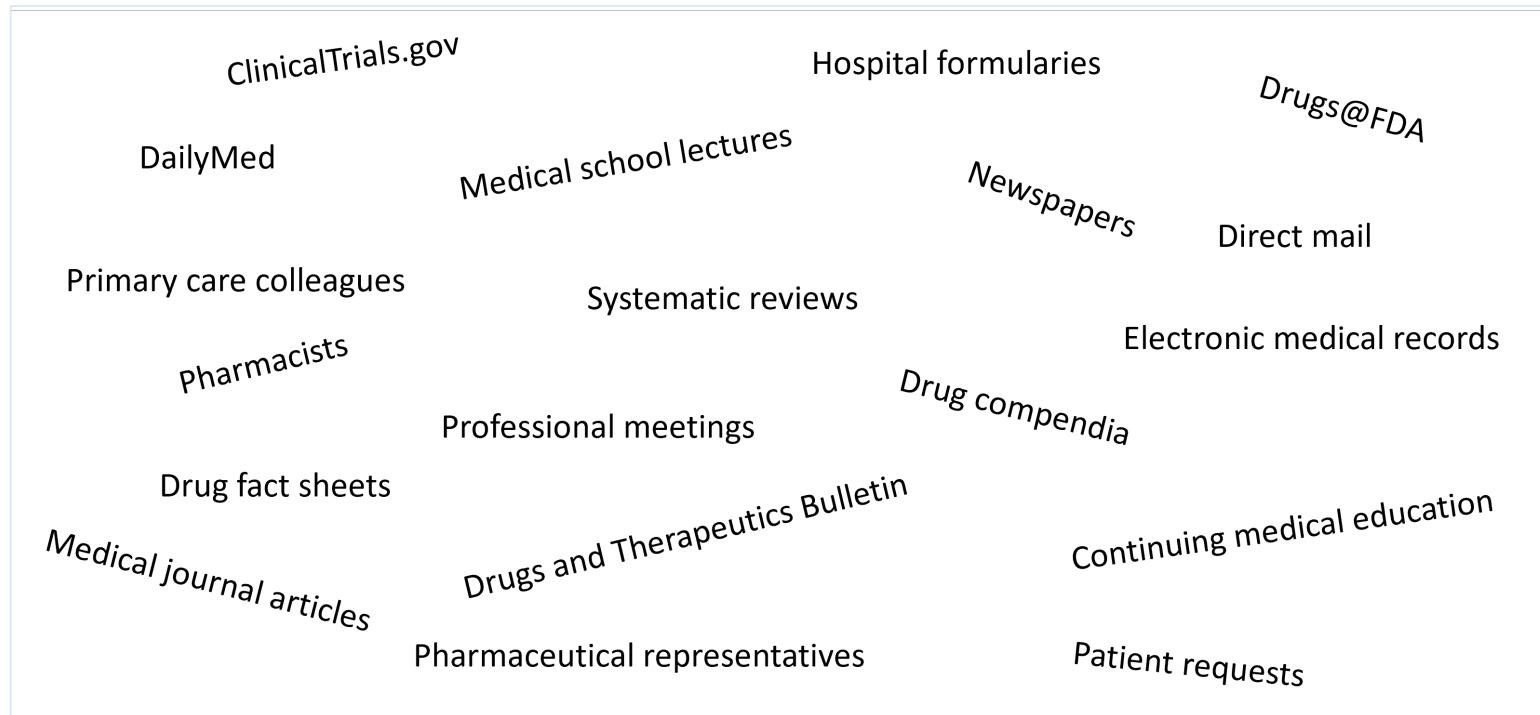
Ozempic Might Help You Drink and Smoke Less

Animal studies suggest GLP-1 drugs alter behaviors associated with reward and pleasure



Source: Subbaraman, N. (2023). *Ozempic might help you drink and smoke less*. The Wall Street Journal. Retrieved November 22, 2024, from <https://www.wsj.com/articles/ozempic-might-help-you-drink-and-smoke-less-a2354ce7>

New Evidence Splashes Down in a Sea of Information



What Effect Does Evidence Have on Utilization?

- ▶ Do some studies have a greater impact than other studies? If so, why?
- ▶ Are there particular types of evidence that are more likely to “move markets”?
- ▶ Are there particular subpopulations of patients or providers that may be more likely to modify their behavior based on emerging evidence?
- ▶ Considering the drivers of the prescription drug life-cycle, are some especially likely to potentiate, or mitigate, the effects of emerging evidence on use?
- ▶ Is there a need for new scientific investigations regarding the effects of emerging evidence on use, and if so, where are the opportunities for knowledge generation greatest?

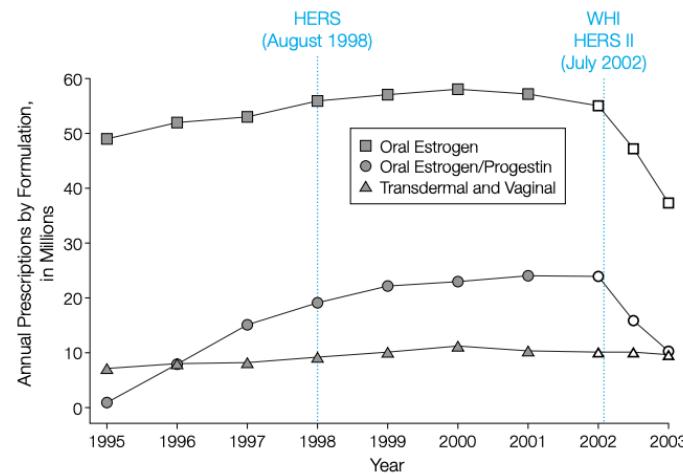
There Are Many Paths Whereby the World May Change

- ▶ Direct impacts of high-profile scientific investigations
- ▶ Indirect effects of evidence on many other forces
 - ▶ Evidence can be incorporated into guidelines
 - ▶ Evidence may impact marketing and promotion
 - ▶ Evidence may modify coverage and reimbursement
 - ▶ Evidence may be integrated within drug compendia
 - ▶ And so on ...

Women's Health Study Provides One Opportunity for Insight

- ▶ Conventional wisdom: hormone replacement therapy (HRT) safe and effective for menopausal symptoms such as hot flashes
- ▶ Conventional wisdom upended by publication of July 2002 Women's Health Initiative (WHI) study
- ▶ Large reductions in oral HRT use following publication of the WHI HERS II landmark trial
- ▶ Results support others showing prescribers may rapidly abandon widely used treatments when high quality new evidence shows harms

Figure 3. Annual Number of US Prescriptions for Hormone Therapy by Formulation, 1995–July 2003



Annualized data for January to June 2002, July to December 2002, and January to July 2003 are included (open symbols). Data are from the National Prescription Audit Plus, IMS HEALTH. HERS indicates Heart and Estrogen/Progestin Replacement Study; WHI, Women's Health Initiative.

Key Features May Be Associated With Greater Impact ...

- ▶ New information about drug risks (rather than benefits)
- ▶ Clinical trials that are definitive (i.e., large, well-conducted, free from bias)
- ▶ Results that have clear implications for clinical practice
- ▶ Results in which dissemination is facilitated, due to high profile nature of study, media attention, or dissemination by scientific community
- ▶ Strength and direction of underlying secular trends prior to publication of new evidence



Regulation

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What the FDA Does

- ▶ Approves new drugs based on:
 - ▶ Medicine is “effective” for intended use
 - Endpoint may be a surrogate such as lowering cholesterol (or amyloid!) as opposed to longer life
 - Typically, two randomized and well-controlled trials are required to demonstrate efficacy; one trial may suffice with “confirmatory evidence”
 - ▶ Medicine is “safe” for intended use
- ▶ Oversees promotional materials
- ▶ Evaluates and responds to post-approval safety concerns

Context of Regulatory Advisories

- ▶ Limited information of risks at time of drug approval
- ▶ Evidence accrues from variety of sources; FDA considers evidence
 - ▶ Legal challenges, media coverage, informal learning, publications
- ▶ Several possible actions that FDA can take short of withdrawal
 - ▶ Risk evaluation and mitigation strategies
 - ▶ Further studies
 - ▶ Labeling changes
 - ▶ Changes in marketing and promotion
 - ▶ Public health advisories
- ▶ Views of scientists, doctors, and lawyers seldom meet; LARGE uncertainties involved; decisions combine FACTS and JUDGEMENTS

Impact of FDA Drug Risk Communications on Health Care Utilization and Health Behaviors *A Systematic Review*

Stacie B. Dusetzina, PhD,* Ashley S. Higashi, MPH,† E. Ray Dorsey, MD, MBA,‡

Rena Conti, PhD,§|| Haiden A. Huskamp, PhD,* Shu Zhu, MPH,†

Craig F. Garfield, MD, MAPP,¶ and G. Caleb Alexander, MD, MS†§#

Objective: To review literature on the impact of The Food and Drug Administration (FDA) drug risk communications on medication utilization, health care services use, and health outcomes.

Data Sources: The authors searched MEDLINE and the Web of Science for manuscripts published between January 1990 and November 2010 that included terms related to drug utilization, the FDA, and advisories or warnings. We manually searched bibliographies and works citing selected articles and consulted with experts to guide study selection.

third examined communications regarding antidepressants. Most used medical or pharmacy claims and a few rigorously examined patient-provider communication, decision making, or risk perceptions. Advisories recommending increased clinical or laboratory monitoring generally led to decreased drug use, but only modest, short-term increases in monitoring. Communications targeting specific subpopulations often spilled over to other groups. Repeated or sequential advisories tended to have larger but delayed effects and decreased incident more than prevalent use. Drug-specific warnings were associated with particularly large decreases in utili-

Examples of US FDA Regulatory Advisories

Class or agent	Date and type	Communication
Antidepressants	October 2004—Black Box warning	Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder and other psychiatric disorders. All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior.
Droperidol	December 2001—Black box warning	Cases of QT prolongation and/or torsades de pointes have been reported in patients receiving Inapsine (Droperidol) at doses at or below recommended doses.
Atypical antipsychotics (metabolic risks)	November 2003—Dear Health Care Provider letter	Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment.
Atypical antipsychotics (mortality)	April 2005—Public health advisory	Treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality compared to the placebo-treated patients.
Over-the-counter cough medicines	January 2008—Public health advisory	These drugs should not be used to treat infants and children under 2 years of age because serious and potentially life-threatening side effects can occur.

Source: Dusetzina, S. B., Higashi, A. S., Dorsey, E. R., Conti, R., Huskamp, H. A., Zhu, S., Garfield, C. F., & Alexander, G. C. (2012). Table 2. Example of safety concern and FDA communication examined. In Impact of FDA drug risk communications on health care utilization and health behaviors: a systematic review. *Medical Care*, 50(6), 466–478.

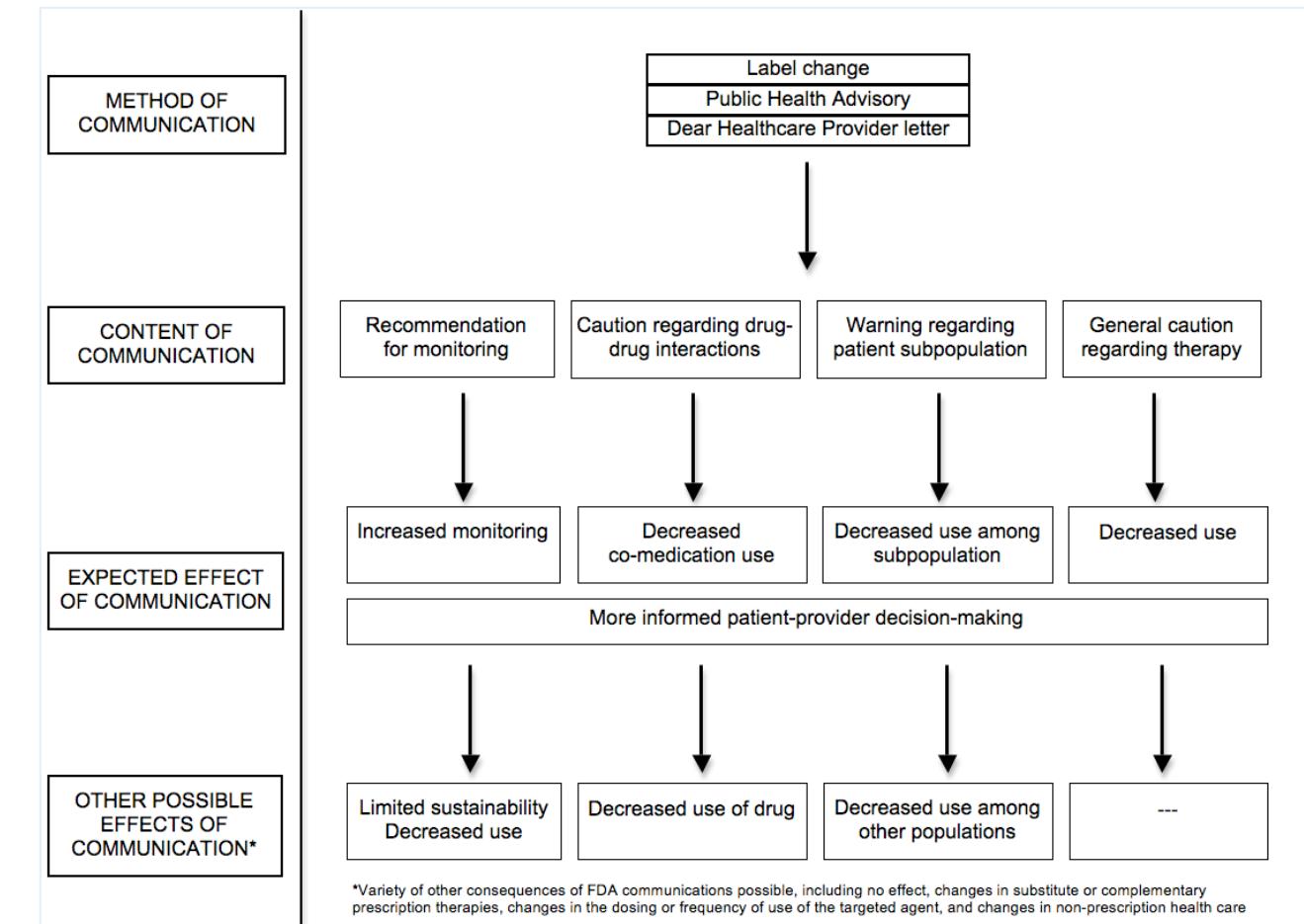
<https://doi.org/10.1097/MLR.0b013e318245a160>

Potential Advisory Impact

- ▶ Decreased physician use of therapeutic class
 - ▶ Among at risk population
 - ▶ Among other populations
- ▶ Nonadherence
 - ▶ Among at risk population
 - ▶ Among other populations
- ▶ Increased switching among therapeutic substitutes
- ▶ Increased nonprescription health care utilization
 - ▶ Emergency department use
 - ▶ Outpatient or inpatient use
- ▶ Decreased sensitivity of general public to safety signals
- ▶ Changes in firm behavior
 - ▶ Pricing
 - ▶ Non-pricing activities (e.g., marketing and promotion)



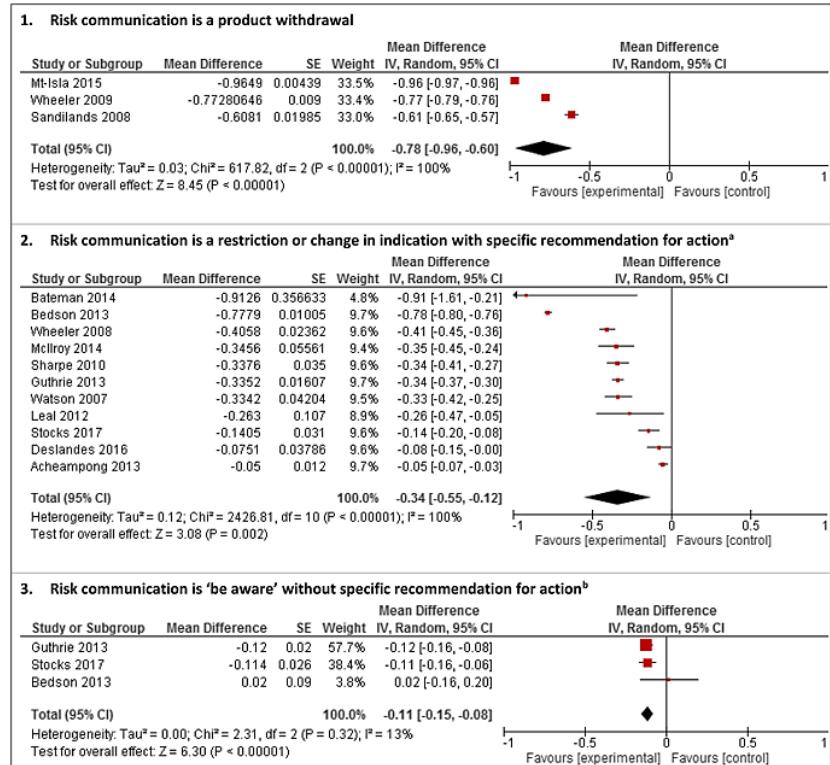
Potential Intended and Unintended Effects of FDA Advisories



Source: Dusetzina, S. B., Higashi, A. S., Dorsey, E. R., Conti, R., Huskamp, H. A., Zhu, S., Garfield, C. F., & Alexander, G. C. (2012). Figure 2. Conceptual approach to systematic review of the effect of the Food and Drug Administration communications. In Impact of FDA drug risk communications on health care utilization and health behaviors: a systematic review. *Medical Care*, 50(6), 466–478.
<https://doi.org/10.1097/MLR.0b013e318245a160>

Do Regulatory Risk Communications Have an “Average Effect”?

- Authors performed systematic review of 40 studies examining 25 specific UK risk communications
- Reanalyzed data using standardized approach (!) to avoid marked heterogeneity in original studies
- Larger effects from withdrawals than indication restrictions than “be aware” communications, also larger effects also seen for direct messaging to providers than general drug bulletins
- As with other work, varied evidence of drug substitution, spillover effects, and unintended consequences



Source: Weatherburn, C. J., Guthrie, B., Dreischulte, T., & Morales, D. R. (2020). Figure 1. Impact at 12 months on prescribing of the targeted drug stratified by type of regulatory action communicated by the risk communication. In Impact of medicines regulatory risk communications in the UK on prescribing and clinical outcomes: Systematic review, time series analysis and meta-analysis. *British Journal of Clinical Pharmacology*, 86(4), 698–710. <https://doi.org/10.1111/bcp.14104>

Drug Risk Communication Can Be Risky!—1

- ▶ “The Great Pill Scare”
 - ▶ Mid-1990s, increasing risk signals from oral contraceptives
 - ▶ Prominent UK warnings to prescribers and general public
 - ▶ Large drops in contraceptives use, increases in unintended pregnancies and abortions

Drug Risk Communication Can Be Risky!—2

- ▶ Thimerosal (ethylmercury) in vaccines
 - ▶ CDC and AAP endorsed “precautionary principle”
 - ▶ Effort to remove ethylmercury from vaccines
 - ▶ Decreases in hepatitis B immunizations, growth of mercury chelating, generation of legal, political, social opposition to vaccines



Coverage and Reimbursement

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Formularies: Fundamental Part of Prescription Drug Benefits

- ▶ A formulary is a list of covered prescription drugs
 - ▶ Drugs on formulary often grouped by generic, preferred brand, non-preferred brand tiers
- ▶ Developed by Pharmacy and Therapeutics (P&T) Committees
 - ▶ Consist of pharmacists and physicians in various clinical specialties
 - ▶ Evaluate new drugs with an emphasis on effectiveness, safety, and outcomes
 - ▶ Products often placed into tiers that determine cost share (e.g., 3, 4, 5)
- ▶ Driving utilization to generic and/or preferred drugs can lower out-of-pocket costs for drugs that are as clinically effective than non preferred drugs
- ▶ Formularies vary with respect to how restrictive they are, where they place products, how aggressively they control access to newer, costlier treatments



Example of Drug Formulary for Nasal Steroids

Product	Tier	Approximate cost/month
Fluticasone (Generic Flonase)	Tier 1	\$21
Triamcinolone (Generic Nasacort)	Tier 1	\$40
Rhinocort AQ	Tier 2	\$125
Nasonex	Tier 2	\$143
Omnaris	Tier 3	\$185
Zetonna	Tier 3	\$130

Drug Utilization Management

- ▶ **Prior authorization:** administrative and/or clinical review prior to dispensing in order to ensure patient fulfills specific criteria to maximize drug safety, effectiveness, and/or value
 - ▶ Typically reserved for select high- or ultra-high-cost therapies that are not widely used and whose safety, effectiveness, and/or value varies markedly based on context of use
 - ▶ Example: access to gene therapy (Zolgensma) for spinal muscular atrophy
- ▶ **Step therapy:** requirement of a “fail first” approach such that individuals must try one medicine before “stepping” through to a second, more costly and potentially more effective treatment
 - ▶ Example: H2-blocker before proton pump inhibitor for uncomplicated reflux
 - ▶ Example: ibuprofen before diclofenac for uncomplicated osteoarthritis
- ▶ **Quantity limits:** restriction on number of pills or total dosage allowed within a given time frame to align with FDA-label and/or clinical practice guidelines
 - ▶ Example: restriction of prescription opioids to no more than 90 morphine milligram equivalents (MMEs) per day

Prescription Drug Cost Sharing Associations With Medication and Medical Utilization and Spending and Health

Dana P. Goldman, PhD

Geoffrey F. Joyce, PhD

Yuhui Zheng, MPhil

MEDICAL PRACTICE IN THE United States has changed dramatically in the last several decades, including an increase in use of prescription drugs. More and better-quality drugs are available to prevent and manage chronic illness, and these

Context Prescription drugs are instrumental to managing and preventing chronic disease. Recent changes in US prescription drug cost sharing could affect access to them.

Objective To synthesize published evidence on the associations among cost-sharing features of prescription drug benefits and use of prescription drugs, use of non-pharmaceutical services, and health outcomes.

Data Sources We searched PubMed for studies published in English between 1985 and 2006.

Study Selection and Data Extraction Among 923 articles found in the search, we identified 132 articles examining the associations between prescription drug plan cost-containment measures, including co-payments, tiering, or coinsurance ($n=65$), pharmacy benefit caps or monthly prescription limits ($n=11$), formulary restrictions ($n=41$), and reference pricing ($n=16$), and salient outcomes, including pharmacy utilization and spending, medical care utilization and spending, and health outcomes.

Key Insights From Systematic Review

- ▶ Copayments, tiering and coinsurance are three main features of drug design that impact use
- ▶ Nearly all evidence is observational, with exception of Rand Health Insurance Experiment
- ▶ Best studies had large samples, variability in benefit design across plans AND time, efforts to control for other factors influencing utilization (data from multiple plans, changes in medical benefits)
- ▶ Patients are responsive to cost-sharing, though changes in utilization are often greater than changes in health, with price elasticity of demand of -0.2 to -0.6
- ▶ Mixed evidence regarding whether elasticities vary markedly across different therapeutic classes
- ▶ Some evidence that prior authorization (PA) is associated with lower adherence; most studies suggest PA associated with lower expenditures on targeted drug class, but no effect on total spending
- ▶ Higher cost-sharing for select groups of chronically ill patients (heart failure, diabetes, schizophrenia) associated with higher emergency department and inpatient services

Drug Utilization Research Study

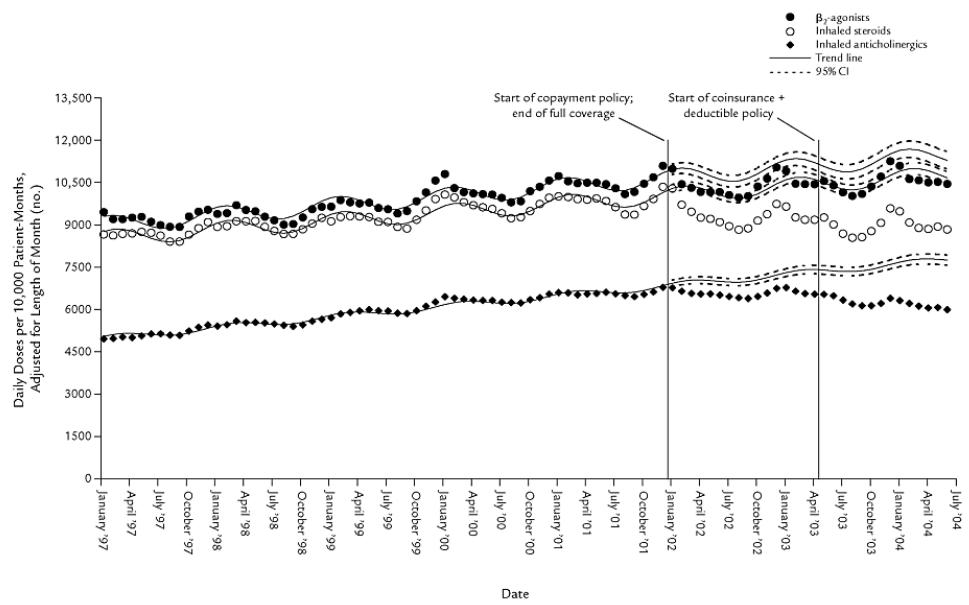


Figure 2. Use of inhaled medications among residents of British Columbia aged ≥ 65 years during changes in prescription drug plans. Copayment policy = policy in effect from January 1, 2002, through April 30, 2003, under which residents aged ≥ 65 years paid Can \$10 or Can \$25 per prescription up to an annual ceiling of Can \$200 or Can \$275, depending on annual family income; coinsurance + deductible policy = policy in effect from May 1, 2003, through June 30, 2004, under which residents aged ≥ 65 years paid a deductible of 0%, 1%, or 2% of their annual income, after which they paid 25% of prescription costs until reaching an annual ceiling of 1.25%, 2%, or 3% of their income.

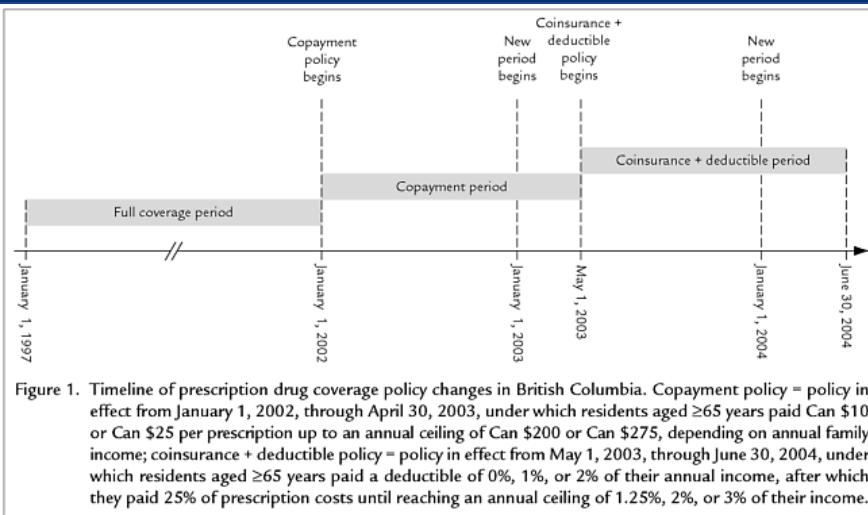


Figure 1. Timeline of prescription drug coverage policy changes in British Columbia. Copayment policy = policy in effect from January 1, 2002, through April 30, 2003, under which residents aged ≥ 65 years paid Can \$10 or Can \$25 per prescription up to an annual ceiling of Can \$200 or Can \$275, depending on annual family income; coinsurance + deductible policy = policy in effect from May 1, 2003, through June 30, 2004, under which residents aged ≥ 65 years paid a deductible of 0%, 1%, or 2% of their annual income, after which they paid 25% of prescription costs until reaching an annual ceiling of 1.25%, 2%, or 3% of their income.

Table I. Components of British Columbia prescription cost-sharing policies.

Policy	Net Annual Family Income, Can \$	Copayment*	Coinurance + Deductible†	Out-of-Pocket Maximum‡
Fixed copayment: January 1, 2002– April 30, 2003	$\leq 50,000$ $> 50,000$	Can \$10 Can \$25	– –	Can \$200 Can \$275
Fair PharmaCare coinsurance with income-based deductible: May 1, 2003–June 30, 2004	$\leq 33,000$ $> 33,000–\leq 50,000$ $> 50,000$	25% 25% 25%	0% 1% 2%	1.25% 2% 3%

*Proportion of net family income from previous year.

†Proportion of drug costs paid by patient after deductible and before out-of-pocket maximum.

Major Change in Pharmaceutical Coverage: Medicare Part D

Table 2. Effect of Medicare Part D on Out-of-Pocket Prescription Expenditures and Utilization

Study Period and Outcome*	Average Adjusted Monthly Effects for Part D-Eligible Seniors†		Difference due to Part D‡		
	Factual Effect	Counterfactual Effect‡	Absolute Change	Relative Change, %	P Value
Ramp-up post-Part D period					
Out-of-pocket cost, \$	39.3 (38.9 to 39.7)	43.1 (42.0 to 44.2)	-3.8 (-4.7 to -2.9)	-8.8 (-6.6 to -11.0)	<0.001
Pill-days	68.2 (67.8 to 68.3)	67.4 (66.8 to 68.0)	0.8 (0.3 to 1.3)	1.1 (0.5 to 1.7)	<0.001
Stable post-Part D period					
Out-of-pocket costs, \$	34.4 (34.0 to 34.8)	39.6 (38.2 to 41.3)	-5.2 (-3.8 to -6.6)	-13.1 (-16.6 to -9.6)	0.003
Pill-days	66.7 (66.3 to 67.1)	63.0 (62.3 to 63.7)	3.7 (3.2 to 4.2)	5.9 (5.1 to 6.7)	<0.001

* The ramp-up period is January 2006 through May 2006, before the deadline for enrollment in Medicare Part D. The stable period is June 2006 through April 2007, after the deadline for Part D enrollment.

† All individual effects were statistically significant.

‡ Counterfactual changes in outcomes (changes that would have resulted if Part D had not been implemented) were estimated by using the generalized estimating equation model described in the Appendix Figure (available at www.annals.org).

Summary

- ▶ Marketing and promotion, emerging evidence, regulation, and coverage and reimbursement represent four key drivers of drug utilization
- ▶ If you want to understand prescription drug utilization, you've got to understand how these factors may change the behavior of prescribers, patients, and other stakeholders
- ▶ There are also many important pharmacoepidemiologic studies that quantify the association between one or more of these factors and changes in the use of a prescription drug or therapeutic class
- ▶ As with other areas of drug development and pharmacoepidemiology, these are dynamic processes—the only constant is change, and there is more good work to be done