UNC Chapel Hill

AN IN DEPTH ANALYSIS OF PHARMACEUTICAL PRICING

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BACKGROUND

Over the last few years, pharmaceutical list prices and spending on pharmaceuticals have been growing at an undesirably high rate. Pharmaceutical pricing has become the focus of political and societal attention due to the substantially high impact of prices on patients. The pharmaceutical pricing process is shrouded in a complicated and confusing system of proprietary contracts. Despite - and partly due to - the complexity and poor understanding of the intricacies of pharmaceutical pricing, it has become a debate with highly polarized, and I would argue uninformed, opinions on both sides.

Pharmaceutical manufacturers justify high prices with the claim that it supports the cost of innovative therapies. Manufacturers argue that drugs that make it to market must assist with supporting the exorbitant research and development (R&D) costs of all the therapies that did not make successful market entrances. Additionally, pharmaceutical manufacturers state that they do not receive the full list price of a medication and that publicly available pricing information does not represent the full picture. They posit that other lesser, well known organizations play a role in supporting the high prices that patients are exposed to and thus should also be held accountable for high prices.

Those that the manufacturers serve are the public. The public understands the least well versed on pharmaceutical pricing process – considering this requires knowledge of insurance contracting, formulary positioning, R&D cost structures, the nuances of international pricing and reference pricing points – and yet, are the most affected by it. The prices paid at the pharmacy counter are palpable and that generates frustration amongst many Americans. The public is often exposed to reports of low prices in other countries and feel that the U.S. healthcare system and American patients, through the higher prices they pay, bear the burden of the low prices paid by

other countries all around the world. The impact of high prices coupled with consumer ignorance and media sensationalization, may lead to consumer outrage and indignation. The media senses this outrage and brings to light scandals, the public rage is further fueled and politicians are incentivized to repeatedly discuss the topic pharmaceutical pricing. Ultimately consumers feel that pharmaceutical firms are taking advantage of them. by nature of the fact that they hold the key to improving life and knowing that patients will pay high prices to obtain that relief. This belief has driven the American public to maintain a sense of cynicism when it comes to pharmaceutical companies. The frustration at high prices, a lack of understanding and publicized examples of corporate greed have brought the pharmaceutical pricing debate to the incredibly tense state in which we currently find ourselves.

SIGNIFICANCE

This is a significant topic for reasons that are personal, political and professional. At the highest level, the issue of pharmaceutical pricing is relevant to anyone who purchases medication in the United States as insurance companies generally do not cover the full price of prescriptions. Moreover, pricing is of the utmost importance for those individuals working in healthcare administration and policy as this will be a topic of debate for the foreseeable future with healthcare reform presently being at the forefront of the presidential legislative agenda. Most notably, pricing is personal as it informs the decisions we make about our own healthcare. When we are prescribed medications and make choices between treatments with our providers, knowledge of the pharmaceutical pricing system, structure and its components can only serve us better as consumers.

When selecting a pricing proposal to support prior knowledge of pharmaceutical pricing is vital. Blindly supporting policies and initiatives without wholly understanding the intricacies

of the industry may be more dangerous than supporting nothing at all. In this paper, I intend to bring awareness to those who seek to understand pharmaceutical pricing in order to be better educated on the pharmaceutical system as a whole. Specifically, I am focused on those individuals who will one day be policymakers and healthcare administrators. Presenting a comprehensive overview of pharmaceutical pricing will help my colleagues make informed decisions on this topic when they are called upon.

Personally, I was drawn to this topic as I have accepted a position with GlaxoSmithKline (GSK) after graduation this May. It is quite likely that my first role will be within the contracting division of GSK which is responsible for creating access for therapies through formulary negotiations with payers. It is very much to the benefit of my professional development to understand the processes used to derive prices for therapies which are new to market. Further, it suits me to have an understanding of how contracting and pricing may change in the future and what the contracting landscape may look like over the course of my career.

Finally, awareness is the first step towards change. It is undeniable that healthcare costs in this country are rising at a rapid rate. In order to take action, we need to develop a deep understanding of the root causes so that we can address them efficiently and effectively. This systematic review will provide insight and hopefully assist with generating some solutions that can be used to restructure the pricing system.

SPECIFIC AIMS

The first aim of this paper is to develop a clear understanding of the prices and business to business transactions in the pharmaceutical pipeline. Specifically, I will outline the distribution of profits amongst the organizations involved in the supply chain. To achieve this aim I primarily utilized grey literature.

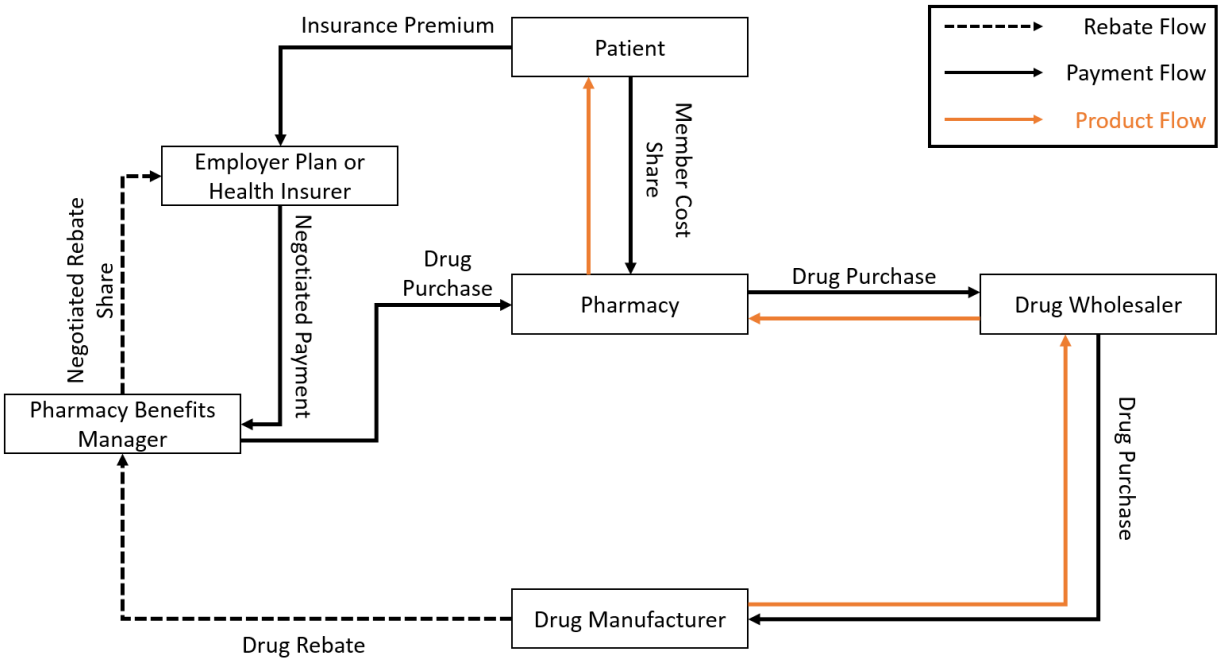
The second aim is to provide a comprehensive analysis of the pharmaceutical pricing process. By reviewing the published literature and tertiary sources, it was apparent that the role of manufacturers in setting high prices for drugs is well documented. As such, throughout this review there will be more of a focus on the aforementioned organizations which contribute to high prices, especially targeting pharmacy benefit managers. Acknowledging that I provide a biased perspective due to the nature of my future employment, I will attempt to provide multiple perspectives to the arguments within this review by examining the perspectives of drug manufacturers, insurance companies and patients.

The third aim is to present the argument that the cause of the pricing epidemic is a lack of transparency and knowledge of the system. In its current state, the pharmaceutical system is a Gordian knot involving countless organizations, contracts and factors influencing prices. Compounding this is the fact that contracts and agreements made to set prices are agreed upon in confidential meetings and unavailable to the public or to lawmakers. I will present data and findings from peer-reviewed literature and tertiary sources to piece together a picture of pricing practices as well as attempt to demystify the contracts between organizations.

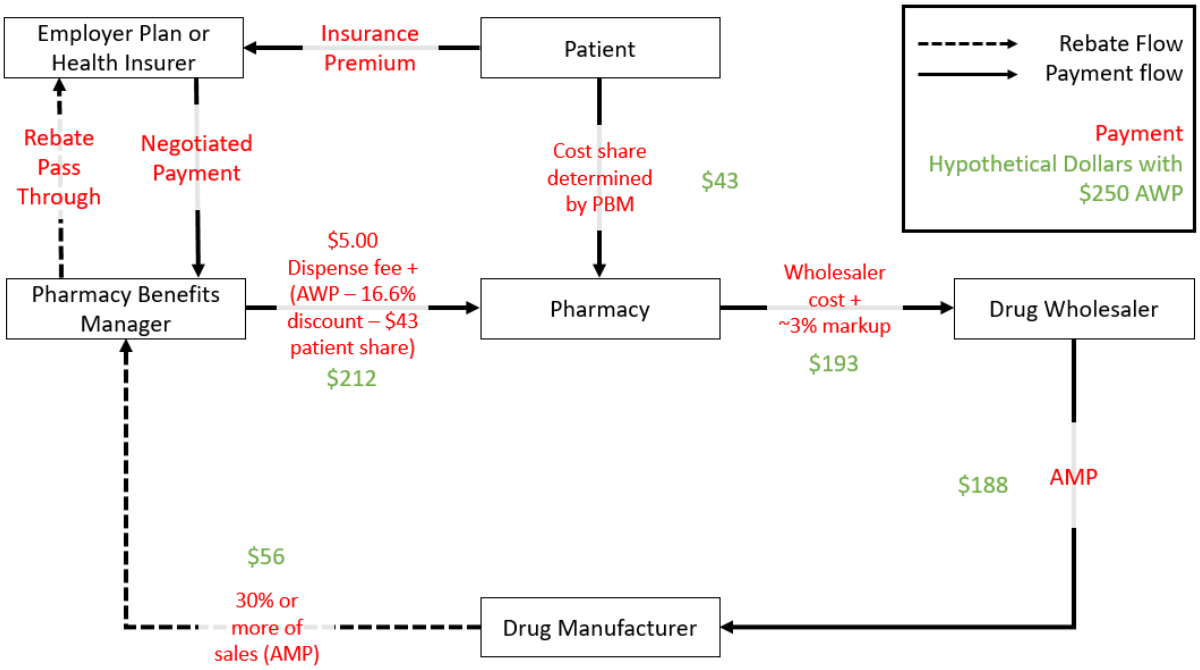
The fourth aim is to explore proposed solutions to the issue in order to better inform the reader on some of the potential solutions currently under consideration. These solutions were drawn from popular political maneuvers that have been proposed to lower prices and actions taken by progressive pharmaceutical companies to address high prices. When considering solutions based with the industry, I focused solely on price hike limits and value based contracting.

CONCEPTUAL MODEL AND HYPOTHESES

The conceptual models below are graphical representations of the pharmaceutical pipeline from the point of manufacture to consumption by the patient. The models document the flow of product, payments and rebates through the system and provide a comprehensive and clear picture of the system. The second model employs the use of inputs derived from research to illustrate the various costs incurred throughout the pipeline. These models are to be used to provide an understanding of where each dollar of a publicized price actually goes. Both models[1] will be more thoroughly discussed in the Following The Money section of this paper.



[1] Fein, P. A. (n.d.). About Drug Channels. Retrieved February 22, 2017, from http://www.drugchannels.net/p/about-blog.html



RESEARCH METHODS

Data was primarily gleaned from grey literature and tertiary sources. Subject matter experts were also consulted through email correspondence and in-person interviews. Jon Easter at UNC's Center for Medication Optimization through Practice and Policy was consulted to clarify industry terms and detail specific pricing processes. Easter is a pharmaceutical industry veteran with a career focused in pharmaceutical policy. Brian Miller, M.D. a Medical Officer for the Center for Drug Evaluation and Research with the Food and Drug Administration was also consulted to provide insight into PBM contracting. Stacie B. Dusetzina Ph.D from the UNC Eshelman School of Pharmacy was consulted to review this paper for accuracy.

Much of the information gathered regarding the current problems with pharmaceutical pricing from the patient's perspective was generated from research involving two recent highly publicized pricing scandals. The Mylan EpiPen and Turing Daraprim scandals were used as case studies for this research as they present two of the most infamous cases in the last decade. Due to

the highly-publicized nature of the cases, information and analysis of these cases was plentiful and provided strong examples of different concepts that I will be touched upon throughout my paper.

EXECUTIVE SUMMARY

Pharmaceutical pricing is a poorly understood yet highly publicized issue. This lack of understanding is the result of a complex system coupled with business to business contracts shrouded in confidentiality between the various organizations involved in the purchase of pharmaceuticals. While pharmacies, physicians, pharmacy benefit managers (PBMs) and pharmaceutical manufacturers all play a role in increasing the cost of pharmaceuticals, the general public is most aware of manufacturers. Consequently, pharmaceutical manufacturers take the brunt of the blame and the penalties for rapid price increases. It is an axiomatic truth that moral misgivings perpetrated by pharmaceutical manufacturers have eroded public trust. Furthering this erosion is the fact that manufacturers continue to set the price of their pharmaceuticals while refusing to reveal exactly what they are paid for a given drug. However, other companies in the supply chain – most notably PBMs – play a large role in price increases and the opacity of the market. The contractual secrecy permeating the entire market is the leading hindrance to a reduction in pharmaceutical prices. Policies and solutions adopted to address the issue of pharmaceutical prices must do so comprehensively – solutions must confront all of the contributing organizations in order to effectively achieve change. The development of successful solutions is entirely dependent upon an understanding of the comprehensive issue and all of its complexity by those proposing solutions. In short, if we are to fix a broken system, we must first understand how it works.

BRANDED DRUGS

Pharmaceutical pricing is subject to wide variations throughout the industry dependent upon a number of factors. In an effort to reduce some of the variability, I have elected to focus specifically on branded non-biologic drugs in the United States. This section gives background on what non-biologic branded products are in order to make the following sections more easily interpretable by laypersons.

Pharmaceuticals can be divided into biologics (large molecule) and what we will call drugs (small molecule). Biologics are medicines which are developed from biological materials (animals, humans, viruses etc.), that typically carry a much higher price and require special handling, administration and monitoring. They are not available at your local pharmacy. Conversely, for the purposes of this paper, drugs are those medications you can buy at your local pharmacy.

Drugs can be separated into the categories of branded and generic. Branded products are new and unique products that have not yet lost patent protection and face no generic competition. Once a branded product loses its patent protection, any company is free to make an exact copy of that drug - a generic - and sell it for much less than the original product.

THE BIG PLAYERS IN PHARMA PRICING AND THEIR PERSPECTIVES

The complexity of pharmaceutical pricing can be partially attributed to the myriad of organizations which have an effect on prices but which are not always easily visible to the public. These include patients, pharmaceutical manufacturers, pharmacy benefit managers, wholesalers and pharmacies.

PATIENTS

In the context of this paper the terms, “the patient”, “the public” and “consumer” are interchangeable. Large swaths of the public believe that pricing in the pharmaceutical industry has become a problem. For those who do not have experience with high personal medication cost, it has been brought to their attention through media coverage of scandals such as Mylan’s EpiPen, Turing’s Daraprim, Eli Lilly’s insulin and Valeant’s business practices. Patients believe that profit is being prioritized above patient lives and societal benefit. Recent scandals plaguing the industry make it easy to see why this is the case. From the public’s perspective, EpiPen manufacturer Mylan pharmaceuticals took advantage of the fact that they have a monopoly on a life-saving anaphylaxis treatment and increased prices by 600%. Martin Shkreli purchased Turing pharmaceuticals and increased the price of a long-available generic drug vital to HIV patients to pocket huge profits. The wider public learns of patients struggling to pay for medications while simultaneously learning of pharmaceutical executives traveling in private jets. These never-ending news headlines have provoked rage and resentment by the public.

Opponents of this public perception posit that public opinion has been unduly influenced by media coverage and political agendas and that regulation cutting into pharma’s profits will have a devastating effect of the flow of new and innovative treatments. Public discussion of pharmaceutical pricing paints a picture of hobbled patients cutting pills in half or going without lifesaving therapies while pharmaceutical executives sit around a boardroom laughing at patients’ misfortune. A Kaiser Family Foundation Survey found that 77% of Americans view present pharmaceutical prices as unreasonable. The same survey found that of the 55% of Americans who take prescription drugs, 73% reported that affording their medication is easy

with only 26% reporting that it is difficult[2]. These statistics highlight the media's role in shaping perception despite a differing reality.

The belief that Americans pay more for drugs than other countries is supported by the literature. However, this data does not necessarily refer to what patients pay at the counter, but rather the entire cost of the healthcare system. Although the American public may perceive a causal relationship between pharmaceuticals and the fact that American healthcare system is very costly, this may not be entirely true. Americans' feelings of contempt may be overly apportioned to the pharmaceutical industry given drug costs make up only 10% of America's 2015 healthcare spending[3]. This evidence suggests that the average American's perspective of pharmaceutical pricing may be distorted due to misinformed and arguably, uniformed reports circulated by media outlets.

MANUFACTURERS

Manufacturers are the pharmaceutical companies that research diseases – often with the aid of academia – and develop and sell pharmaceuticals. While some overlap does exist, manufacturers are divided into two groups: generic and branded manufacturers. For the purposes of this paper, branded manufacturers will be the main focus. Although the average consumer may only be aware of a handful of manufacturers, there are hundreds of pharmaceutical companies operating within the United States. Due to the resulting competition, firms often have a pharmaceutical area of specialty such as a disease state (i.e. diabetes) or something larger, such

[2] Kirzinger, A., Wu, B., & Broadie, M. (2016, September 29). Kaiser Health Tracking Poll: September 2016. Retrieved February 13, 2017, from http://kff.org/health-reform/report/kaiser-health-tracking-poll-september-2016/

[3] "National Health Expenditures 2015 Highlights" (PDF). Centers for Medicare and Medicaid Services. Retrieved February 12, 2017.

as a body system (i.e. respiratory). Some of the largest branded manufacturers in the U.S. include Pfizer, Johnson & Johnson, Roche and Novartis.

The main argument presented by pharmaceutical companies in defense of their pricing philosophy is that the prices they set and the revenues that they generate go into funding the discovery of innovative therapies. Further, they argue that without the benefit of the revenues they obtain, the world would have fewer innovative and life-saving therapies. An often-quoted statistic to uphold that assertion is, that for every one drug which makes it to market, thousands failed costing billions at the company's expense. Opponents of this position argue that revenue generated from the exorbitant prices is actually largely spent on advertising and not R&D. According to data from healthcare research firm GlobalData, 9 of the 10 biggest pharmaceutical manufacturers spent more in advertising than in R&D[4]. This begs the question: Are pharmaceutical companies are truly using their revenues to develop cutting edge, life-saving pharmaceuticals or are they using the money to push expensive treatments on patients that may be served equally well by lower cost alternatives?

Another justification that manufacturers have put forth is that downward pressure from payers has necessitated price increases in order to meet the financial expectations of their investors. A good example of this is Amgen's blockbuster rheumatoid arthritis drug Enbrel. According to Bloomberg, third quarter 2016 gross sales for Enbrel were $2.1 billion with net sales of only $1.4 billion[5]. The $700 million difference was attributed to discounts offered to

[4] Swanson, A. (2015, February 11). Big pharmaceutical companies are spending far more on marketing than research. Retrieved March 19, 2017, from https://www.washingtonpost.com/news/wonk/wp/2015/02/11/big-pharmaceutical-companies-are-spending-far-more-on-marketing-than-research/?utm_term=.b54b54c5140c

[5] Langreth, R., Keller, M., & Cannon, C. (2016, June 29). Decoding Big Pharma's Secret Drug Pricing Practices. Retrieved February 7, 2017, from https://www.bloomberg.com/graphics/2016-drug-prices/

PBMs. To fully understand this statistic, one must first understand the system in which drugs are purchased and distributed. We have not yet explored this system, so for now we will simply say that PBMs through their purchasing power have the ability to lower the profits of drug manufacturers. Many of these claims made by manufacturers present a persuasive argument, but those arguing against manufacturers would claim that it doesn't tell the whole story.

Marcia Angell, author of The Truth About Drug Companies, further expands upon the previous statement in her book[6] citing that, R&D spending isn't as high as manufacturers suggest. For example, drug companies can receive a 50% tax credit on expenses related to testing orphan drugs or testing drugs for which "there is no reasonable expectation that the cost of developing and making [the] available in the U.S." will be recovered from sales. Moreover, that there are many drugs for which the research portion of the R&D costs are borne not by manufacturers, but by academic institutions with federal grant funding, thus offsetting some of the R&D costs manufacturers often discuss. This returns us to our question of whether high prices are really funding breakthrough R&D. Evidence suggests that the answer is that a percentage is spent on R&D while perhaps more is spent on advertising to sell existing drugs. Nonetheless, without high drug sales, costs would have to be cut somewhere – like R&D - to maintain maximal profitability. The fact of the matter is that the issue is circular and much more complex than either side would have you believe.

PHARMACY BENEFIT MANAGERS (PBMs)

As stated by the American Pharmacists Association, "PBMs are primarily responsible for developing and maintaining the formulary (a cost control tool), contracting with pharmacies, negotiating discounts and rebates with drug manufacturers, and processing and paying

[6] Angell, M. (2006). *The truth about the drug companies: how they deceive us and what to do about it*. Melbourne: Scribe.

prescription drug claims"[7]. Health plans, self-funded companies and - less commonly - government programs purchase PBM services to control pharmacy expenditures through the aforementioned methods. PBMs do not generally offer their own insurance products (with the exception of some Part D products) but instead sell their logistical infrastructure and bargaining power. Some examples of the largest PBMs include Express Scripts, CareMark (CVS), Catamaran and Optum (UnitedHealth Group).

PBMs argue that they act as a gateway by using their purchasing power to keep costs down. They contend, that without them, the costs of medication would run rampant. As mentioned above, PBMs utilize a tool known as a formulary to control drug spending. A formulary is a tiered system of insurance coverage for pharmaceuticals where the amount of coverage is determined by drug cost, efficacy and availability of alternative therapies. Manufacturers negotiate with PBMs offering them rebates on drugs in exchange for favorable position on formulary. A rebate is a payment made from a manufacturer to a PBM after purchase for the purpose of refunding some of the purchase price. A better formulary position equates to better and sometimes exclusive coverage by the PBM for a given drug. PBMs maintain that the exclusion of coverage for drugs that experience hyperinflationary price increases, are overly expensive given their benefits or which have cheaper alternatives stems the flow of healthcare expenditures[8].

Opposition argues that pushing such large rebates requires manufacturers to raise prices which increase the PBM's profit. We will explore this in more depth later, but higher rebates narrow profits and thus incentivize manufacturers to push prices higher to maintain or widen

[7] "Pharmacy Benefit Management" (PDF). American Pharmacists Association. July 9, 2009. Retrieved February 3, 2017.

[8] PBMs Will Save Nearly $2 Trillion in Prescription Drug Costs over the Next Decade. (n.d.). Retrieved March 21, 2017, from https://www.pcmanet.org/pcma-pbms-will-save-nearly-2-trillion-in-prescription-drug-costs-over-the-next-decade/

their profit margins. A second argument which is often made against PBMs, is that they negotiate low prices for drugs, accept the rebates yet fail to pass on these savings to their customers. Such that although the price of the drug is dramatically decreased through negotiations with the PBM, the patient never feels the price decrease at the pharmacy counter and that those savings instead go to the PBM's bottom line. Again, a lack of transparency clouds the ability to clearly see where the money goes. To that end, this paper details the rebate process and the flow of money from manufacturers and analyzes the supply chain from manufacturer to patient in an attempt to clarify that process for readers.

PROVIDERS AND PHARMACIES

Providers and pharmacies are the most visible members of the pharma system to patients. A provider is any person or institution that provides care to a patient. This includes doctors, physician's assistants, hospitals, nursing homes etc. Pharmacies are the institutions which fulfill doctors' medication orders and dispense medications to patients. For most pharmaceuticals, the pharmacy is the last link in the supply chain before the product reaches the patient.

PBMs, not manufacturers, generally negotiate directly with pharmacies and control what a patient pays out of pocket. The details of contracting will be discussed in more depth later, but PBMs negotiate both the price paid for the drug and the fee to dispense the medication. The three biggest PBM's control 80% of the market and as such, wield immense leverage in negotiations[9]. For small pharmacies, these negotiations may be detrimental enough to put them out of business. If a small pharmacy has little negotiating power with both a large PBM and a large wholesaler (their supplier), then they risk operating at a loss. Pharmacies perceive that the deals PBMs

[9] Lopez, L. (2016, October 21). Here's how a $50 drug ends up costing you $700 in America's healthcare system. Retrieved March 15, 2017, from http://www.businessinsider.com/pharmacists-blame-pbms-for-high-cost-of-nexium-2016-10

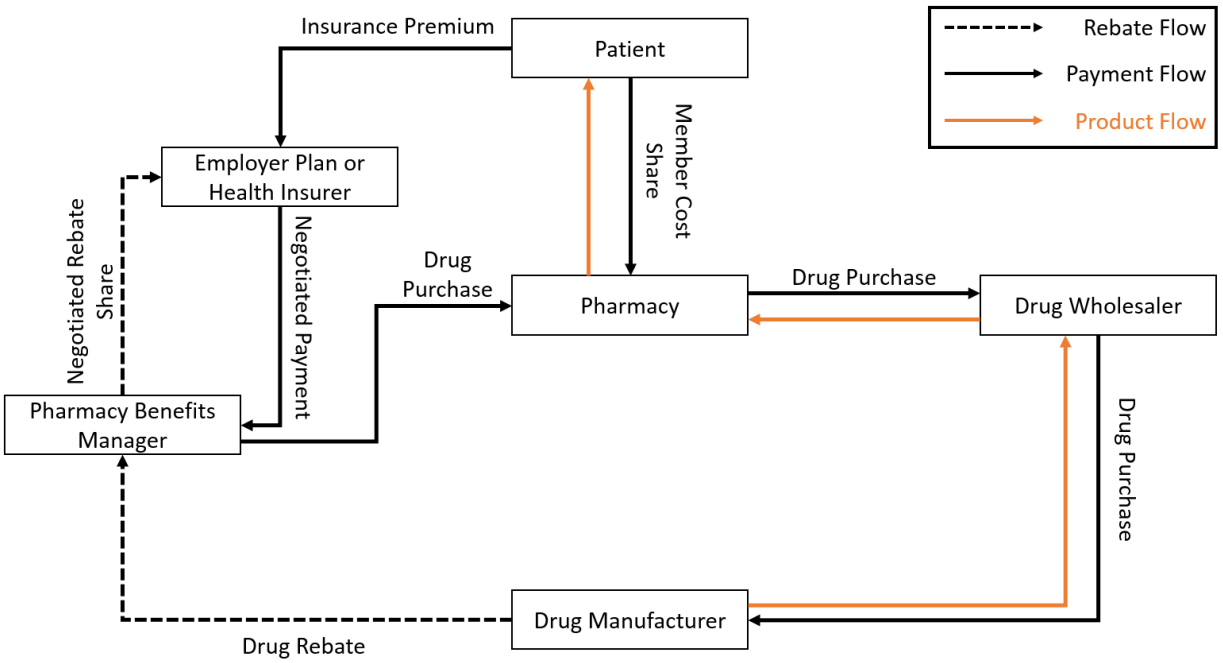
receive are highly lucrative and economically driven rather than a means to reduce drug costs across the industry. The end result of this motivation being that PBMs are motivated to not to cover the best or lowest priced medication, but those that are the most profitable for them.

WHOLESALERS

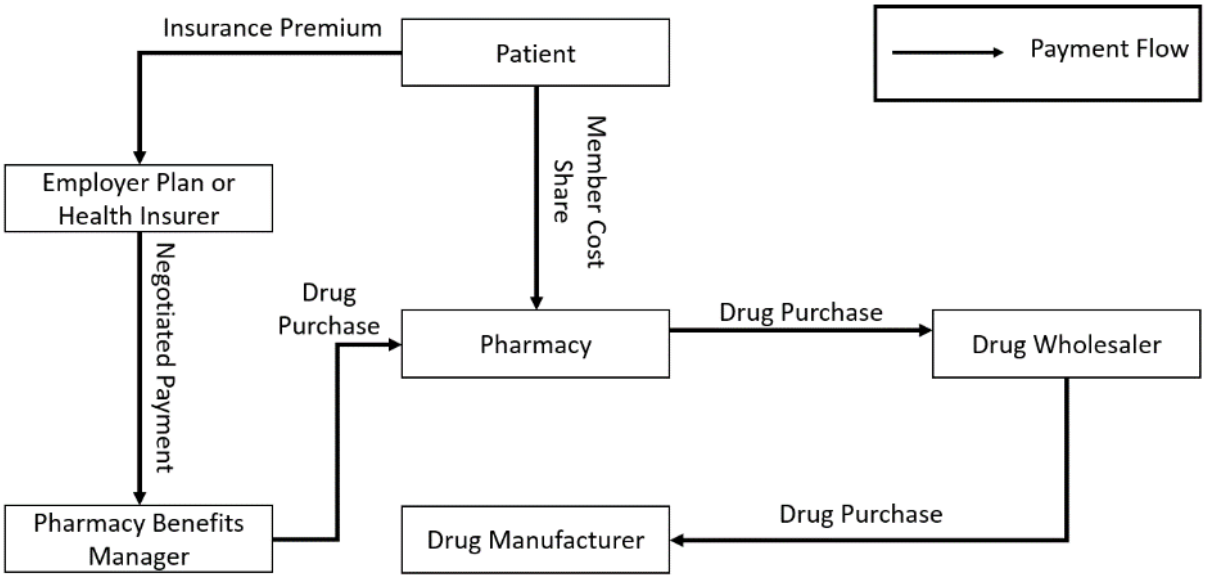
Out of all of the organizations we will discuss, *wholesalers* are likely the one of which the public is least aware. Wholesalers specialize in logistics and can be thought of is a middle man between the manufacturer and the retail pharmacy. The wholesaler purchases products from the manufacturer and then distributes products to pharmacies, hospitals or other providers. Similar to manufacturers, wholesalers can specialize in purchasing and distributing specific products (i.e. generics, specialty drugs and/or branded drugs) or working with certain providers (hospitals, skilled nursing facilities etc.). Some of the largest wholesalers in the U.S. include McKesson, Cardinal Health and AmeriSource Bergen.

THE SUPPLY CHAIN

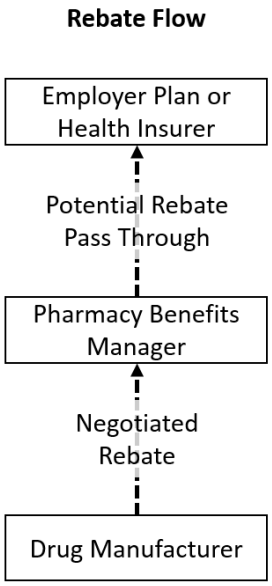
The model below from the Health Strategies Consultancy LLC illustrates the complex relationship between all of the parties involved in the distribution chain from manufacturer to patient. As a disclaimer and for the sake of simplicity and understanding, this graphic does not depict all of the payments and rebates that may arise in the supply chain. The model is a representation of the most common payments and rebates. Depending on the nature of the contract, other payments/rebates may be made between the organizations in this model to reduce risk due to volatile prices, for patient education or as bonus payments for various incentives.



To begin analyzing this process map, the *product flow* must be identified in isolation from the actual prices/markups incurred at each transaction. Once the flows are established, different prices will then be layered in at each point in the process. The product flow (to the right) is the most intelligible of the three flows. Pharmaceuticals are created by the manufacturer and sent to the wholesaler. The wholesaler then ships the product from its warehouses to their pharmacy customers. Finally, the patient goes to the pharmacy, collects and takes the prescription.



Payments are more intricate as there are payments covering both services (insurance) and the physical product (medication). On the insurance side, the patient pays a monthly premium to the insurance company for their health insurance. The health insurance company then contracts the management of the prescription drug benefit to a PBM. Many Americans obtain health insurance through their employer who may also contract with a PBM on the employee's behalf. The remaining payments cover the physical product – the medication. The wholesaler pays the manufacturer for the drug. The pharmacy subsequently buys the drug from the wholesaler and finally, the pharmacy charges both the patient and the PBM once the drug is dispensed. The amount paid by the patient for any given medication is predetermined by the PBM according to the patient's plan. As we will see when we explore the drivers of high prices, the PBM's determination of cost sharing is important as it suggests that PBMs should be more highly scrutinized when addressing medication pricing. Finally, the PBM pays the outstanding balance to the pharmacy. As stated before, in contracts between large PBMs and small pharmacies, the PBM payment may not cover the pharmacy's acquisition cost of the drug.



The final flow in the diagram - the rebates - may be the most difficult to understand due to the general public's lack of familiarity with the concept. A rebate is an amount paid after a purchase has been made. The concept is quite similar to the mail-in rebates many consumers receive when they buy consumer goods. When a drug company negotiates with a PBM, the two items being negotiated are the rebate – often referred to as a discount – and the formulary position. As you'll recall from earlier, a formulary is the tiered list of drugs that the PBM will cover. A better formulary placement lowers the medication cost a patient is exposed to. A lower cost in turn increases the likelihood that a doctor will prescribe and a patient will purchase the medication. In the case of drugs with multiple competitors, a PBM may decide to cover only one drug, effectively providing the chosen drug with a monopoly. In exchange for a more favorable position on formulary or a monopoly, drug manufacturers pay a rebate to the PBM. Once the PBM pays the pharmacy for the drug, the PBM will request a rebate payment from the manufacturer which, in effect, lowers the end price of that drug. Depending on the nature of the contract, the PBM may pass through all or some of the manufacturer rebate to the organization which hired them (either the health insurance plan or the employer).

FOLLOWING THE MONEY

To quote the only pharmacist in Congress, Rep. Buddy Carter, "nobody knows where the money goes because there is no transparency. That's the real problem."[10] Having established a basic understanding of the flow of product, payments and rebates, I will attempt to solve that

[10] Staton, T. (2016, September 22). Lawmakers smack Mylan CEO Bresch for pay, plane and pricing at EpiPen hearing. Retrieved February 15, 2017, from http://www.fiercepharma.com/node/355501

problem. Doing so will require a deeper understanding of who pays what and what exactly each group is left with once all transactions are completed. To begin, a base understanding of terms and the types of prices that exist must be established and are outlined directly below. These explanations have been adapted from the Kaiser Family Foundation definitions.

WHOLESALE ACQUISITION COST (WAC)

Despite it being defined as the price paid by a wholesaler for drugs purchased from the wholesaler's supplier, the WAC does not reflect all available discounts and as a result is not the actual price paid to a manufacturer. The WAC should be considered only as the starting point for negotiations between wholesalers and manufacturers. The WAC is the price often discussed in the media and is determined by pharmaceutical manufacturers after consideration of a variety of factors. The manufacturer uses algorithms and computer programs that analyze the competitive landscape for the product, the cost of similar products, expected market share, forecasts of script volume, research and development costs, marketing costs and other variables. This data is used to develop what they believe to be an optimal price for the drug and is published as the WAC. The actual price that is ultimately paid by wholesalers to manufacturers is the average manufacturer price (AMP)[11].

AVERAGE MANUFACTURER PRICE (AMP)

The average price paid to manufacturers for a drug by wholesalers for drugs distributed to retail pharmacies. As WAC is the starting point for negotiations between manufacturers and wholesalers, the AMP is the ending point. It is the average of what is paid after all rebates,

[11] "Medicaid Drug Price Comparisons: Average Manufacturer Purchasing Price to Published Price" (PDF). Office of Inspector General. 2016. Retrieved January 21, 2017

chargebacks or other adjustments. Revealing the different prices paid would strengthen the resolve of wholesalers in negotiations and weaken the negotiating power of manufacturers. This price is not made available to the public due to fears that the transparency would endanger the competitive position of manufacturers in negotiations.

ACTUAL ACQUISITION COST (AAC)

The AAC is average net cost of a drug to the pharmacy from a wholesaler. It accounts for rebates, chargebacks and other adjustments and thus reflects the true price paid by the pharmacy.

AVERAGE WHOLESALE PRICE (AWP)

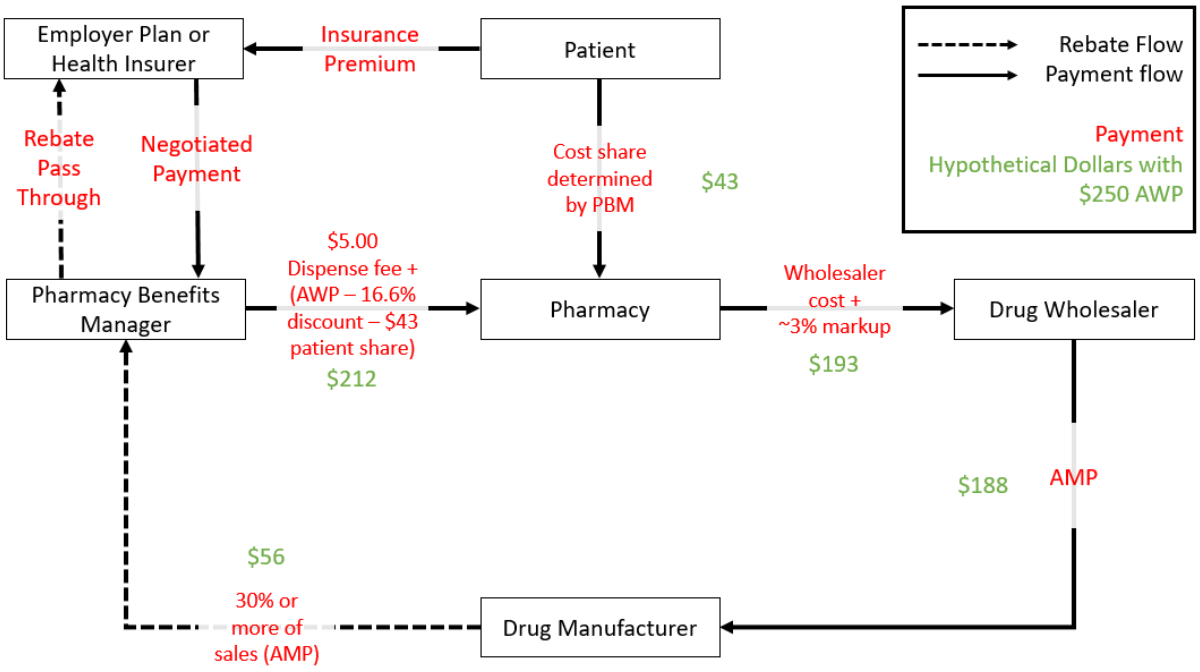
The AWP is defined as the national average of list prices charged by wholesalers to pharmacies. The name and definition of this price are misleading because "list prices" do not account for rebates and adjustments. As a result, after negotiations, wholesalers actually sell to pharmacies at a price based on WAC. AWP is calculated and published by independent companies which generally set AWP at 20% above the WAC. Similar to a car's sticker price, AWP's main use is as a basis for negotiation by payers, governments and pharmacies to determine retail prices and rebates[12]. Many states also use AWP as a starting point to establish Medicaid reimbursement rates[13].

The diagram below illustrates the flow of money through the system. A disclaimer, this model is driven by data from multiple sources, in particular, the numbers presented in the diagram are based on tertiary sources.; one of the biggest shortcomings of data and statistics is

[12] Anderson, L., PharmD. (2014, March 04). Average Wholesale Price (AWP). Retrieved February 20, 2017, from https://www.drugs.com/article/average-wholesale-price-awp.html

[13] "Medicaid Covered Outpatient Prescription Drug Reimbursement Information by State Quarter Ending September 2016" (PDF). Medicaid.gov. September 30, 2016. Retrieved February 10, 2017.

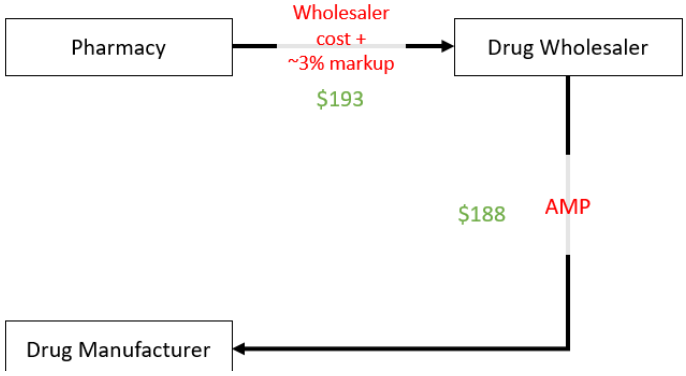
that in the right hands they can be manipulated to serve any purpose. Rebates vary significantly by product. This diagram and the accompanying analysis serve only as an example to provide the information required to think critically when engaging in the pricing debate and to ask the right questions.



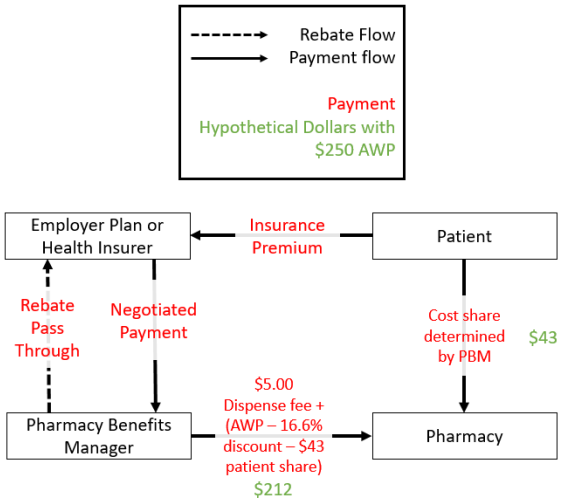
Following the AARP's 2016 research report which provided an average WAC (manufacturer established list price) for a year's supply of branded drugs of ~$3,000[14], we can deduce a monthly WAC of $250 and an AWP of $300 (120% of the WAC). A 2005 OIG report found AMP (the actual price paid to the manufacturer) to be 25% below WAC and 59% below

[14] "Trends in Retail Prices of Prescription Drugs Widely Used by Older Americans, 2006 to 2013" (PDF). AARP. February 2016. Retrieved February 3, 2017.

AWP on average. Reducing the WAC by 25% brings us to the AMP of $188 paid to the manufacturer by the wholesaler[15]. Then the wholesaler sells to the pharmacy at a 3% markup[16] which brings the pharmacy's cost to $193. Out of the $5 markup ($193- $188) comes the wholesaler's profit.



At this point, we shift from WAC based pricing to AWP based pricing. The pharmacy receives a payment from both the patient and the PBM. The patient pays the pharmacy an amount determined by their insurance plan. This fee can be a fixed amount known as a co-payment, a percentage based calculation (coinsurance) or can be set up in many other ways. For example, in a high deductible plan, the patient faces the total cost of the medication until a certain out-of-pocket spending limit is reached and the patient's insurance coverage kicks in. A 2016 survey of employer sponsored health plans by the Pharmacy Benefit Management Institute (PBMI) provides some insight into patient cost sharing. The report found that patients in the plans they surveyed paid on average $30.46 for a 30-day supply of a



[15] "Medicaid Drug Price Comparisons: Average Manufacturer Purchasing Price to Published Price" (PDF). Office of Inspector General. 2016. Retrieved January 21, 2017

[16] Barlas, S. (2015, March). Employers and Drugstores Press for PBM Transparency: A Labor Department Advisory Committee Has Recommended Changes. Retrieved February 3, 2017, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357353/

preferred branded drugs and $55.56 for a 30-day supply of a non-preferred branded drugs[17]. I have taken an average of the two numbers to arrive at an out of pocket cost of $43. The out of pocket cost will be much higher for patients on less comprehensive plans such as a high deductible plan.

The pharmacy's payment from the PBM is comprised of two parts: the price of the medication and the dispensing fee. The dispensing fee is a fee for service payment made for the dispensing of medications to the patient. For the medication price, online drug encyclopedia Drugs.com and the PBMI employer sponsored plan survey found that on average, PBMs pay pharmacies AWP (120% of the manufacturer set price) minus 16.6%. The PBM will pay this amount less any patient cost sharing ($43 in our example) outlined in the insurance plan. In our example, this brings the price to $212 paid by the PBM. From the $19 difference between what the pharmacy pays the wholesaler ($193) and what they collect from the PBM ($212) comes the pharmacy's profit.

The PBM primarily collects money from two sources. Firstly, it collects a premium from the health plan or plan sponsor for offering their services as a third-party administrator. The plan sponsor is the organization that sets up the health insurance plan. For self-funded employers, the company itself is the plan sponsor. As discussed earlier, the PBM's services include negotiating prices, processing claims, establishment of formularies, creation of pharmacy networks and other services.

One benefit of the PBM's negotiating power, is the rebate the PBM is able to negotiate from the manufacturer in exchange for a favorable position on their formulary. Although rebates

[17] "2015-2016 Prescription Drug Benefit Cost and Plan Design Report" (PDF). Pharmacy Benefit Management Institute. 2016. Retrieved February 3, 2017

are highly variable from drug to drug, according to research from consulting firm ZA Associates, conducted by analyzing manufacturer financial statements, the average rebate for a drug is 30% of sales. This number was established by examining manufacturers' reported gross sales and net sales (gross sales less rebates)[18]. Sales are the AMP as this is what the manufacturer is actually paid after accounting for all adjustments. In our example, that 30% results in a rebate of $56 from the manufacturer to the PBM in addition to the money being paid to the PBM by the plan sponsor/health plan for the PBM's services. The rebate may or may not be shared with the health plan/plan sponsor. Later on, we will delve deeper into the data surrounding PBM rebate sharing.

The second way in which PBMs profit is through the contract design with the health plan or plan sponsor. PBM contracts can be designed as either spread based contracts or pass-through contracts[19]. In a spread pricing arrangement, the PBM pays the pharmacy a contracted amount for a drug and charges a higher price than the pharmacy cost to the health plan/plan sponsor. The spread is the difference between what the PBM charges the health plan/plan sponsor for the drug and the PBM's payment to the pharmacy. In addition to the spread, the PBM may retain some or all of the rebate that they negotiate from the manufacturer. In our example, the PBM would charge the health plan/plan sponsor an amount in excess of the $212 they paid to the pharmacy. In addition, they would take some or all of the $47 rebate negotiated from the manufacturer. The PBM's profit would be the amount charged to the health plan/plan sponsor in excess of $212, their share of the $56 manufacturer rebate and the payment they receive from the health plan/plan sponsor.

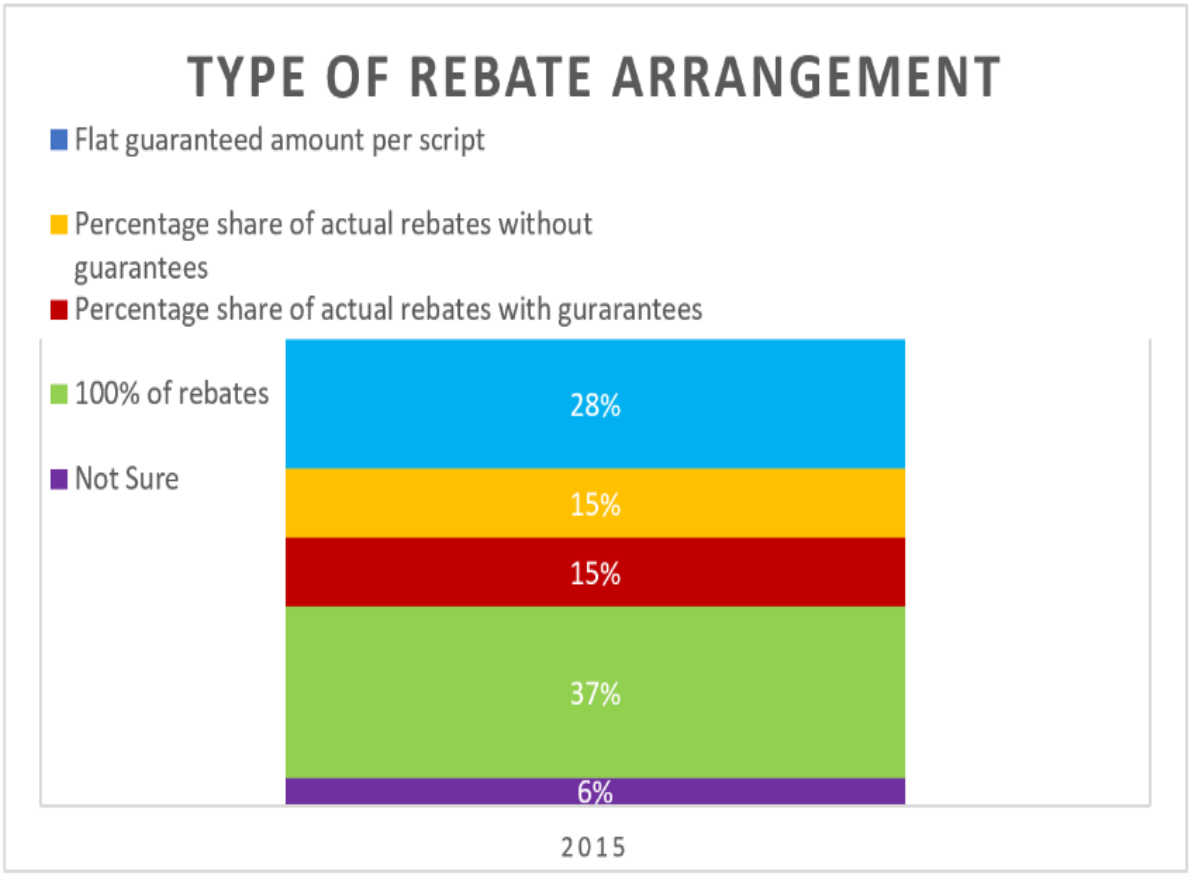
[18] Herper, M. (2014, November 20). Inside The Secret World of Drug Company Rebates. Retrieved February 5, 2017, from http://www.forbes.com/sites/matthewherper/2012/05/10/why-astrazeneca-gives-insurers-60-discounts-on-nexiums-list-price/#316c7e3a4fd6

[19] Barlas, S. (2015, March). Employers and Drugstores Press for PBM Transparency: A Labor Department Advisory Committee Has Recommended Changes. Retrieved February 3, 2017, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357353/

Under a pass-through-pricing arrangement, the health plan/plan sponsor pays fees to a PBM for their services but does not pay a spread on medications. The fees may be fixed per claim that is processed by the PBM or set up as another arrangement. The health plan/plan sponsor then pays the PBM the exact amount paid to the pharmacy for the drug (and nothing more). Finally, the PBM will pass the entire rebate through to the health plan/plan sponsor[20]. Under a pass-through contract in our model, the PBM would charge the health plan/plan sponsor the pharmacy cost of $212 and pass to them the entire rebate of $56. The health plan/plan sponsor would pay the PBM a set rate for every payment that the PBM processed. Under pass-through-pricing, the PBM's profit comes from the rate for processing each claim and the original payment by the health plan/plan sponsor for the PBM's services.

[20] "Pharmacy Benefit Management: Pros and Cons of Various Approaches" (PDF). Snook. T. D. Filipek. T. M. 2011. Retrieved March 21, 2017

The 2016 PBMI report on prescription drug benefits provides insight into just how much of the rebates are going to PBMs. As shown in the chart below, only 37% of plan sponsors receive the full rebate. Others receive some variation of a percentage share or, more commonly, a



flat amount per script regardless of the negotiated rebate. Of those receiving the flat amount, the median and mean rebate dollars shared with plan sponsors for 30-day and 90-day branded prescriptions are shown to the left. Given the knowledge that rebates average about 30% of manufacturer sales (AMP) and the AMP of a 30-day supply from our example is $188 (or $564 for 90 days) we can deduce that the total rebates for 30 - day and 90 - day supplies are $56.80 and $169.20 respectively. Using the mean rebate share figures of $23.80 and $31.70, we see that for

Flat Guaranteed Rebate Amount by Prescription Type		
Prescription Type	Mean	Median
Branded 30 day supply	$23.80	$22.50
Branded 90 say supply	$31.70	$30.00

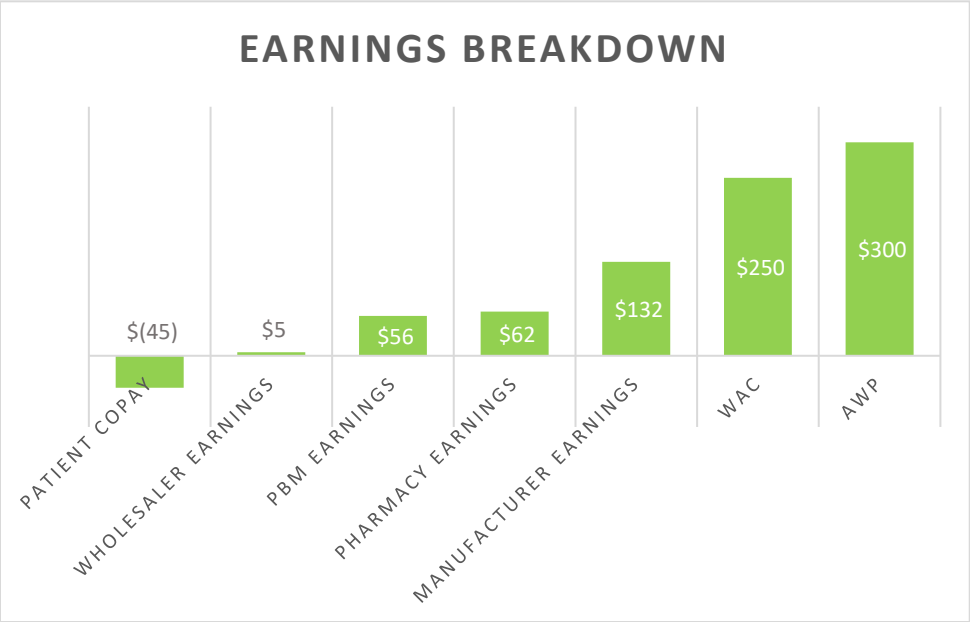
Total Rebate Paid By Prescription Type		
Prescription Type	AMP	Total Rebate
Branded 30 day supply	$ 188.00	$ 56.40
Branded 90 say supply	$ 564.00	$ 169.20

a 30-day supply of medication under a flat guarantee rebate share, the PBM keeps $32.60 ($56.40 total rebate - $23.80 shared with health plan/plan sponsor) of the $56.40 total rebate or 58%. On a 90-day supply under a flat guarantee rebate share, the PBM keeps $137.50 ($169.20 total rebate – $31.70 shared with health plan/plan sponsor) of the $140.40 total rebate or 81%. This level of intricacy and complexity is a large part of why drug pricing is so difficult to understand. This information serves to show that the problem cannot be attributed to one group or organization, but that it is a systematic issue. It also begins to open our eyes as to how much information the public is truly lacking when this issue is discussed.

I will now use our example to further illustrate how public perception of pharmaceutical pricing is skewed. The "Earnings Breakdown" graphic on the following page shows the cash inflows and outflows from our example. These numbers do not represent profit as they only account for the costs we've discussed and do not include the various other costs of doing business. They also do not account for all of the rebates, discounts and chargebacks which may be paid to adjust profitability. However, this model does serve to illustrate the point that we must dig deeper to truly understand where the money is going.

In our example, through media coverage and price publication the public would see the WAC (aka list price) of $208. However, as we can see in the Earnings Breakdown graphic, the *manufacturer* would actually receive $132 ($188 AMP price to wholesaler less $56 rebate to PBM) - around 53% of the WAC price. Assuming a spread based contract where the *PBM* keeps 100% of the manufacturer rebate, the PBM earns $56 – around 22% of the WAC. They also keep any spread between what they charge the health plan/ plan sponsor and what they pay the pharmacy. This is in addition to the contracted premium payment made to the PBM by the plan

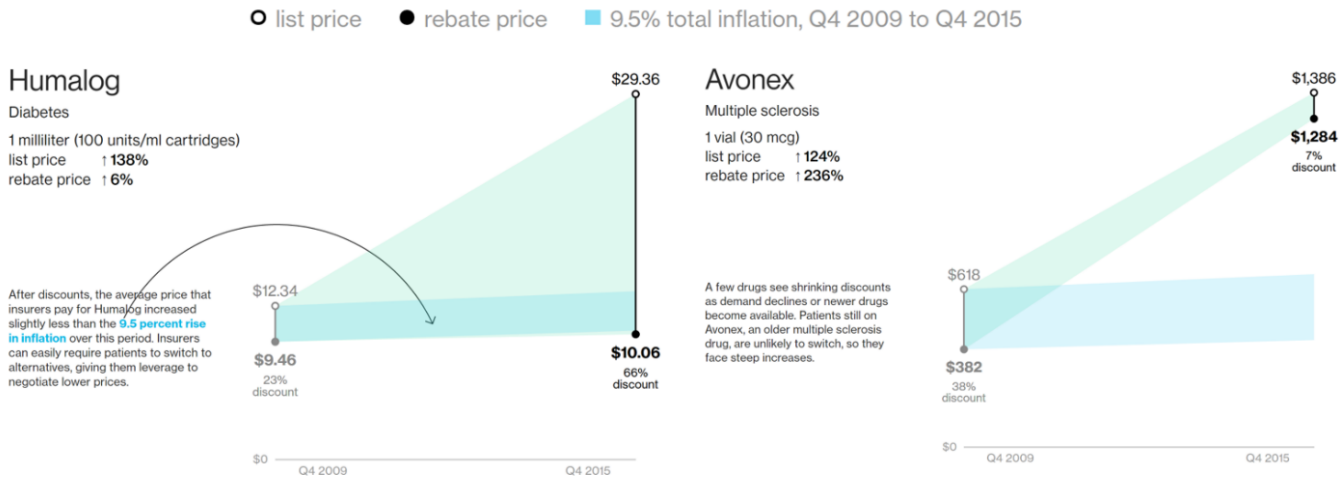
sponsor/health plan. The average spread is unknown and the premium payment is not tied to a specific drug. For those reasons, they are not accounted for in the $56 shown here. The *pharmacy* would pay $193 to the wholesaler and receive the PBM payment of $212 plus the patient copay of $43 – resulting in earnings of $62 (~25% of the WAC). The *wholesaler* after paying $188 to the manufacturer and charging the pharmacy $193, earns $5 (2% of the WAC). The WAC does matter and should be known to the public as it is often used to set patient cost sharing rates. However, after seeing these numbers, it goes without saying that the issue of pharmaceutical pricing is much more complex than the WAC price hike that we read about in the papers.



A real-world example of the pervasive nature and damning consequences of the lack of information relating to the distribution of money through the system is readily available in one of the most highly publicized scandals to date. Mylan – the company which makes EpiPen – has become a target of intense scrutiny after it came to light that the WAC of the EpiPen went from $100 in 2007 to $600 in 2016. In an interview with CNBC, CEO Heather Bresch shone the spotlight on PBMs, saying that over half of EpiPen's list price goes to the PBM in the form of a rebate.

Not only does the EpiPen scandal showcase how the lack of information influences public opinion, but it also illustrates why the transparency this paper attempts to provide is so important. Politicians had been denouncing pharmaceutical prices for months before Mrs. Bresch's testimony. However, it wasn't until after Mrs. Bresch's comments and a letter from the CEO of the National Community Pharmacists Association to the House Committee on oversight and Government Reform calling out the PBM's role in raising EpiPen's price that Congress began to investigate PBMs[21]. The lack of investigation into these areas of the business highlight the importance of drug pricing education. Neither the public nor our nation's politicians should be calling for drastic changes to drug pricing with incomplete information as this is how the implementation of ineffective or even harmful "solutions" may take place.

As we delve deeper into rebates, you will find that they are highly variable depending on the medication. The size of a rebate depends on factors such the availability of competing products, doctors' willingness to change prescribing habits, the drug's effectiveness and more.



[21] Staton, T. (2016, October 04). With new calls for congressional hearings, PBMs could be next on Capitol Hill's hot seat. Retrieved February 5, 2017, from http://www.fiercepharma.com/pharma/new-calls-for-congressional-hearings-pbms-could-be-next-capitol-hill-s-hot-seat

The graphic below[22] illustrates how our current practice of judging drugs and their manufacturers based solely on their WAC can result in erroneous conclusions.

Both Humalog and Avonex have experienced large and rapid list price (WAC) increases. Yet, the difference in rebate growth is staggering. For Humalog, despite a 138% increase in list price, the net price to PBMs (price paid after rebates) has only risen by 6%. In contrast, Avonex has seen a list a 124% increase in list price and the net price growth has outpaced even that at 236%. This means that the manufacturer of Avonex was able to raise the price faster and higher than the rebates the PBM was able to negotiate. The discrepancy is likely due to the fact Humalog is an insulin which treats diabetes, a common disease, that has many competitors whereas Avonex treats multiple sclerosis which has much lower prevalence and fewer treatment options. Solely knowing the increase in a drug's list price (WAC) is not sufficient to fully understand the problem nor to solve it. Many more questions must be asked if we are to pass informed judgement and draft effective solutions.

Outlining the rebate system stirs an important question: If a PBM demanding a rebate from a manufacturer is essentially the PBM stating "*your drug is not worth what you are claiming. In order to buy it, you will have to lower the pric*e.", one must ask why the price is set above the value which the market has attributed to it in the first place. I will attempt to answer that question in the following section.

WHY DO WE HAVE HIGH PRICES?

The four contributors to high prices (aside from the opacity this paper aims to reduce) covered in this paper are as follows: a pharmaceutical delivery network which incentivizes high

[22] Langreth, R., Keller, M., & Cannon, C. (2016, June 29). Decoding Big Pharma's Secret Drug Pricing Practices. Retrieved February 7, 2017, from https://www.bloomberg.com/graphics/2016-drug-prices/

prices, the design of the American Healthcare system, manufacturer practices and PBM benefit design. Each of these factors plays a large role in the setting of and patient exposure to high medication costs.

DESIGN OF THE DELIVERY NETWORK

The design of the pharmaceutical delivery network is such that most organizations within it benefit from price hikes. As **manufacturers** increases their published price (WAC), the amount they receive from the wholesaler increases. This is because the AMP price the manufacturer receives from the wholesaler is WAC minus 25%. The **wholesaler's** markup is based on a percentage increase over their cost (AMP), so a higher WAC mean a higher AMP which nets the wholesaler larger profits. The **pharmacy's** spread is increased because they buy at the wholesaler's cost (AMP aka WAC – 25%) + 3% and sell at a price based on AWP (120% of WAC). The **PBM** benefits because the rebates from which they benefit are set as a percentage of AWP. An increase in WAC increases the AWP which in turn increases the size of the rebate. This process alone makes it easy to see why this system is so poorly understood, especially given the fact that most of these prices and discounts are not generally made public.

DESIGN OF THE AMERICAN HEALTHCARE SYSTEM

Another flawed system which contributes to the sting of high prices felt by patients is the American healthcare system. Our current system leaves large holes of uninsured patients that bear the full cost of care, that has been driven higher and higher over time. Those who are uninsured pay the full cost of drugs when they go to the pharmacy because uninsured patients do not benefit from the lower prices that are negotiated by large insurers. Evidence of this is provided by research from the Public Interest Research Group (PIRG) report titled *Paying the*

Price 2006 found that uninsured patients paid 60% more than the federal government[23]. This cultivates many of the stories involving uninsured or underinsured patients having to go without medication due to an inability to pay. Major coverage of these instances distorts perception and leads the public to believe that many more patients than is likely true are sacrificing health for lack of money.

DATA EXCLUSIVITY, M&A AND DRUG FLIPPING

Supplementary to the systematic incentives and flaws are three manufacturer practices that encourage increases in prices. The first is the use of an FDA rule known as data exclusivity, the second, a heightened level of M&A deals and the third, a practice known as drug flipping. Data exclusivity is offered to manufacturers by the FDA and prohibits the use of the original producer's clinical trial data for approval of a generic version of the drug. The data exclusivity granted by the FDA is separate from a patent – which will be discussed later - offered by the US Patent Office. The FDA's creation of data exclusivity arose because manufacturers argued that clinical trials were incredibly expensive and that allowing other companies to use that data for free constituted an unfair advantage. Without access to the clinical trial data to submit with their approval application, generic manufacturers cannot obtain FDA approval of their generic version of a drug unless they run their own costly trials. Due to the large expense associated with running clinical trials, any such attempt would make the endeavor unprofitable for the generic manufacturer. For new molecular entities (new pharmaceuticals) the data-exclusivity period is 5 years, for orphan drugs (those with less than 200,000 patients) the period is 7 years and for

[23] "Paying the Price 2006: The High Cost of Prescription Drugs for Uninsured Americans" (PDF). U.S. PIRG Education Fund. July 11, 2006. Retrieved February 3, 2017.

changes to existing drugs, the period is 3 years[24]. The delay of any competing products allows manufacturers to maintain their monopoly and their control over the market price.

Another cause for high prices is the buying and selling of companies or parts of companies known as mergers and acquisitions (M&A). Often these deals involve very large payments/purchases in return for promising drugs which have often times not yet made it to market. Whether or not consolidation is good or bad for market prices is debatable. Regardless of the economic arguments, it is a fact that pharma deal prices have increased 400+% in the last two years and that money has to be made up somewhere. In 2016, the median revenue premium paid for pharma acquisitions was 38%; that is contrasted with 8% for 2014[25]. What companies are doing is compensating for a lack of innovative products in their own pipelines. Through their purchase, they are betting on the promising drugs that the acquired company has under development. According to Bernstein Analyst Tim Anderson, "Winning a bidding war when it comes to acquiring biopharmaceutical companies almost always equates to overpaying". If a company overpays or if the promising drugs they were hoping for don't succeed, the company has few options. One of the most effective ways for them to mitigate the financial impact of a poorly priced purchase is to raise top line revenue by increasing the price of their products.

A specific form of M&A that pharma partakes is known as drug flipping. Drug flipping involves a company buying an older medication from another and then increasing the price to make the deal profitable. The most notorious case of drug flipping is Turing Pharmaceutical's Daraprim under Martin Shkreli. Under Shkreli's ownership Daraprim went from $13.50 per pill to $750 per pill. Many other drugs have followed this same scheme, Actimmune (434% price

[24] Angell, M. (2006). *The truth about the drug companies: how they deceive us and what to do about it*. Melbourne: Scribe.

[25] Helfand, C. (2017, January 04). Overpay much? Pharma's deal prices have quadrupled in the last two years. Retrieved February 5, 2017, from http://www.fiercepharma.com/pharma/overpay-much-pharma-s-deal-prices-have-quadrupled-last-two-years

hike) and Denavir (372% price hike) just to name a few[26]. Companies are able to take these price hikes due to inefficiencies in the market. The purchasing companies target older drugs because their profits have become stagnant, sales may be falling and thus the rights to the drugs can be purchased at a low price. Generally, the drugs have few competitors and are smaller drugs which are able to go unnoticed as PBMs focus their negotiation efforts on top selling drugs. A commonly offered defense by drug flippers is that they are adjusting prices to be market efficient and that the previous owners mispriced the medication. The question you may be asking yourself is: *why would the drug's original owner have a medication priced so low to begin with if the market could bear a much higher price*? Craig Garthwaite, a health economist at Northwestern University proposes that it's a matter of leadership[27]. Many of the drug flipping companies are owned and operated by private equity firms (i.e. Turing pharmaceuticals) whereas the original owners are often established pharmaceutical companies run by industry veterans. The original owners keep the price low to avoid scrutiny from regulators and therefore protect their portfolio of other drugs. A private equity company does not have that concern. They enter the purchase as a short-term investment, increase the company's profitability and then sell it at a higher price reflecting the higher revenues to pocket the profit. There is no fear of regulatory scrutiny or backlash on other drugs because it is a one-time transaction with fairly rapid turnaround time.

PHARMACY BENEFIT MANAGERS

The final cause of high prices we will investigate are the PBMs. We will analyze manufacturer price hiking in response to PBMs, PBM's ability to obtain rebates and lower drug

[26] Langreth, R. (2016, November 02). Dealmakers Behind Soaring Drug Prices Hit the Jackpot. Retrieved February 5, 2017, from https://www.bloomberg.com/news/articles/2016-11-02/buy-and-flip-booms-in-drugs-market-as-private-equity-moves-in

[27] Kliff, S. (2015, September 25). A health economist explains the real reason American drugs are expensive. Retrieved February 5, 2017, from http://www.vox.com/2015/9/25/9393805/american-drug-prices-economist-interview

costs as well as what happens to the dollars a PBM is able to shave off of the price of pharmaceuticals.

The three largest PBMs, Express Scripts, Caremark and OptumRx (a subsidiary of United Health Group) make up ~80% of the market covering 180 million lives between them[28]. This concentration of lives grants them incredible buying power and the ability to demand larger and larger rebates from manufacturers. Manufacturers, knowing that a larger percentage of the price will be returned to the PBM in the form of a rebate, increase prices in order to achieve their financial targets. Pratap Kedkhar, a principal at pharmaceutical consulting firm ZS Associates, stated that his firm found that rebates cut $40 billion out of drug sales every year; we've already covered that the average size of a rebate is 30% of sales[29]. In addition to rebates, PBMs are increasingly incorporating a price protection clause into their contracts that provides an increase in rebates as a percentage of the list price if the drug's list price exceeds a pre-specified amount[30]. Again, this incentivizes the uncontrollable upward spiral of high prices we observe today. As rebates increase, the manufacturer raises prices to maintain profit. In response to the price increase, the PBM increases the rebate and the cycle repeats itself such that we see cases like EpiPen more frequently.

[28] Staton, T. (2016, October 04). With new calls for congressional hearings, PBMs could be next on Capitol Hill's hot seat. Retrieved February 5, 2017, from http://www.fiercepharma.com/pharma/new-calls-for-congressional-hearings-pbms-could-be-next-capitol-hill-s-hot-seat

[29] Herper, M. (2014, November 20). Inside The Secret World Of Drug Company Rebates. Retrieved February 5, 2017, from http://www.forbes.com/sites/matthewherper/2012/05/10/why-astrazeneca-gives-insurers-60-discounts-on-nexiums-list-price/#316c7e3a4fd6

[30] Koons, C. (2016, September 21). Blame Game: The $130 Billion in Fees Mylan Says Pushes Up Prices. Retrieved February 5, 2017, from https://www.bloomberg.com/news/articles/2016-09-21/blame-game-130-billion-fees-that-drugmakers-say-push-up-prices

The opaque rebate system also incentivizes a much more sinister practice known as "rebate pumping". Rebate pumping is when a PBM favors a higher priced drug on formulary over a lower cost alternative because they make more on the rebate. As an example, take a contract where a PBM negotiates a rebate of 20% off of list price. If the PBM is offered the choice between a $500 drug and a $100 drug, the PBM may be incentivized to cover the more expensive option. This is because under the $500 drug, the rebate will be $100 and for the $100 drug it will be $40. What allows this to happen is the lack of transparency which keeps this hidden from the public. A real- world example of this is the Nexium scandal where Medco was favoring Nexium over cheaper alternatives. Ultimately, AstraZeneca, which manufactures Nexium was fined $7.9 million by the DOJ for providing what the DOJ found to be kickbacks to Medco. Medco was later purchased by ExpressScripts.

Earlier while tracking the flow of money through the system we analyzed manufacturer rebate sharing agreements between PBMs and plan sponsors/health plans. Dr. Patricia M Danzon, Professor at the University of Pennsylvania's Wharton Business School stated, "most PBMs do not disclose to employers either the price that they pay to retail pharmacies or drug acquisition costs for their mail operations, which makes the PBM spread nontransparent to sponsors,"[31]. A consequence of the lack of transparency is that it creates an opportunity for PBMs to take a large share of rebates. Instead of the money flowing back to health plans/plan sponsors to lower premiums or co-payments, it may be going to the PBM's bottom line.

An audit carried out by Pharmacy Outcomes Specialists examined PBM spread based contracts and found that for Lipitor an unspecified PBM charged a plan sponsor $21.60 for a

[31] Barlas, S. (2015, March). Employers and Drugstores Press for PBM Transparency: A Labor Department Advisory Committee Has Recommended Changes. Retrieved February 3, 2017, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357353/

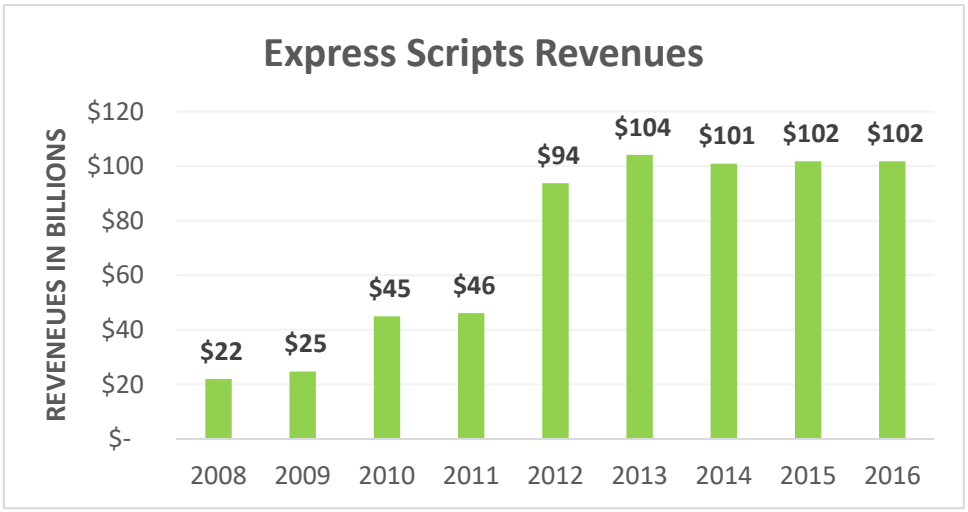
month's supply of Lipitor, paid the pharmacy $10.83 and pocketed the $10.77 difference (50% of the plan sponsor cost). The same audit found that a PBM charged a plan sponsor $5.65 for a month's supply of Ambien, paid the pharmacy $1.88 and pocketed the $3.77 (67% of the sponsor cost). These numbers do not even account for the rebate paid from the manufacturer to the PBM which would lower the true price paid by the PBM even farther[32]. In another example The National Center for Biotechnology recently published the story of Robert Schenk, an administrator of the Meridian Health Systems' employee plan. He was in the unique position of both overseeing the contract with PBM Express Scripts while simultaneously holding access to Meridian Health Systems' outpatient pharmacy financial records. Schenk found that, Express Scripts was charging the Meridian plan $92.53 for generic amoxicillin filled at an outside pharmacy. He then looked at Meridian Health Systems Pharmacy's contract with Express Scripts and found that they were being paid $26.91 to fill the same prescription. Extrapolating that the payments made to Meridian Health Systems' pharmacy and the outside pharmacy were likely similar, he deduced that Express Scripts was pocketing the $65.62 spread on generic amoxicillin (71% of the sponsor cost)[33].

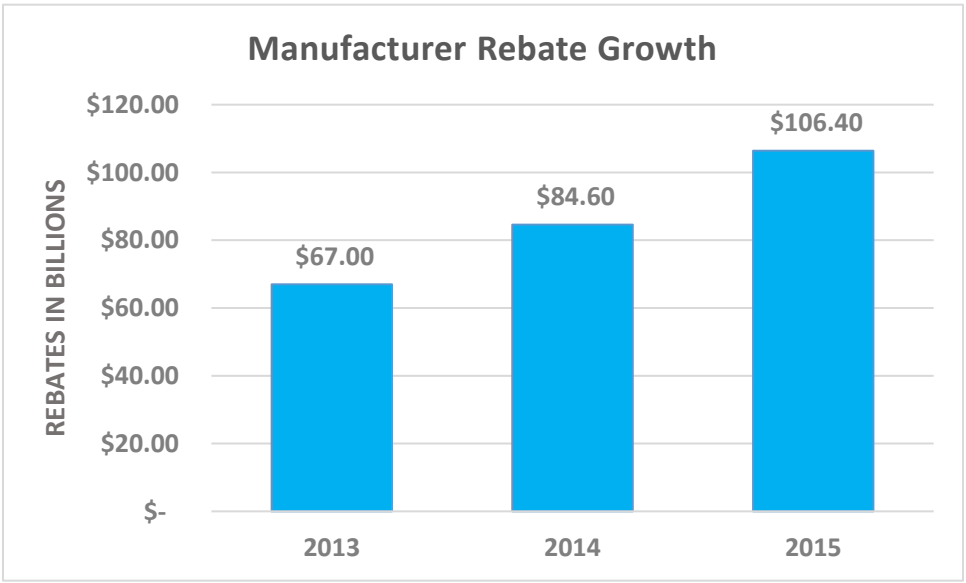
Despite the high margins and lack of transparency, spread pricing is perfectly legal and there is no law which sets limits on the spread a PBM can create. It is the presence of both the system's complexity and non-existing transparency that allows for them to take advantage of these market inefficiencies. In lieu of comprehensive data, which would allow for a more robust

[32] O'Donnell, J. (2014, March 03). Do drug benefit managers reduce health costs? Retrieved February 5, 2017, from http://www.usatoday.com/story/money/personalfinance/2014/03/03/pharmacy-benefit-managers-healthcare-costs-savings/5495317/

[33] Barlas, S. (2015, March). Employers and Drugstores Press for PBM Transparency: A Labor Department Advisory Committee Has Recommended Changes. Retrieved February 3, 2017, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4357353/

analysis, these scenarios are the best data we have and they do help to explain where some of the savings negotiated through rebates end up.





Additional evidence of PBM profiteering can be found by comparing Express Scripts revenues over the last 8 years[34] with the growth in manufacturer rebates from 2013 to 2015[35]. I use Express Scripts revenue as they are the largest PBM and the only one which has easily accessible revenue figures. While these numbers do not provide substantial evidence to claim that PBMs are hoarding manufacturer rebates or putting upward pressure on prices, the correlation between rebate size and PBM profit is alarming. It would

[34] Lopez, L. (2016, September 12). These companies you've never heard of are about to incite another massive drug price outrage. Retrieved February 3, 2017, from http://www.businessinsider.com/scrutiny-express-scripts-pbms-drug-price-fury-2016-9

[35] "The Pharmaceutical Supply Chain: Gross Drug Expenditures Realized By Stakeholders" (PDF). Valverde A. Blalock S. Berkeley Research Group. 2017. Retrieved March 19, 2017

appear that the increase in rebates – which are touted by PBMs as lowering the overall cost of drugs – is in lock-step with an increase in PBM revenues.

Revenues may also be growing through the use of little known tools which are gaining more attention. One such tool is known as a co-pay clawback. A co-pay clawback is a situation in which an insurer's plan requires the patient to pay a co-pay amount larger than the price they negotiated with the pharmacy. The pharmacy collects the co-pay and sends any amount in excess of the price back to the PBM as profit. A May 2016 investigative report by Fox8 News in Cleveland,[36] uncovered this practice and it has resulted in a lawsuit against OptumRX, a subsidiary of UnitedHealth Group. The report found an example of two drugs – Sprintec and Valsartan. OptumRx was buying Valsartan for $14.43, requiring a $30 co-pay and *clawing back* or requiring the pharmacy to send them the extra $15.57. For Sprintec, OptumRx was paying $11.65 to the pharmacy and requiring a $50 co-pay. The $38.35 in excess was sent from the pharmacy back to United as a *clawback.* Tools such as *clawbacks* and others, of which we may not be aware, provide some additional insight into why our drug prices are so high[37].

THE ROAD AHEAD

Now understanding the issue and its complexity, we will evaluate potential solutions. With the nation in an uproar about the prices of pharmaceuticals we can be sure that there exists no shortage of politicians proposing solutions in an effort to mollify their constituencies. There have also been proposals put forth by private citizens, governmental organizations, non-profit organizations and even pharmaceutical manufacturers. In this paper, I will focus on those which

[36] Wright, L. Z. (2016, May 04). Zurik: Copay or you-pay? Prescription drug clawbacks draw fire. Retrieved March 13, 2017, from http://www.fox8live.com/story/31891070/zurik-copay-or-you-pay-prescription-drug-clawbacks-draw-fire

[37] Kass, D. (2016, November 06). UnitedHealth Sued Again Over Prescription Copay Clawbacks - Law360. Retrieved March 10, 2017, from https://www.law360.com/health/articles/863155/unitedhealth-sued-again-over-prescription-copay-clawbacks

are most well-known and those which seem most feasible. These are industry self-regulation, value based contracting, drug re-importation, increasing negotiating power of States and Medicare, boosting competition and improving transparency.

INDUSTRY SELF-REGULATION

Industry self-regulation has been touted by many pharmaceutical manufacturers as being the best and most efficient way of bringing down pharmaceutical prices. It is certainly the most easily implemented solution, given that the only necessity for its implementation is the will of drug manufacturers to make an attempt. However, it has the downside of being the solution least believed to be effective due to the public's cynicism of manufacturers' ethical principles perpetuated by a history mired in scandals. Its successful implementation must also jump the hurdle of shareholder's financial interest conflicting with lower prices. Most shareholders want to see a company make as much money as possible and while the executive team has the power to make and enforce price pledges, they are hired by shareholders through the board.

The first major inroads into industry self-regulation after scrutiny of drug prices increased came in September of 2016 from Allergan, Plc. In September, Allergan forged a social contract with the public to limit price increases in the face of price gouging scandals involving Martin Shkreli's Turing Pharmaceuticals, Mylan's EpiPen and Valeant Pharmaceuticals. The contract states that Allergan will limit prices increases to once yearly and that the percentage increase will be limited to single digits. After Allergan released their pledge, Novo Nordisk and AbbVie soon followed suit and joined the pledge. While this approach provides promise if the industry can bring most manufacturers into the fold, it may be too little too late. In light of recent scandals and media coverage, the public distrust of pharmaceutical manufacturers runs deep and it will be difficult to persuade them that the industry is capable of putting patients above profits. The

skepticism of the ability for self-regulation to succeed is compounded by the fact that a rift exists between company executives as to what form self-regulation should take. For example, Regeneron's CEO Len Shiefler stated that he did not view price limit pledges as the path forward. The logic he offered was that drugs should be priced to value and that any price raising without additional indications or new effectiveness data proves that the industry is not pricing medications according to their value. His view is that the entire process used to decide on prices is flawed and must be changed. Fragmentation amongst the key stakeholders necessary to make this strategy work make its effective implementation improbable[38].

Critics of this approach would say that while limits on price increases address the issue of aggressive price hikes, it neglects to address the fundamental issue of high price setting. The argument being that limiting a $90K drug to a 9% price hike each year instead of addressing the underlying issue of high prices does little to reduce the cost of these medications.

VALUE BASED CONTRACTING

A close cousin of industry self-regulation is the trend in manufacturers and PBMs embracing value based contracts and value based pricing as a means of addressing the pricing issue. Value based contracting is any arrangement whereby the price paid for a drug is directly tied to the benefits that it has for a given patient. It is often put more simply as *paying for drugs that work*. These arrangements can take many forms and have already been utilized by companies such as Novartis Amgen, J&J, Express Scripts, Cigna, Roche, etc. -. Signaling that this solution may be here to stay is the fact that value based purchasing is expected to grow. In 2015, 14% of U.S. payers had value based contracts in place with 30% planning to strike such

[38] Staton, T. (2017, January 12). AbbVie chief joins the 10% price-hike pledge, but other CEOs aren't buying it. Retrieved February 7, 2017, from http://www.fiercepharma.com/pharma/abbvie-chief-adds-his-company-to-10-price-hike-pledge-but-other-ceos-aren-t-buying-it

deals within a year [39]. Under one such contract between Cigna and Novartis, the amount Cigna pays for Entresto – a heart failure drug – will vary based on the rate of heart related hospitalization for Entresto patients. Another contract between Amgen and Harvard Pilgrim Health Care for Repatha – a cholesterol drug – dictates that Amgen's rebate to Harvard Pilgrim will vary depending on a patient's cholesterol levels. These arrangements are attractive as they provide a win-win for payers, patients and manufacturers given that the drug works. If the drug doesn't work, supporters argue that the arrangements are a win for the overall system as manufacturers producing effective drugs will be rewarded and the development of more effective drugs would be pursued. A common criticism against these types of arrangements is its ability to disentangle the multitude of contributing factors for any given outcome. For instance, if Cigna refuses full payment to Novartis because an Entresto patient was hospitalized for a heart attack, it may be unclear whether the heart attack was due ineffective medication, an oversight on the part of the physician, a lack of medication persistence/adherence on behalf of the patient or any number of other factors which may affect heart health.

INCREASING NEGOTIATING POWER OF MEDICARE

Despite some manufacturer's opposition to take on the risks involved with these contracts, they may soon have little say in the matter due to proposed changes in Medicare Part B. Part B covers medications administered by a healthcare professional in a healthcare facility. Professionally administered drugs are typically purchased by the provider from the manufacturer or wholesaler. Medicare Part B then reimburses the provider 106% of a price called Average

[39] Staton, T. (2016, May 11). Cigna inks results-based deals on pricey Amgen, Sanofi PCSK9 meds. Retrieved February 7, 2017, from http://www.fiercepharma.com/pharma/cigna-inks-results-based-deals-pricey-amgen-sanofi-pcsk9-meds

Sales Price (ASP). ASP is the weighted average of all non-Federal sales to wholesalers after any discounts, rebates or other adjustments[40].

On March 8th 2016, the Centers for Medicare & Medicaid Services (CMS) released a rule proposal that included potential tests to be carried out on Medicare Part B drug payments. This proposal was subsequently retracted in December 2016, but it provides an indication of what future policy to address pricing may resemble[41]. The proposed rule contained many potential changes but two were related to pay for value: indications based pricing and risk-sharing agreements. Technically, the changes would not allow Medicare to negotiate prices, but instead would likely use waivers for the Center for Medicare and Medicaid Innovation (CMMI). The proposed test of indications based pricing would have involved varying the payments for drugs on their proven clinical effectiveness for a given indication. One of the results of this approach would have been that Medicare's Part B payment for a drug would vary depending on what it is used for. The risk-sharing agreements proposed by CMS for Part B would have been very similar to those already in place in the private market. These declarations are notable because the private market as a whole tends to follow the direction of CMS.

Due to strong opposition from physicians and manufacturers, the Obama administration halted the proposal in December of 2016. Despite its defeat, the move is important as its feasibility may be boosted by mounting public pressure and bipartisan support of Medicare negotiation. It is not unreasonable, to assume that a similar rule could be reintroduced successfully and that these initiatives would spread into Part D which comprises the bulk of

[40] Glied, S., & Haninger, K. (2017, February 21). Medicare Part B Reimbursement of Prescription Drugs. Retrieved March 22, 2017, from https://aspe.hhs.gov/report/medicare-part-b-reimbursement-prescription-drugs

[41] CMS proposes to test new Medicare Part B prescription drug models to improve quality of care and deliver better value for Medicare beneficiaries. (2016, March 08). Retrieved February 5, 2017, from https://www.cms.gov/Newsroom/MediaReleaseDatabase/Press-releases/2016-Press-releases-items/2016-03-08.html

Medicare spending. The impact of value based contracts in Part D may have the potential to make a noticeable change in American pharmaceutical spending. Additionally, if such a rule were adopted into Part D, we would expect to see private payers forge similar deals with manufacturers.

The other side to Medicare negotiation is to forego VBP and focus only on allowing Medicare to negotiate on behalf of all Part D participants. In the current state, private insurance companies compete to enroll Medicare beneficiaries into their Medicare Part D plans. They then negotiate with manufacturers to lower the prices. If CMS were permitted to negotiate prices on behalf of all 44 million beneficiaries, the consolidated buyer power would be more powerful than it is in today's splintered system. This increase in negotiating power could push prices down. Opponents may argue that due to the high levels of consolidation already present in the PBM market, that Medicare negotiation would not have much effect on lowering the prices which have already been negotiated.

The last potential side effect we will discuss, and perhaps one of the most influential, is the resulting price transparency that would permeate the market if the entire Medicare program were permitted to negotiate prices. In the current market, the price paid for a drug by any individual customer is known only to a select few organizations. If Medicare were able to negotiate prices and those prices became public knowledge, payers would have much more leverage in their negotiations with manufacturers and could put additional downward pressure on the prices that they are charged[42].

[42] Staton, T. (2016, December 21). It's the same song, but a brand-new verse for 2017's drug-pricing debate. Retrieved February 5, 2017, from http://www.fiercepharma.com/node/364641

BOOSTING COMPETITION AND IMPROVING TRANSPARENCY

In addition to permitting negotiation at the federal level, some efforts have been made to allow for states to negotiate prices with manufacturers. Although the legislation was struck down, in late 2016 California made an effort to allow the state to lower the prices it pays through a bill known as the California Drug Price Relief Act (Proposition 61). The legislation attempted to prohibit the state from paying more for prescription drugs than the Department of Veterans Affairs in any arrangement where the state is the ultimate payer[43]. In the current system, the VA receives an initial 24% discount off of a price known as the Non-Federal Average Manufacturer's Price (NFAMP) of a drug and then is able to negotiate even lower prices from there. The NFAMP is unimportant for our purposes, but for reference it is the average price paid by non-federal wholesalers to the manufacturer including any rebates or discounts[44]. The defeat of such a bill in one of the nation's most liberal states paints a bleak picture for the passage of similar legislation in other states. Nevertheless, the defeat of Proposition 61 has not deterred other states from making like-minded attempts. Other states have introduced similar legislation believing that there is a possibility these laws could gain traction as the pressure and scrutiny on drug prices intensifies[45].

In a January 2017 release, Governor of New York, Andrew Cuomo released the blueprints for such a plan. The legislation would allow the state of NY to effectively cap drug

[43] What you need to know about Prop. 61, the spendy prescription drug measure on November's ballot. (2016, November 04). Retrieved March 21, 2017, from http://www.latimes.com/politics/la-pol-ca-proposition-61-prescription-drug-prices-20160915-snap-htmlstory.html

[44] "Government Price Reporting – Staying Ahead of the Curve on Problems and Solutions" (PDF). Nuget, J. T. 2005. Retrieved February 3, 2017

[45] Weintraub, A. (2016, November 17). Analysts to Wall Street: Don't celebrate yet. The drug-pricing brouhaha is far from over. Retrieved March 10, 2017, from http://www.fiercepharma.com/pharma/analysts-to-wall-street-drug-pricing-brouhaha-far-from-over

prices in the state through Medicaid negotiations[46]. The plan calls for an independent review board to establish fair prices for certain medications. The Medicaid program would then pay the recommended price to the drug manufacturer. Furthermore, the price established by the review board would serve as a cap for all sales of that medication in NY state with any amount charged over the recommended price to be charged back to manufacturers as a surcharge. While similar bills have been introduced and killed in the past, this bill if passed would open pharmaceutical prices to the same transparency effects we explored with Medicare negotiation. It would also set a precedent for other states to follow suit and impose price capping legislation of their own. The drugs which would be subject to such a price cap were not outlined, but the legislation focuses on specialty medications, generics and those which have seen exorbitant (yet to be defined) price hikes.

LEGISLATION TO INCREASE COMPETITION

An additional avenue being proposed to lower prices is the passage of legislation to increase competition in the market. The proposals fall into three main categories: improving access to generics, re-importation of drugs from abroad and weakening the protections afforded to branded drug manufacturers.

Generic Access

To augment the ability of generics manufacturers to compete with branded manufacturers, both the Increasing Competition in Pharmaceuticals Act (Senate) and the Lower Drug Costs Through Competition Act (House) have been put forth for consideration. The Increasing Competition in Pharmaceuticals Act would require that the FDA review process be

[46] Governor Cuomo Presents 33rd Proposal of the 2017 State of the State: Protect New Yorkers from Soaring Prescription Drug Prices through a Groundbreaking Three-Pronged Approach. (2017, January 12). Retrieved February 7, 2017, from https://www.governor.ny.gov/news/governor-cuomo-presents-33rd-proposal-2017-state-state-protect-new-yorkers-soaring-prescription

limited to 5 months for generic versions of drugs that are experiencing a shortage or that have a monopoly[47]. Under normal circumstances, this process takes on average 10 months.

In addition to the expedited review, the bill provides a voucher for generic manufacturers which develop generic versions of drugs that are experiencing a shortage or that have a monopoly[48]. The vouchers would shorten a process which takes on average 10 months (and sometimes much longer) to a maximum of five months and could be used on any other generic drug made by the company or be sold to another generic manufacturer. The Lower Drug Costs Through Competition Act is remarkably similar to The Increasing Competition in Pharmaceuticals Act except that it calls for a six-month maximum review period as opposed to five months[49]. One unintended – but positive as it relates to lowering prices – outcome of bills such as these is that they provide a disincentive for price flipping. We discussed that drug flipping occurs primarily with drugs which have little to no competition. As barriers to generic manufacturing are lowered, the number of drugs which benefit from monopolies will begin to shrink and the opportunities to flip drugs will decline.

Re-Importation of Drugs from Abroad

Another often discussed method of increasing competition in the pharmaceutical market is to allow for the re-importation of drugs from foreign countries. Currently the FDA may allow importation of up to a 90 supply of foreign medication for personal use. This only applies under

[47] Brennan, Z. (2013, March 03). More Competition: Senator Proposes New Priority Reviews for Some Generics, New Voucher Program | RAPS. Retrieved February 20, 2017, from http://raps.org/Regulatory-Focus/News/2016/03/03/24466/More-Competition-Senator-Proposes-New-Priority-Reviews-for-Some-Generics-New-Voucher-Program/

[48] Willis, D. (2016, March 1). S.2615: Increasing Competition in Pharmaceuticals Act. Retrieved February 15, 2017, from https://projects.propublica.org/represent/bills/114/s2615

[49] The Lower Drug Costs Through Competition Act: Prioritized Review for Some ANDAs . . . and a Priority Review Voucher. (2017, February 01). Retrieved February 15, 2017, from http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2017/02/the-lower-drug-costs-through-competition-act-prioritized-review-for-some-andas-and-a-priority-review.html

certain circumstances and in order to qualify for legal importation of foreign medications, additional requirements must be met. The conditional circumstances and requirements make drug re-importation impractical for many if not most patients[50].

It has been established that U.S. payers pay more than many countries for the same medications due to the utilization of single-payer systems and enhanced price regulations in other countries. As a result, there is a belief that the high prices in the U.S. are subsidizing lower prices in other countries. Consequently, drug re-importation is an idea that has garnered support from both Democrats and Republicans. Despite bipartisan support from Bernie Sanders, Hilary Clinton, Barack Obama, John McCain and Donald Trump to name a few, many bills attempting this change have been struck down. Present levels of public outrage and political scrutiny may, however, create an opportunity for new attempts at legislation to succeed.

Recently, one such act, titled An Act to Facilitate the Personal Importation of Prescription Drugs from International Mail Order Prescription Pharmacies (aka The Maine Pharmacy Law), made headlines when it was passed, as the first of its kind, then subsequently overturned by a federal judge[51]. The Maine Pharmacy Law allowed for pharmacies that were not licensed in Maine to practice pharmacy in the state. The effect being that residents of Maine would have uninhibited access to medications from pharmacies in Canada, the U.K, New Zealand and Australia. Although the law was struck down, on the basis that importation falls under the purview of the federal government and that the legislation violated federal law, it is a

[50] Mohammed, R. (2016, March 09). Cheap Drugs from Canada Won't Reduce U.S. Drug Prices. Retrieved February 29, 2017, from https://hbr.org/2016/02/why-importing-cheap-pharmaceuticals-from-canada-wont-work)/

[51] Silverman, E. (2015, February 25). Federal Judge Overturns Maine Prescription Drug Law. Retrieved February 15, 2017, from https://www.wsj.com/articles/federal-judge-overturns-maine-prescription-drug-law-1424882855

great example of how frustration with the price of pharmaceuticals can advance legislation and propose drastic changes to address prices[52].

Re-importation would allow U.S. consumers to obtain their drugs at lower prices from foreign pharmacies that are able to strike better deals with manufacturers. Proponents of this type of legislation argue that the imported drugs, are the same drugs at the same dosages that patients receive in the United States. Opponents of re-importation argue that it undermines the FDA and threatens the safety of American patients. Further, they claim that it cannot be assured that imported drugs, and the plants which produce them, have been subject to the same level of rigor, scrutiny and investigation as drugs reviewed by the FDA and as such, the integrity of medications flowing to American patients would be compromised. Thus, as the restrictions and controls over the supply of medications are loosened, it becomes inherently easier for unverified medications to enter the supply chain. The result being that counterfeit medications could be mixed into the supply of drugs flowing into the U.S. which could have devastating ramifications for patients.

Weakening of Patent Protections

In addition to re-importation, a proposed cost control tool is the weakening of patent protections afforded to branded pharmaceutical products. The simplest explanation of pharmaceutical patents is that they last 20 years and protect the novel inventions of pharmaceutical manufacturers from the development of generic versions of their drug. But of course, like all other aspects of the U.S. healthcare system, the topic of drug patents is much more complex. Firstly, while a drug patent lasts 20 years, it takes on average eight years from the

[52] Maine Drug Importation Law Ruling. (2015, March 05). Retrieved February 20, 2017, from http://www.cisbydeloitte.com/cis-compliance-blog/maine-drug-importation-law-ruling/

time the manufacturer files an investigational new drug application to the market arrival of a drug. The eight-year time to market is largely comprised of time spent on development, clinical trials and the FDA approval process. The ramification of this delay is that the patent only protects on average 12 years of drug sales as opposed to 20. Each year of additional patent exclusivity could add billions of dollars in sales for the company and provides an enormous incentive for pharmaceutical manufacturers to vigorously protect their patents and extend exclusivity. Patents are often proposed as a point of intervention because any extension of exclusivity allows for manufacturers to keep the price high.

There are many ways for a manufacturer to extend the patent life of their product or otherwise protect it from competition. These include: patent extensions for drugs tested in children, new drug formulations, approval of new delivery mechanisms, new uses, changes in a drug's chemistry, combinations with other drugs, etc.[53]. This section will review the basics of exclusivity protection and focus on the proposed reform of some of the most highly-utilized tools: The Drug Price Competition and Patent Term Restoration Act (aka Hatch-Waxman Act), a practice known as *pay for delay* and the Bayh Dole Act.

Hatch-Waxman Act

The Hatch-Waxman Act, was ironically was passed in an effort to decrease the time to market for generic versions of drugs from generic manufacturers. The original idea was to simplify the FDA approval process for generic manufacturers and mitigate the damage to branded manufacturers due to patent loss while a drug was under development and FDA review. Some of the most potent patent protection offered under Hatch-Waxman is the inclusion of a

[53] Finkel, R. (2012, August 26). How Long Is A Drug Patent Good For? Retrieved February 6, 2017, from http://www.drugsdb.com/blog/how-long-is-a-drug-patent-good-for.html

five-year extension of a drug's patent life to in an effort to compensate for the time a drug spends under FDA review prior to approval. In the spirit of full disclosure, while Hatch-Waxman does grant a 5-year extension, the act also caps the patent life after FDA review to 14 years[54]. The second layer of patent protection within Hatch-Waxman is a provision addressing unauthorized generic approval applications. A generic manufacturer can claim that the original patent is invalid or that their drug does not infringe on the existing patent and then apply for approval of a patented drug before its patent expires. The original manufacturer then has the option to sue the generic company. If that happens, Hatch-Waxman mandates an automatic 30-month stay of the generic manufacturer's approval application. This stay is equivalent to a 30-month exclusivity extension. Furthermore, a manufacturer can file other patents - known as secondary patents - throughout the life of the original drug patents, thus providing an opportunity to seek consecutive 30-month stays of approval based on litigation alleging violation of the secondary patents. The first generic company to successfully challenge a drug's patent and win FDA approval is granted a six-month exclusivity period as a reward and an incentive for challenging the pharmaceutical company[55]. During the six-month exclusivity period, only the original manufacturer and the generic company which successfully challenged the patent can market the drug. As mentioned before, each extension extends the monopolistic state of the market and allows manufacturers more power to keep prices high.

It may now be apparent why some are calling for the reform of Hatch-Waxman. Specifically, there have been calls to restrict the types of patents which manufacturers can use to trigger the 30 month stay provision. I believe that a more viable reform would eliminate the stay

[54] Finkel, R. (2012, August 26). How Long Is A Drug Patent Good For? Retrieved February 6, 2017, from http://www.drugsdb.com/blog/how-long-is-a-drug-patent-good-for.html

[55] Angell, M. (2006). *The truth about the drug companies: how they deceive us and what to do about it*. Melbourne: Scribe.

provision altogether, allow the generic manufacturer to pursue approval, while simultaneously fighting the litigation and then holding the generic manufacturer liable for loss of sales if it is found that they did indeed violate a patent. Proposed Hatch-Waxman reforms all center around reducing the ability of manufacturers to fend off generic competition through the legal loopholes – as they are called by the law's critics – mentioned above[56].

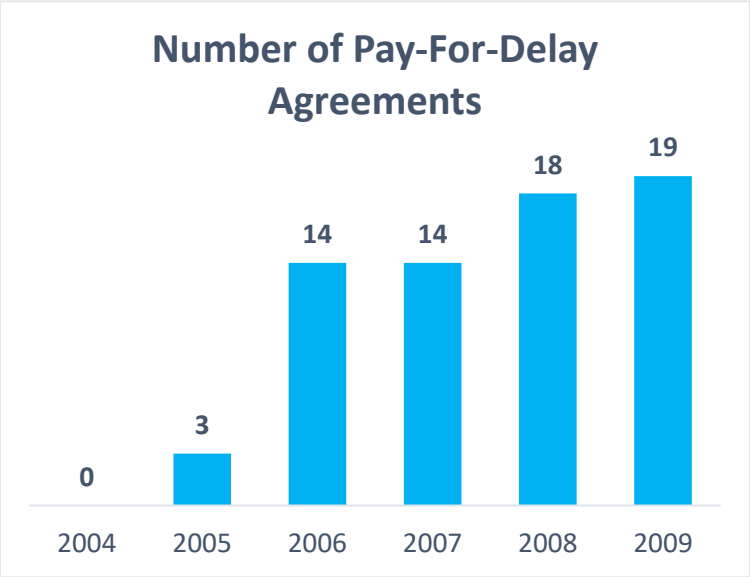
Pay for Delay

An unintended consequence of Hatch Waxman is known as Reverse Payment Patent Settlement, or more commonly, pay-for-delay. To explain the process of pay-for-delay, imagine that a generic manufacturer has applied for the approval of a drug that is currently patented by a branded manufacturer. The branded manufacturer then brings a lawsuit against the generic manufacturer. Consequently, the branded manufacturer calculates the cost of losing exclusivity in the market and the generic manufacturer calculates the potential sales from releasing the drug. The branded manufacturer offers to settle the litigation with the generic manufacturer in exchange for a payment to the generic manufacturer that would be beneficial for both parties. The generic company accepts, the development of the generic version of the drug is delayed for a pre-specified period of time and the branded manufacturer maintains exclusivity on the drug.

If this sounds like illegal collusion or a violation of anti-trust law to you, you are not alone. Opponents of these arrangements claim they are ethically dubious at best and illegal at worst and are calling for prosecution of companies engaged in such deals. The hope is that the threat of prosecution will deter companies from engaging in pay-for-delay, increase competition in the marketplace and bring down prices.

[56] Angell, M. (2006). *The truth about the drug companies: how they deceive us and what to do about it*. Melbourne: Scribe.

So far, the tactic of prosecuting pay-for-delay to reduce prices seems to be the one of the most feasible and actionable as pay-for-delay has already grabbed the attention of the FTC. In 2010, the FTC published a study which found that these deals cost $3.5 billion every year and revealed the growth in pay-for-delay (shown below). As a result of these findings, the FTC made a crackdown on pay-for-delay one of its top priorities[57].



Pointing to their success in reducing these deals, another FTC report found that pay-for-delay deals as defined by the FTC were down from a high of 40 in 2012 to 21 in 2014[56]. Furthermore, the Supreme Court in 2013 in FTC vs Actavis passed down a ruling which made the prosecution of pay-for-delay deals by the FTC easier. The ruling expanded the antitrust principles under which the FTC was able to bring a lawsuit against participants of pay-for-delay deals[58]. Now an abundance of pay-for-delay cases have been brought to court (most unsettled and at various levels of litigation)[59], and in May of 2016 the FTC won a $1.2 billion settlement with generic manufacturer Teva Pharmaceuticals for their part in a pay-for-delay deal.

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[57] "Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. Overview of Agreements Filed in FY 2014. A Report by the Bureau of Competition." (PDF). Federal Trade Commission. Retrieved February 8, 2017.

[58] "Federal Trade Commission v. Actavis Inc Et Al." (PDF). Supreme Court of the United States. October 2012. Retrieved February 15, 2017.

[59] Lipman, M. (n.d.). Law360's Pay-For-Delay Cheat Sheet For 2015. Retrieved February 12, 2017, from https://www.law360.com/articles/608357/law360-s-pay-for-delay-cheat-sheet-for-2015

The FDA has made significant progress in reducing the amount of pay-for-delay deals[60]. However, it is as of yet unclear whether this tactic will be effective in noticeably reducing drug prices. While data is not yet available, basic economic theory would lead us to believe that as competition improves, prices will begin to fall.

Proponents of pay-for-delay deals argue that settlements maximize societal benefit. What they are implying is that the societal cost incurred through the maintenance of the high price of the drug is outweighed by the costs the settlement avoids. These costs include the high costs of litigation, the use of government resources to settle cases and the time and resources diverted away from developing new treatments to fight legal battles. Lastly, manufacturers defend their legal right to engage in pay-for-delay. From their perspective, if a patent is being violated, they as the inventor have the right to defend their patent and that any resulting settlements fall within the confines of the law.

Bayh Dole Act

The Bayh-Dole Act (aka the Patent and Trademark Law Amendments Act of 1980) allows for inventors – usually from small businesses or universities – to pursue ownership and patents for inventions that are a product of government funded research. Prior to Bayh-Dole, inventions which were developed using government funded research were property of the U.S. government[61]. The problem with this system was two-fold: First, it diminished incentives for innovation by removing ownership. Second, at the time of the Act's passage, the U.S.

[60] Schencker, L. (2016, January 14). Drugmakers' pay-for-delay deals fall following Supreme Court decision. Retrieved February 20, 2017, from http://www.modernhealthcare.com/article/20160114/NEWS/160119926

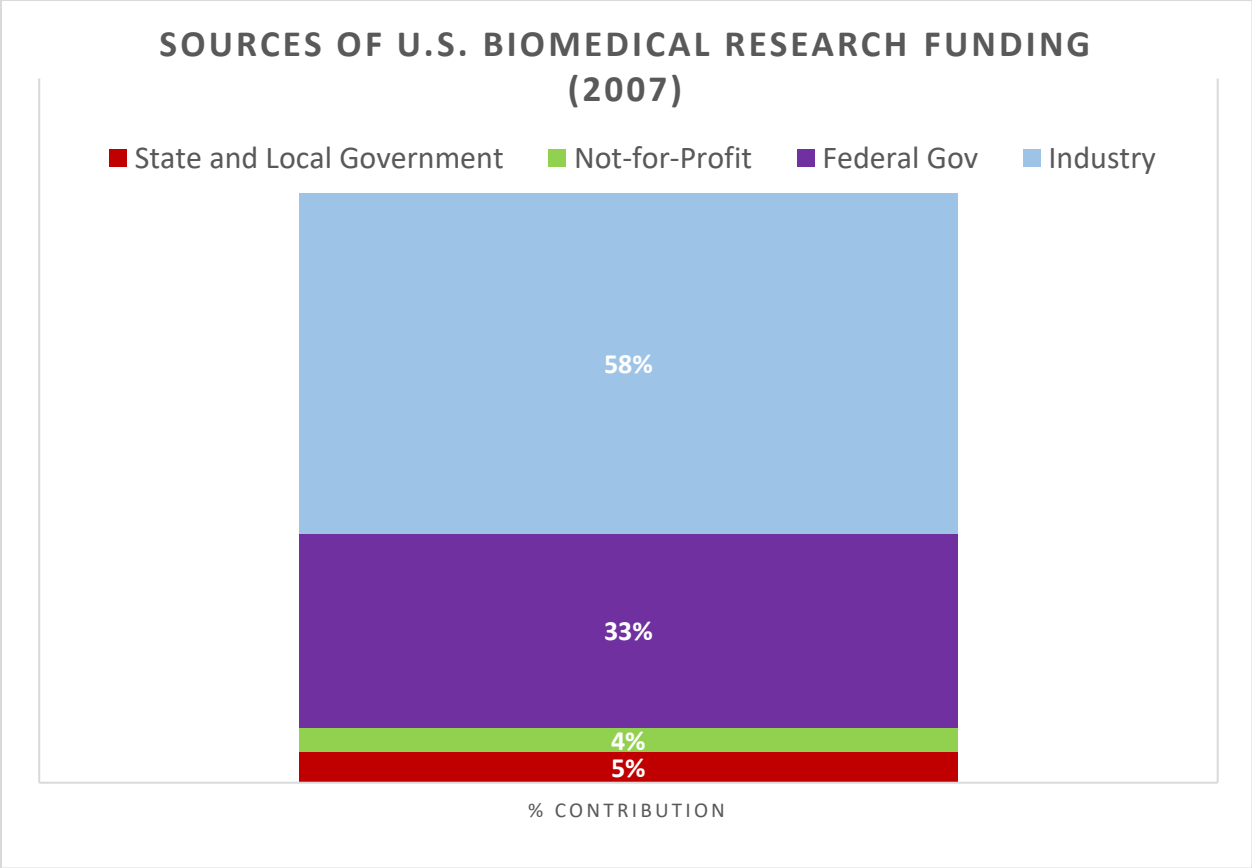
[61] Stevens. A (2004) The Enactment of Bayh–Dole Journal of Technology Transfer 29:93–99

government had commercial licenses for only 5% of the 29,000 patents that they owned[62]. Through the ownership transition facilitated by Bayh-Dole, inventors could now own their inventions regardless of if their funding source was governmental. Once inventors established ownership, they could license them to a large manufacturer and collect royalties on resulting sales. Thus, the transfer in ownership to inventors was effectively a transfer of both the flow of profits and pricing away from the federal government and into the hands of manufacturers.

This begs the question, "how much was the government giving up with Bayh-Dole?" The results (on the following page) of a report published in JAMA show the breakdown of biomedical research funding in the U.S.[63] Displayed is the fact that, in the U.S., the government funds a significant portion of biomedical research. If Bayh-Dole were to be repealed or reformed, the U.S. could own all of the drugs resulting from this research.

[62] U.S. Government Accounting Office (GAO) Report to Congressional Committees. May 7, 1978. "Technology Transfer, Administration of the Bayh-Dole Act by Research Universities"

[63] Dorsey, E. R. (2010). Funding of US Biomedical Research, 2003-2008. *Jama,303*(2), 137. doi:10.1001/jama.2009.1987



To truly understand the magnitude of the government's losses, we need to know how many drugs stem from the 33% of biomedical research that is federally funded. According to Marcia Angell M.D., author of *The Truth About Drug Companies and How They Deceive Us*, 33% of all drugs marketed by major manufacturers are licensed from universities or small biotech companies[64]. Multiplying the 33% of drugs that are licensed by the 33% of funding that comes from biomedical research, leads us to the following conclusion: ~16.6% of drugs marketed by major manufacturers are a result of federal research. Supporters of reforming Bayh-Dole are furious that the government and American taxpayers fund the invention of drugs that manufacturers turn around and gouge them for. They submit that by allowing the federal

[64] Angell, M. (2006). *The truth about the drug companies: how they deceive us and what to do about it*. Melbourne: Scribe.

government to retain or reclaim ownership of the ~16.6% of drugs which benefit from federally funded R&D, the government could stymie rise in spending on pharmaceutical products. Of course the flip side of this argument is that, by removing incentives for innovation, the flow of innovative new therapies will slow and any commercial uses that may have been developed would be seriously encumbered by the fumbling and inefficiency of government systems. In my opinion, it seems a good solution to imbue government funding contracts with clauses that allow the government to exercise a *clawback* of ownership for products birthed from federal funding once revenues of the product reach a certain level. This way, the government could protect the public from exorbitant spending on drugs which they've paid to develop and inventors would still have an incentive to innovate.

CREATING TRANSPARENCY TO HAVE DRUG REBATES UNLOCKED ACT

The final reform we will review involves improving transparency in the PBM contracting process. In my opinion this would be one of the most effective tools in reducing the cost of drugs in the U.S. While I believe that it is the most effective proposal, it lacks feasibility, as the industry will lobby hard against any such legislation and conservatives will argue that it hurts competition in the marketplace. On March 15, 2017, Senator Ron Wyden proposed the Creating Transparency to Have Drug Rebates Unlocked Act (C-THRU). This legislation would require PBMs to disclose, by publishing on CMS' website, information on the size of manufacturer rebates and the spreads charged to customers. Furthermore, after two years of reported data, this legislation would require a minimum share of rebates and discounts to be shared with health plans/plan sponsors in order to lower patients' premiums and cost sharing. Finally, this legislation would require that cost sharing for Medicare Part D be based on PBM negotiated

prices which would lower the cost of drugs to Part D participants. Presently Part D cost sharing is a percentage of the pre-rebate cost of the drug the plan[65].

Throughout this paper, I have provided evidence that the major cause of high prices is a lack of transparency within the system. This legislation would be the first step in wiping the glass and allowing the public to look into the system and see where their money is going. While the initial PBM transparency would go a long way in lowering prices, the true value of the passage of this bill would be the precedent which it sets. If legislation improving PBM transparency were passed, it would undoubtedly be followed by proposals to increase transparency of other organizations contracts as well. Eventually, what you would have would be a fully transparent chain from manufacturer to patient.

Unfortunately, the negative ramifications of such legislation for the industry are such that its passage is highly unlikely. Although one would expect rebate transparency to improve public perception of manufacturers and reduce the blame attributed to them, this legislation will most likely be strongly opposed by both PBMs and manufacturers. Their opposition poses a huge threat to the legislation. According to the LA Times, the pharmaceutical industry has 1,266 lobbyists in Washington and has been known to spend hundreds of millions of dollars fighting legislation[66].

The reason PBMs may oppose C-THRU is evident. If rebate contracts were to become public, PBMs would face increased scrutiny over their profit margins and inevitably their profits

[65] "Summary of The Creating Transparency to Have Drug Rebates Unlocked (C-THRU) Act" (PDF). U.S. Senate. 2017. Retrieved March 19, 2017

[66] Sanders, B. (2016, October 21). Bernie Sanders: Stand up to Big Pharma greed. Vote yes on Proposition 61. Retrieved March 22, 2017, from http://www.latimes.com/opinion/op-ed/la-oe-bernie-sanders-yes-on-proposition-61-20161021-snap-story.html

would be pushed lower. Manufacturers may oppose it because their rebates would be made public knowledge and their competitive edge in any given rebate negotiation would be demolished. It can be thought of like this: if it becomes public knowledge that Express Scripts is receiving an $80 rebate for a given drug, other PBMs will want to know why they aren't being offered the same deal. In this scenario, manufacturers would be forced to offer everyone the rebate negotiated by the most powerful PBM, or forego coverage with those companies with which the manufacturer is unwilling to give said discount. On these grounds, both manufacturers and PBMs will fight this legislation with veracity and both industries command considerable lobbying power.

As we have just reviewed, there are many ways to approach the problem of high drug prices. The complexity of the issue allows for many avenues to solve the issue. Some approaches such as self-regulation are easy to implement but may be ineffective. Others such as Medicare price negotiation, patent reform and improving transparency would be highly effective but are likely to be defeated before they can be implemented. And some such as value based contracting and drug re-importation have proven some semblance of feasibility while questions of their effectiveness will be answered with time. Solving a problem without full information is unlikely to bear fruit and may in fact do harm (as some would argue Bayh-Dole and Hatch-Waxman did). For that reason, it is my belief that until we have transparency within the system, effective reform will be nearly impossible.

CONCLUSION

If nothing else, this analysis has proven that the pricing of pharmaceuticals is a complex and ever-evolving labyrinth involving multiple organizations. The lack of transparency involved only further impedes any attempt to understand it. In many instances, it appears that the financial

benefit provided through higher prices serves as a major motivation for the organizations involved in this system. This may or may not be the case; however, it demands then that blame for higher prices not be attributed to one group but rather to the design of the entire system.

To improve this system, we cannot look exclusively at list prices or organizations in isolation. Instead, we must analyze the system in its entirety and review the various components that contribute to higher prices. As we have reviewed, these components include, legislation, profiteering, flaws in our healthcare system and inadequate coverage. Yet, despite these concerns, I believe that the most contributory is the lack of transparency. Since the industry benefits from the contractual secrecy, it will use all of its political power to hinder any attempts to improve transparency. But in this highly-polarized time, regardless of political affiliation, increasing transparency must be the concluded solution. For those who support a market driven system, transparency will allow the market to more accurately ascribe value to medications and to PBM services. The manufacturers and PBMs that are able to maintain profit margins while keeping prices low will be rewarded with higher sales and those that cannot will be driven out of the market. For those who support lower prices for drugs and less corporate profiteering, increased transparency will push prices lower. And for this to be successful, all organizations must be made transparent simultaneously, as any other option would unduly and unfairly affect the ability of transparent firms to compete against those which remain shrouded in secrecy.

Until transparency in drug pricing is improved, I urge you to use the information within this analysis to ask informed questions that will fully develop your understanding. If you are given the list price of a drug, know that it is the WAC. Ask what the manufacturer is actually receiving, what the PBM is paying and about the size of the patient co-pay. Learn whether the drug was purchased by another manufacturer before a price hike and whether the PBMs, pharmacies and

wholesalers are profiting from and contributing to a higher price. Research whether the drug has been granted monopolistic coverage by PBMs and how much the manufacturer is spending on advertisements for the drug. Figure out how much patent life remains on the drug or if generic competition is being stifled. After reading this analysis, I hope I have armed you with the knowledge to ask and answer these questions. Use the answers you obtain to inform your stance on the issue as well as the solutions you put forth.

X [redacted]

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