The Ethics of High Drug Prices

DONALD MILLER, PHARM.D.

PROFESSOR OF PHARMACY PRACTICE

Drug Goes From $13.50 a Tablet to $750, Overnight

Specialists in infectious disease are protesting a gigantic overnight increase in the price of a 62-year-old drug that is the standard of care for treating a life-threatening parasitic infection.

The drug, called Daraprim, was acquired in August by Turing Pharmaceuticals, a start-up run by a former hedge fund manager. Turing immediately raised the price to $750 a tablet from $13.50, bringing the annual cost of treatment for some patients to hundreds of thousands of dollars.

Sept 20, 2015 NY Times https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html

Specialty Drugs

What you would guess the price of Humira is? Of Cosentyx?

Humira list price is about $60,000/year.

Cosentyx list price is about $69,000/year at a maintenance dose.

Similar biologic drugs may cost from $30,000 to $100,000/year.

All prices are “list” or wholesale price.

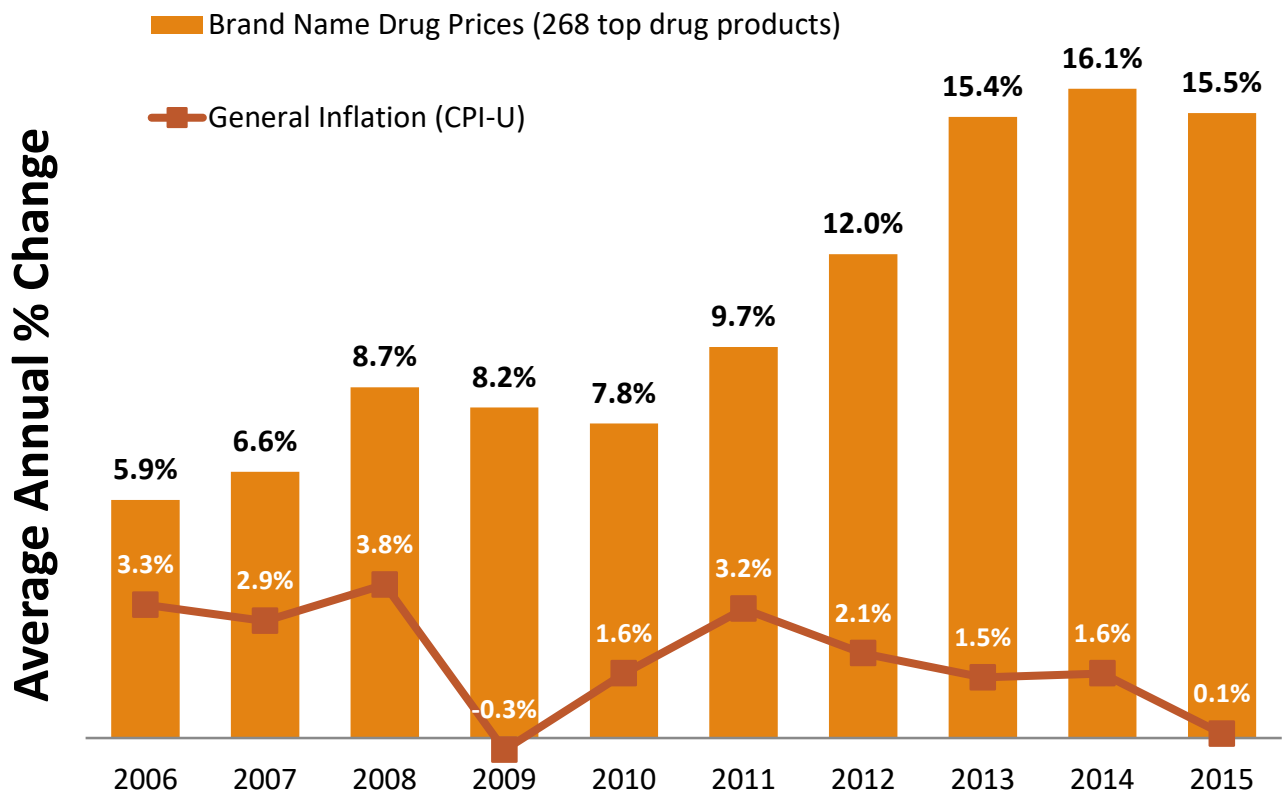
The average cost of specialty drugs for cancer or rheumatoid arthritis, exceeds the median U.S. household income.

At $300,000 a year, Sarepta's new drug is considered a steal

Sarepta Therapeutics Inc.'s eteplirsen, the first approved treatment for the rare, degenerative disease Duchenne muscular dystrophy, will cost patients on average about $300,000 a year.

Though not exactly a steal, even by pharmaceutical price standards, Wall Street analysts were expecting a much higher number — as much as more than twice the figure — and even hailed the price as a "bargain."

https://www.marketwatch.com/story/at-300000-a-year-sareptas-new-drug-is-considered-a-steal-2016-09-20



Average Brand Name Drug Prices vs. General Inflation Rate by Year

Schondelmeyer, S, Purvis, L. Trends in Retail Prices of Brand Name Prescription Drugs Widely Used by Older Americans 2006 to 2015 (internet). 2016 December. Available from: https://www.aarp.org/content/dam/aarp/ppi/2016-12/trends-in-retail-prices-dec-2016.pdf

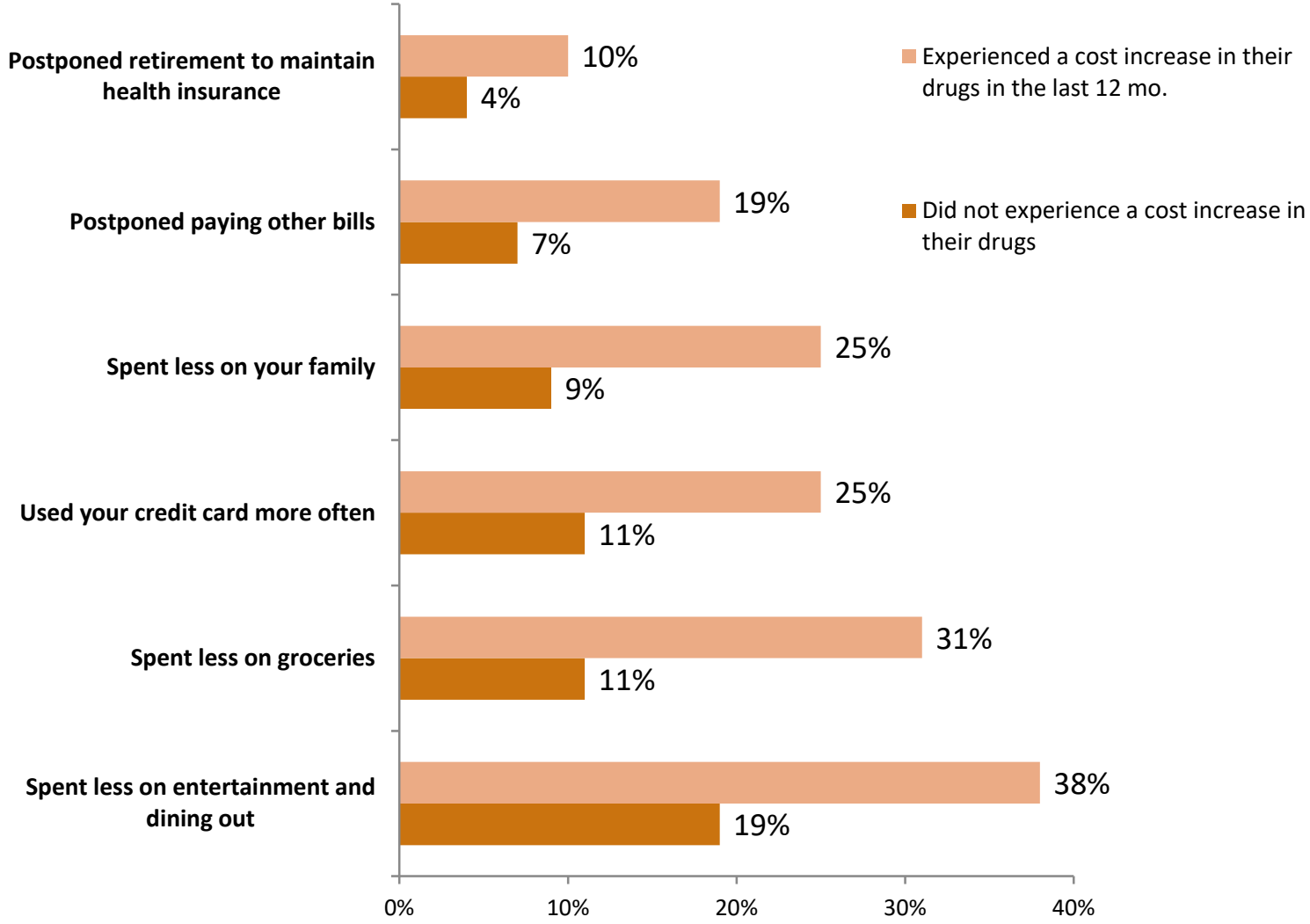
Consequences of High Drug Costs

Patients do not fill prescriptions. In 2016 20% of U.S. adults reported not filling a prescription due to cost (Health Aff 2016;35:2327-36).

When prescriptions are filled, adherence to medication is poor. Many ration their own drugs by not taking them as often as they should, split their tablets without first talking with a doctor, or use expired medication.

State and federal budgets are strained by the diversion of resources to drugs.

Patients face delays in getting insurance approval to use expensive drugs.



What has been done in the last 12 months in order for patients to afford their prescription medication.

Skinner, G. As Drug Prices Increase, Quality of Life Goes Down (internet). 2016 June 21. Available from: https://www.consumerreports.org/drugs/as-drug-prices-increase-quality-of-life-goes-down/

What is Driving Increased Prices?

ARE THEY JUSTIFIED?

Trump: 'Nobody knew health care could be so complicated'

By Kevin Liptak, CNN White House Producer

Updated 4:10 AM ET, Tue February 28, 2017

MORE FROM CNN

Heavy snow brings travel c
to UK

Sirius XM faces celebrity b
after Steve Bannon rejoins

Possible Drivers of Increasing Drug Costs

Better, more complex, drugs and greater demand.

Pharmacy Benefit Managers.

The opaqueness of the system.

Excessive FDA regulation.

Cost of development (why are generics increasing?).

Excessive patent extensions on drugs.

Cost of Drug Development

Updated estimate of cost to develop a new drug was updated to about $2.5 billion (2013 dollars), according to the Tufts Center for the Study of Drug Development (a drug company supported center). Based on analysis of 10 companies and 106 products (87 chemicals and 19 biologics). Based on $1.4 B out of pocket and $1.1 B in capital costs from lost investment and unsuccessful projects.

Post-marketing costs can add another $300 M on average.

http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study

Increase due to complexity of studies. FDA review time not a major factor – better FDA review times actually drove down capital costs since 2000.

Are U.S. prices justified by R&D? No. https://endpts.com/do-big-rd-budgets-justify-us-premium-drug-prices-no-way-analysts-scoff/

Cost of Drug Development

Researchers analyzed U.S. Securities and Exchange Commission filings for 10 drug companies that received FDA approval for a cancer drug from January 1, 2006, through December 31, 2015 and *had no prior drugs approved*. Cumulative R&D spending was estimated from initiation of drug development activity to date of approval. Earnings were also identified from the time of approval to the present. The 10 companies had a median time to develop a drug of 7.3 years. Five drugs received accelerated approval from FDA and 5 received regular approval. The median cost of drug development was $648.0 million. The median cost was $757.4 million for a 7% opportunity cost and $793.6 million at a 9% opportunity cost.

With a median of 4.0 years since approval, the total revenue from sales of these 10 drugs since approval was $67.0 billion compared with total R&D spending of $7.2 billion ($9.1 billion, including 7% opportunity costs). The researchers concluded the cost to develop a cancer drug is significantly lower than prior estimates, and that revenue far exceeded costs.

JAMA Internal Medicine 2017;177:1569-75

Patent Games

Although market exclusivity on brand-name drugs typically expire after about 12 years, manufacturers have discovered a number of end-runs to box out generics.

They have learned to defend exclusivity by getting additional patents on formulations, by changing formulation (e.g. longer-acting dosage forms) just before generic competition comes out, and by paying generic manufacturers to delay introduction of competing products (pay-for-delay deals).

Others have resorted to filing citizen petitions, which delay generic competition by raising public concern about the drug in question. Yet another tactic entails negotiating exclusive deals—such as bundled discounts—with drug plans so that more expensive medications are favored.

Patent Games

Brand-Name Combo Drugs May Cost More Than Buying The Drugs Separately, Study Indicates.

Reuters (8/21) reports researchers have found that brand-name medicines “that combine multiple drugs into a single” tablet “may be more expensive than buying each drug separately.” The researchers looked at data on 1,500 medicines from 2011 to 2016 that accounted for the most spending by Medicare Part D drug plans in 2015 and identified “29 brand-name combination pills with generic alternatives available.” They found that “for the ten most costly brand-name combo pills, Medicare could have spent $2.7 billion less if generic alternatives had been prescribed instead.”

Allergan Transfers Patent To Native American Tribe To Protect Drug From Generic Competition.

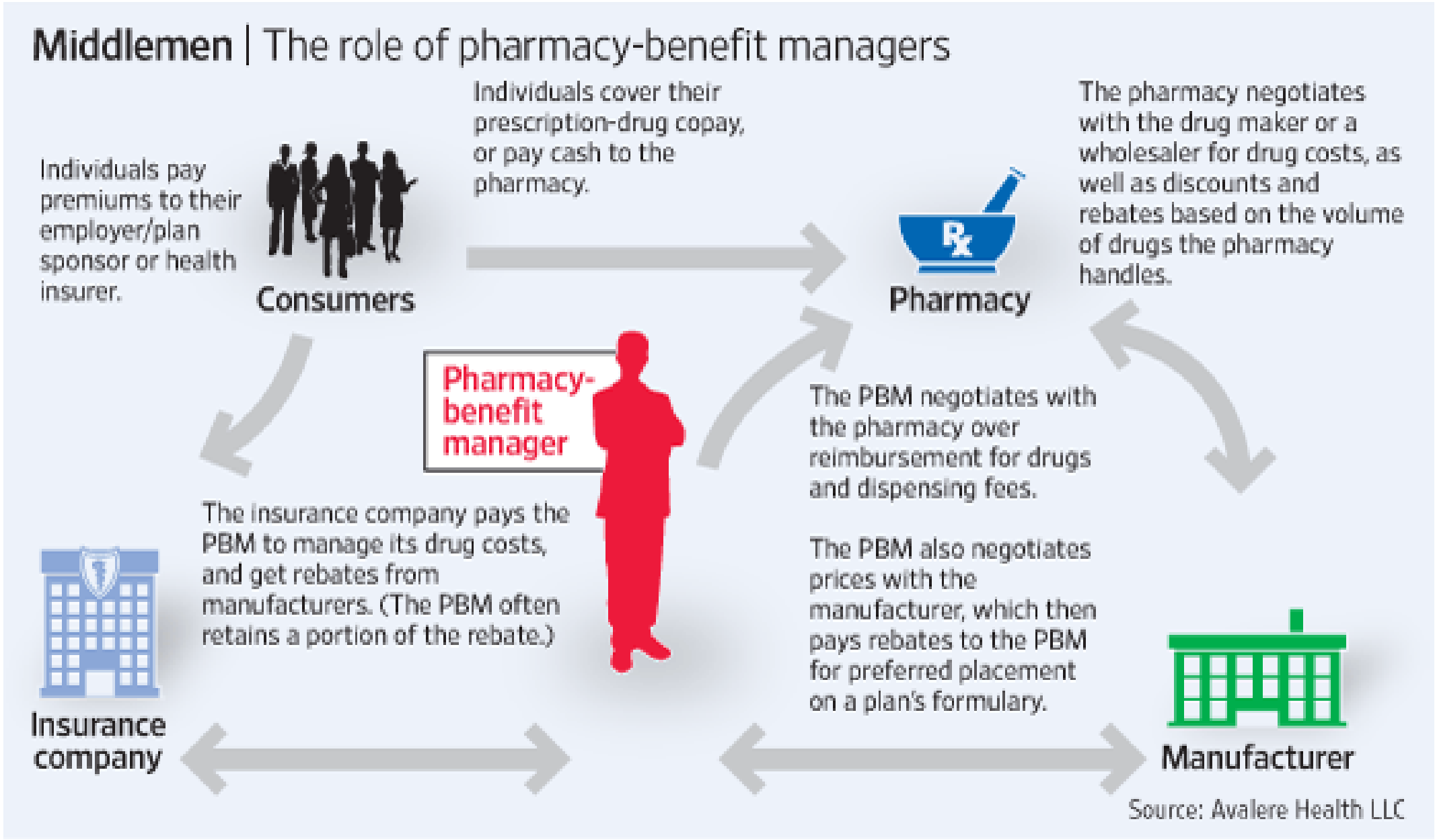
The New York Times (9/8/17) reported that Allergan "transferred its patents on a best-selling eye drug to the Saint Regis Mohawk Tribe in upstate New York — an unusual gambit to protect the drug from a patent dispute." Pursuant to the deal, Allergan pays the tribe $13.75 million and in exchange, the tribe claims "sovereign immunity as grounds to dismiss a patent challenge" to the dry-eye drug Restasis (cyclosporine ophthalmic emulsion). The tribe "will lease the patents back to Allergan, and will receive $15 million in annual royalties as long as the patents remain valid." The move created "speculation about whether other drug companies would soon follow suit in order to protect their patents from challenges through a patent-review process that the industry despises."

Bloomberg News (9/9/17) reported that "there's a legal basis for the strategy," as the Patent Trial and Appeal Board "recently ruled in two cases that state-university-owned patents aren't subject to the review process because states have sovereign immunity." However, "the university was the original owner of the patents."

Would give tribe only $15 million in annual royalties despite $1.4 billion in annual drug revenue.

How are Drugs Actually Paid For?

CONNECTING THE DOTS



https://www.investopedia.com/articles/markets/070215/what-pharmacy-benefit-management-industry.asp

Overview

List prices are set by the manufacturer, but do not reflect what is typically paid for the drug.

Middlemen (Pharmacy Benefit Managers) negotiate discounts and rebates and include non-cash considerations such as preferred status on formularies.

Insured patients pay only the co-pay out-of-pocket, which insulates them from the true prices. Co-pays vary depending on the insurance plan and which “tier” of coverage it is on. Deductibles may be need to be met first, and co-insurance may require paying a fixed percentage of cost.

Pharmacies collect the co-payments but pass them on to PBMs which later reimburse the pharmacy a negotiated rate. Co-payments may actually exceed cash drug cost and pharmacy reimbursement.

Things work differently for private insurance payer, hospitals, physician-purchased drugs, and public payers (Medicare, Medicaid, VA, Tri-Care, etc.).

JAMA 2018;319(March 13):1042-3 JAMA 2018;319(March 3):1045-6

Pharmacy Benefit Managers (PBMs)

Intermediaries hired by employers or insurance companies to manage drug costs by administering drug claims, negotiating with manufacturers and pharmacies for discounts and limits on drug availability. For example, BCBS of ND contracts with Prime Therapeutics.

PBMs lower the price that manufacturers receive by getting direct discounts on long term contracts (either a set amount or percentage).

The difference between list price and what the manufacturer actually receives can be very substantial (a hepatitis C drug with a list of $90,000 for a course of therapy can be reduced to less than $20,000 after the discounts and rebates are factored in). PBMs claim to pass these rebates to the insurers, but due to the opaque nature of their contracts, quite a bit of these funds may go to their own bottom line (on top of basic fees the insurer contacts with the PBM for). Neither the manufacturer nor PBM need to disclose the actual agreements which are closely held secrets for each agreement.

PBMs are very large companies (only 3 dominate most the U.S.), and are extremely profitable ($130 billion annually in drug spending goes to PBMs). As middle men, they do not add direct value to health care but DO soak up health care dollars for shareholders. Not licensed or regulated in any way!

Problems With PBMs

More expensive brand name drugs may actually be listed as “preferred brands” by PBMs because they get a better contract with the manufacturer, OR because of bigger cash rebates to the PBM, but this does not necessarily mean the patient pays less! Advantage to the payer and PBM has priority over the patient.

Some insurers require a set co-payment for each prescription — say, $15 or $20 — even when the insurer reimburses the pharmacy at a much cheaper rate. When insurers seek deals for generic drugs, they often do so in bundles, reaching agreements for groups of different drugs rather than getting the lowest price on every drug.

When pharmacies enter a contract with PBMs, languages in those contracts prevent pharmacists from telling customers about more affordable prescriptions. The drug that they're receiving might be cheaper if they pay cash for it rather than running it through their insurance carrier. Overpayments on co-pays may be as common as 25% of all prescriptions (JAMA 2018;319:1045-6).

Consumers also may face penalties if they pay cash to save money. In many cases, insurers won’t let them apply those purchases to a deductible or out-of-pocket spending maximum.

Rebates

Pharmaceutical companies set a high “list price” for a drug, and then lower the cost for health plans through giving hefty rebates in *exchange for the broadest access to patients*.

Rebates have a federal “safe-harbor” protection from anti-kickback laws. The anti-kickback law makes it illegal to pay an incentive for drugs or services that Medicare, Medicaid or other federal healthcare programs cover.

But rebates are secret and make it difficult to know what is really being paid for any given drug. Rebates may give PBMs an incentive to prefer MORE EXPENSIVE drugs so they can pocket larger rebates!

Manufacturers claim they are forced to increase list prices due to the rebates. PBMs claim they pass on all rebates and manufacturers are simply deflecting blame for high prices.

Rebates on expensive drugs are usually spread over the entire PBM business, to subsidize beneficiary premiums, rather than applied to the sick patients who are paying for the drug. Thus, the sick actually subsidize the healthy! PBMs argue this is necessary to hold down costs for all, but it is in fact a redistribution of fixed savings to healthier persons.

Deflecting Blame

Pharma, under attack for drug prices, started an industry war
Washington Post (01/03/18)

The pharmaceutical industry lobby spent 2017 working to redirect public anger about drug prices to PBMs, in the process bringing a long-simmering feud between two big health industry players into the open. **The drug companies' fight with PBMs and insurers has helped thwart any real action on the issue of drug pricing—splintering the problem into a multi-industry echo chamber of accusations that is hard to comprehend, much less solve.** PBMs say they typically pass along 90% of the savings they negotiate to customers, and point to data showing no link between drug price growth and rebates.

Prior Authorizations

A requirement that prescribers receive prior approval to prescribe a drug if their patient is to get reimbursement by their insurance plan.

Biggest problem is long delays in actually getting the approval. While sometimes they take just a couple of days, PAs can delay even life-saving chemotherapy/ oncology drug approval by a month or more. In the meantime patients suffer or worry unnecessarily, or simply decide to use less effective alternatives.

Contacting a PBM can use up 30 minutes or more of staff time, and/or another 30 minutes or more completing paper work and documenting information in the medical record. May occur even for generic drugs like prednisone, pain drugs, etc.

Tiered Formularies

Payers use tiered formularies (drug lists), meaning a patient's cost-sharing obligation varies by category.

- Tier 1 drugs may have no co-pay requirement and consist of generic drugs.
- Tier 2 drugs are mostly preferred brands and have modest co-payments.
- Tier 3 consists of non-preferred and specialty drugs that are high cost. In order to discourage utilization, *these drugs require prior authorization*, a steeper co-pay and co-insurance. In response, pharmaceutical companies may offer co-payment assistance that attenuate the patient's obligation but encourages use of the expensive drug.

Tiering reduces spending on expensive drugs, and is also a tool to bring pharmaceutical companies to the negotiating table for rebates. On the other hand, it makes it difficult for patients to obtain appropriate drugs.

Policy Options for Holding Down Prices

ALEXANDER GC, ET AL. PHARMACOTHERAPY 2017;37(11):1469-78.

Attempts to Control Prices

Free Markets/Greater Competition/More Generic Drugs

Greater Transparency in Pricing (PBMs, rebates)

Drug Company Patient Assistance Cards and Programs

Importing Drugs

Reference Pricing

Value Pricing

Regulation and Limits on Costs (FDA has no role).

Free Markets - Does Competition Keep Prices Down?

HHS Secretary Azar said the White House wants to drive competition by allowing more branded and generic drugs. "The more drugs that are out there," he said, "the lower the prices are going to be.“ *Azar talks prescription drug prices in Miami, Miami Herald (06/20/18)*

However, substantial evidence shows drug pricing does not conform to usual economic models. Patent monopolies (among other things) allow pricing well above an expected market price (Pharmacotherapy 2017;37:14-69-78).

Yes, for generic drugs. Generics in general cost less than innovators. The more competitors for generic drugs, the less prices increase. (Annals of Internal Medicine 2017; 167:124-151).

Drug shortages are almost invariably associated with increases in price.

However, introduction of new drugs in the same general class does not lower prices. New drugs typically are priced in the same range as competitors and existing competitors often raise prices.

Arthritis drugs show how U.S. drug prices defy economics *Kaiser Health News (12/22/17)*

The laws of economics suggest that introducing multiple new drugs for a condition should bring prices down over time, but the experience with rheumatoid arthritis (RA) shows how that is not always the case. The cost of the first RA drug has climbed from $10,000 per year when it debuted a decade ago to more than $40,000, despite competition from a number of similar products.

https://www.medscape.com/viewarticle/890699?nlid=119874_865&src=WNL_mdplsfeat_180102_mscpedit_rheu&uac=19003PJ&spon=27&impID=1524813&faf=1#vp_2

New Approach to Generic Competition

Hospitals Join Together To Start Their Own Drug Company.

The Washington Post (9/5, Johnson) reports that a group of about 500 hospitals, including seven large hospital systems, and three philanthropic groups are launching a “mission-driven, not-for-profit generic drug company, Civica Rx, to take some control over the drug supply” and reduce the effect of “price spikes on old drugs and long-lasting shortages of critical medicines.” The venture “will focus initially on establishing price transparency and stable supplies for 14 generic drugs used in hospitals.” The Post says Civica Rx’s “first drug could hit the market next year.”

Transparency in Pricing

It has been suggested that drug prices should be included in direct-to-consumer advertising.

Bloomberg News (7/10/18) reports some pharmaceutical companies "are canceling or reducing planned price increases in the U.S., following a new California drug pricing transparency law and continued political pressure over pharmaceutical costs." The California state law, which went into effect earlier this year, requires pharmaceutical companies "to give insurers, governments and drug purchasers advance notice of large price increases, as a way of publicly pressuring pharmaceutical companies to keep prices down."

More important, elimination of, or full transparency in rebates would make it easier to detect abuses. Squeezing PBMs to reduce their profits seems to be an approach that everyone can agree on.

Drug Company Coupons and Assistance

For low income patients, companies do often provide drugs at a substantial discount or offer to pay co-insurance.

Manufacturers may offer coupons or drug cards to lower (or even eliminate) out-of-pocket costs, but insurers still have to pay their share. This results in incentives to use expensive drugs and drive up overall spending on drugs (not allowed on government plans).

“As prices climb, Vyera has followed what has become a familiar pharmaceutical effort to shift attention and costs, launching what it calls the Daraprim Direct program. Commercially insured patients can get a company-sponsored coupon that guarantees they will pay no more than $10 out-of-pocket. Uninsured patients at 500% or less of the federal poverty level will not pay anything”.

Drug Importation

Companies Associated With Canada Drugs Plead Guilty To Charges Of Selling Counterfeit, Misbranded Drugs In US.

The Wall Street Journal (12/15/17) reported several companies controlled by Canada Drugs, an online pharmacy, have agreed in a US federal court to plead guilty to charges of selling counterfeit or misbranded drugs. The companies agreed to pay a $5 million fine and $29 million in compensation for illegal sales, and also to cease illegal sales in the US. Kristjan Thorkelson, the founder of Canada Drugs, agreed to plead guilty to a criminal charge.

See more on counterfeit issues at NEJM 2017;377(Oct 26):1699-1700.

Temporary importation could work to fight small generic monopolies like Daraprim, or for drug shortages. FDA has formed a working group to study.

However, the U.S. market is much larger than that of Canada, Australia, etc. It is impossible to import our whole supply, especially since the same manufacturers produce the major drugs in all countries.

Reference Pricing

In this system, similar drugs are grouped by therapeutic class, and payment is limited for all to the lowest price (or median, etc.) drug in the class. If patients want a more expensive drug, they must pay the difference (unless an exception is granted).

In one experiment using this approach by an alliance of private payers, there was a $1.34 million reduction in expenses to employers and a $120,000 increase in employee co-payments versus a comparison group (New Engl J Med 2017;377:658-65).

Value-Based Pricing (Outcomes-based Contracting)

Essentially a “money-back guarantee”, so that price is refunded to consumer (or payer) if the drug does not work. Other companies have proposed discounts, not all money back arrangements.

Sounds better than it would work in real life. Company can simply price the drug high enough to compensate for a small refund or discount rate.

Several problems in practice – patients/insurers must actively apply for a refund, prove the drug did not work (which can be subjective), changing insurance coverage over time could limit incentive to pursue refunds, must be able to distinguish effect of drug from other treatments and events going on with a particular patient. (Ann Intern Med 2018;168:888-9)

Reducing Patent Protections

Fight gaming in the system by excessive patents and exclusivity agreements.

Preventing pay-for-delay agreements.

Shortening patent periods and **putting some in the public domain, based on amount of public research funding**.

Limits on cost of drugs developed with federal or public dollars.

- CAR-T cell therapies were developed through basic research at the University of Pennsylvania, yet the first marketed products is priced at $475,000 for a course of therapy in treating childhood leukemia.

Regulation and Stronger Negotiation

The New York Times (11/30/17) reports the **National Academy of Sciences** "called...for sweeping changes in the pricing, sale and promotion of prescription drugs to make lifesaving treatments more affordable without discouraging the development of new medicines." The academy said in a new report, "**The federal government should consolidate and apply its purchasing power to directly negotiate prices** with the producers and suppliers of medicines."

Most countries control prices and pay based on **cost-effectiveness (**a **value-based** model). Centralized advisory boards determine efficacy and cost-effectiveness. Prices are set based on reference to similar drugs and price in similar countries.

Government can potentially negotiate or even set prices on drugs prescribed for federal programs, *but drug companies can simply recoup profits in the private market.*

Setting limits on drug prices for all customers is commonly done in other countries, but would require a major change in philosophy in the U.S.

Why is Nothing Happening?

“Full of sound and fury, signifying nothing.”

All potential solutions atre hamstrung by the complexity of the system(s), each part controlled by different players watching for their self-interest. The huge scale of the health care enterprise, and its multiple subsystems, makes it almost totally resistant to change.

Azar Takes a Victory Lap

Congressional Quarterly (8/20/18) reports, "The prices of 60 percent fewer brand name prescription drugs increased since the Trump administration released its drug pricing blueprint in May, compared with the same period last year, Health and Human Services Secretary Alex Azar said Monday." The article says this announcement "came as Azar took a 100-day victory lap on the release of" the Trump Administration's drug pricing blueprint. He is quoted as saying, "The pharmaceutical industry has responded with real changes that will benefit patients, not out of any altruism on their part, but rather they're skating to where they see the puck is going."

The Washington Examiner (8/20/18) reports that the Administration contends "the president's blueprint to tackle high drug prices is already sparking a 'sea change' that's prompting pharmaceutical companies to lower prices." In addition to fewer price increases, the Administration said there are "54 percent more generic and brand drug price decreases compared to the same period in 2017." Dan Best, special adviser to Azar on drug pricing reform, stated, "I don't want to speak specifically for the manufacturers, but it is unprecedented to see action like that."

Turing Pharmaceuticals CEO Defends Drug Pricing

STAT (12/4/15) reports that Turing Pharmaceuticals CEO Martin Shkreli "rejected fresh criticism that he went back on his promise to lower the price of the life-saving medicine Daraprim." **At a health industry gathering, Shkreli said, "Our shareholders expect us to make as much as money as possible." He added, "That's the ugly, dirty truth."**

High Prices are a Moral Requirement?

A pharma executive has defended his decision to raise the price of an antibiotic mixture to more than $2,000 a bottle, arguing there was a “moral requirement to sell the product at the highest price”. Last month, Nostrum Laboratories, a small Missouri-based drug maker, more than quadrupled the price of a bottle of nitrofurantoin from $474.75 to $2,392.

Nitrofurantoin is an antibiotic used to treat bladder infections that was first marketed in 1953, which appears on the World Health Organization’s list of essential medicines.

https://www.ft.com/content/48b0ce2c-b544-11e8-bbc3-ccd7de085ffe

Or http://www.630wpro.com/news/report-pharma-exec-says-he-had-moral-requirement-to-raise-drug-price-400/

The industry is all about maximizing shareholder profit. It has lost any real concern for public good. PBMs, while carrying out a useful function, have bloated into highly profitable businesses by taking large cuts as middlemen.

Is Current Drug Pricing Ethical?

There is currently no check on drug prices, and there is a poor link between value and price. It is clear that a considerable profit is going to manufacturers and PBMs. Pharmaceutical companies are free to charge whatever the market will bear, particularly when there is no or little choice about using a product.

Consumers have a choice about when and whether to buy a new auto, phone, a new iPad, etc., but typically need their medicine and have no true negotiating power. No one voluntarily seeks out chemotherapy for cancer, etc. withot need. In addition, the consumer relies on an outside agent (physician) for decisions about choice. Thus, drug pricing is essentially no different than gouging customers who desperately need supplies during a natural disaster.

Is the drug industry the same as any other? Is there an ethical imperative to keep prices low for consumers and payers? Or is it perfectly ethical to let the free market work and to maximize profits for shareholders at the expense of consumers? How can public policy balance these competing imperatives?

Is There a More Ethical Framework?

Our current drug pricing is purely based on a business model in which the opportunity to make money supposedly raises the wealth for all, and innovates to find solutions.

A different model, used by most countries, is a public health model, in which the priority is overall health of the population. This is the thinking that leads to universal health care, subsidized care, and regulation of drug prices to assure access to medications.

Within this model of thought, there are many models for delivery in other countries that still preserve markets and competition (e.g. mandatory nonprofit insurance plans). It is a false dichotomy to pit free enterprise against common good.

Bottom Line

Short-term solutions can focus on:

- Greater transparency of the pricing and distribution system to expose abuse
- Eliminating some patent protection games and keeping some patents in the public domain

Some regulation of prices based on cost-effectiveness could curb drug spending considerably (either by limiting payment, or threatened exclusion of drugs from coverage with poor cost-effectiveness).

Long term, a more universal or centralized system of health care could lead to additional simplification and transparency on pricing that would hold down costs, and make price negotiation much simpler.