1 INTRODUCTION

Everyone has a limit. Every budget has an end point. Although sellers would love to raise prices continually, it doesn't take fancy economics to know that, at some point, the money runs out. Why isn't that basic principle working as expected in the pharmaceutical industry? Instead, drug prices are rising continually and reaching astronomical levels, with no end in sight. In May 2018, analysts reported that a company is contemplating a US$1.5 million price tag for its new hemophilia cure.[1] (The current hemophilia therapies already cost an astounding $580,000–800,000 per year.[2]) Along the same lines, Spark Therapeutics' cure for a rare form of blindness will cost $850,000,[3] rivaling Novartis' planned $475,000 price tag for its Car-T drug Kymriah.[4]

Even outside the eye-popping headlines, prescription drug prices across the board have risen to an alarming and puzzling level. A government inspector general's report found that the high cost of brand medications for common conditions (diabetes, high cholesterol, and asthma) were the true problem for patients on Medicare.[5] In fact, pharmaceutical companies have raised the prices most sharply for commonly used medications such as these.[6] Similarly, an analyst report concluded that in 2016, the average price for a set of specialty drugs known as "orphan drugs" was $140,000 a year and the average price of ordinary drugs was almost $28,000 a year.[7]

The list price of drugs tells only part of the story, given the many rebate and discount processes that exist within the industry.[8] Nevertheless, real spending for drugs is rising as well. According to the Health and Human Services Inspector General's report, even after accounting for rebates, Medicare spending for branded drugs still rose 62 percent between 2011 and 2015.[9] Worse yet, the department responsible for Medicare and Medicaid projects that the increase in

national prescription drug spending will more than double in 2018 from the prior year's significant rise.[10] In 2017, this increase in spending outpaced increased healthcare spending as a whole and the 2017–18 consumer price index (CPI).[11] All of this, despite the fact that roughly 80 percent of the prescriptions in this country are filled using generic drugs.[12]

No one would ever suggest that spending within the healthcare system follows an ordinary, rational model. The patient as consumer does not absorb the full costs of health care, given the effects of private insurance and government programs.[13] Nor does the consumer possess full information about the products purchased or the cost of choices, and even physicians may experience information gaps. Most important, the value consumers place on their own lives creates distortions that differ from buying choices in ordinary markets. Nevertheless, dollars are finite, and some limits must exist.

One can see the mounting pressure in government budgets, which are struggling to cover the cost of new, expensive medicines. If the Defense Department had treated all Veterans Administration (VA) patients infected with hepatitis C in 2015 using the breakthrough cure Sovaldi, the $12 billion cost would have accounted for 20 percent of the department's annual medical budget – just for treating a single disease.[14] With budgets in the home, patients report rationing or forgoing medications for lack of funding.[15] This is precisely the type of boundary point that should create pressure to reduce prices. And yet the rise persists.

This book analyzes and explains the phenomenon, which has puzzled modern commentators and policymakers alike. Why do drug prices stubbornly continue to rise, despite the promise of competition from generic drugs? Quite simply, the phenomenon occurs because internal incentives push every market participant toward behaviors that increase prices, knocking out the normal checks that should operate as brake-points on the market.

At the center of the system lies the highly secretive and highly concentrated industry known as "pharmacy benefit managers" (PBMs). These middle players negotiate prices between branded drug companies and those who pay the bills, arranging for rebates from various drug companies. They also establish the formularies, which are

the schedules that set the terms on which patients can access particular drugs and the reimbursement rates patients will get. The PBM middle players are supposed to act to ensure good bargains for patients and health insurers, but the reality is far from that ideal. Moreover, the system is deeply hidden. The contracts between drug companies and the PBMs are a closely guarded secret, with the details known only to the drug companies and the PBMs themselves. Government entities and the private insurers who pay the bills are not permitted to see the full terms of the contracts. Even their auditors generally are not permitted full access to the contract terms.[16] Those who pay are given periodic rebates without full information regarding the actual net pricing for any particular drugs. Markets thrive on information, and, from the standpoint of competition, such an industry design is problematic.

Despite the extreme secrecy, details have begun to seep out – through case documents (including recent contract disputes among parties), government reports, reports to shareholders, state Medicaid actions, and industry insider reports. Piecing together information from these original sources, this book presents – for the first time – a full picture of the perverse profit-taking incentive structures in the industry. The book demonstrates the way in which encouraging consumers to use drugs with higher prices operates in the interests of so many players – including doctors, clinics, hospitals, PBMs, brand drug companies, health plans, patient assistance programs, and patient advocacy groups. Payment flows are structured so that higher prices benefit the intermediaries who should be the watchdogs for the patients. Given these incentive structures, higher-priced drugs receive more favorable reimbursement treatment, and patients are channeled toward more expensive drugs.

The system also operates to support competition-free zones for pharmaceutical companies. The perverse incentive structures allow pharmaceutical companies to share monopoly profits with parties at each level of the market, maintaining their position at the top and ensuring that lower-priced competitors cannot knock them off their perch. In exchange for financial payoffs, structured in different ways to appeal to different groups, drug companies can ensure that, as lower-priced substitutes enter the market, those firms cannot gain a foothold.

The system fits within a larger framework in which drug companies block competitors – even paying them to stay off the market for periods of time. It is a win–win for everyone – except, of course, for consumers, taxpayers, and society in general.

Thus, this book describes the way in which the system creates incentives for prices to rise unchecked and for consumers and taxpayers to experience harm. The book also proposes approaches to better align incentives and analyzes the flaws in some popular proposals. Specifically, Chapter 2 of the book describes the extent of the rising prices and economic effects. Chapter 3 describes how incentive structures in place for PBM middle players and insurance companies drive prices higher. Chapter 4 explains how incentive structures in place for pharmacies, doctors, and patient groups drive prices higher. Chapter 5 explains the broader framework within which drug companies keep lower-priced competitors out, demonstrating that, in the process, companies are largely recycling and repurposing old drugs, rather than creating new ones. Chapter 6 suggests how to begin realigning the industry's incentives with society's interests. Each chapter begins with a short summary, for those who like to skip around.

2 THE LANDSCAPE

2.1 BRANDED PRESCRIPTION DRUGS

Research and development in the pharmaceutical industry is a long and arduous affair. Scholars disagree over the full extent of the cost to bring a drug to market. Nevertheless, no matter how one slices the numbers, it takes many years, and the cost is substantial, with estimates ranging from US$161 million to $2.5 billion for a single drug to get to market.[1]

The pharmaceutical industry in the United States has introduced extraordinary advances in health care. One cannot overemphasize the major life improvements over the last century that flow from innovation in prescription medications, including new life-saving antibiotics, treatments for pain, psychopharmacological treatments, and cancer drugs. As one physician pointed out to me, former US President Jimmy Carter is now approaching three years since his diagnosis with metastatic cancer, thanks to a drug that did not exist a decade ago. Pharmaceuticals also constitute a major export for the United States, with domestic companies accounting for 45 percent of the global market.[2]

To incentivize this substantial and uncertain investment, new drugs are generally protected by a patent, which prevents others from copying the drug and competing in the market. Other regulatory awards, for activities such as engaging in new studies or pediatric analyses, can extend that protection for limited periods of time.[3] When the various patent and regulatory protections that allow a period of time for recoupment of investment have expired, the Hatch-Waxman system for approval of generic drugs steps in to expedite the entry of generic competitors.[4]

Not all patent-protected drugs represent major healthcare innovations. Some are merely combinations of existing medications that can be purchased for less individually, such as Treximet, a migraine medicine that combines an old migraine medicine and naproxen.[5] Others are tweaks of existing medicines, with dosage or delivery system altered in an effort to obtain additional protection.[6] As detailed in Chapter 5, the patent and exclusivity system, unfortunately, incentivizes this type of behavior.

The price of a generic drug averages 75–90 percent below the cost of the original branded drug.[7] This price reduction tends to happen across time, with the largest reduction occurring as more generic drugs become available on the market.[8] This, of course, is when the generic market is working at its best, which is not always the case. Some scholars have observed generic drugs experiencing high prices or sharp price increases.[9]

During the period of protection for a branded drug, however, monopoly pricing reigns. There may be drugs within the same general class of medications that can serve as therapeutic alternatives, but most branded drug companies enjoy considerable freedom in setting the price in the United States. With any commodity in a monopoly price setting, of course, the upper bounds of pricing are set by the limits of the budgetary capacity of those consuming the product.[10] No budget is endless, and all goods must compete to some extent with other items in the consumer's basket. After all, I will pay only what I am willing to pay – I want to provide for my family and go to the movies once in a while – and what I can afford to pay – I have to eat, keep a roof over my head, and buy a coat so I can survive in the winter.

Health, however, is no ordinary expenditure, and the healthcare industry is an odd market.[11] Although patients are the ultimate consumers of prescription drugs, they lack full information and may be insulated from the full costs in a variety of ways.[12] For example, employer-provided health insurance is subsidized by federal and state governments, in the form of tax advantages for the employers and employees.[13] Insurance itself can insulate users from the full costs of their care, spreading the cost across a pool of other workers and across time. For many of those without a connection to employment, Medicare, Medicaid, government health plans, and other government programs absorb much or all of the cost.

The patient also suffers from an information disadvantage in health care, relying on the expertise of healthcare professionals. With prescription medication in particular, consumers are not able to make the purchasing choice; rather, the physician makes the ultimate decision regarding what to prescribe. And, as will be described in detail below, the purchasing preference for both doctor and patient may be influenced by the insurer's willingness to reimburse for the medication, as well as by less savory aspects, including direct-to-consumer advertising[14] and drug companies courting physicians.[15] Accurate information on both the price and quality of healthcare services can benefit consumers, both by helping them to become better shoppers and also by spurring competition among providers along both price and quality dimensions.[16] However, delivering that information in an easily understandable format – and one that is not drowned out by other messages such as advertising – can be challenging.[17]

Most important, buying decisions for health care do not follow ordinary economic logic, stretching the boundaries of rationality.[18] My own life may be of incalculable value to me – well beyond what my budget or society's budget can rationally afford. That may be true even when the likelihood of successful treatment is low or the additional lifespan provided is no more than weeks or months.[19] And when someone else is paying the bill, the value to me, measured by my willingness to consume the good, could become infinite. Of course, not all prescription drug buying decisions are a matter of life and death, but the general irrationality of health decisions can distort ordinary purchase choices in a society whose citizens generally exist well beyond the subsistence level. All of this suggests that the normal budgetary limitations that a monopolist might face have less force in the healthcare system.

Even within the distorted world of health care, however, prescription drug prices stand out, rising faster than any other form of healthcare spending, including hospitalization and nursing home care.[20] In a 2017 report to Congress, the Medicare Payment Advisory Commission (MedPac), a nonpartisan legislative branch agency, reported that, between 2006 and 2014, drug prices in Medicare Part D rose by an average of 57 percent cumulatively, with dramatic increases in 2013–14 in particular.[21] One industry report for 2016 projected that

prescription drug prices would rise 11.6 percent for Americans younger than 65 and 9.9 percent for older adults, compared to wage increases projected for that year of 2.5 percent.[22]

Some price rises stand out in particular. A report from the U.S. Government Accountability Office estimated that, between 2000 and 2008 alone, 416 branded products displayed extraordinary price increases.[23] Those increases mostly ranged from 100 percent to 499 percent.[24]

Such price increases are driven by rising prices in branded medications. According to the generic pharmaceutical industry group, although branded drugs account for only 11 percent of prescription volume in the country, they account for 74 percent of the spending.[25] Thus, although the pharmaceutical industry correctly points out that generic medications represent most of the prescription volume in this country, and the U.S. Food and Drug Administration (FDA) approves a vast number of new generics every year,[26] the year-to-year increases in the prices of branded drugs, along with higher prices for new branded drugs, are swamping the savings from generic competition.[27]

Consider, first, list prices. The list prices for branded medications continue to rise sharply. The list prices for branded drugs rose 12.4 percent in 2015 and increased 10 percent or more annually for each of the prior three years.[28] Although there may be some moderation in pricing as a result of public pressure, the general trend of increasing prices appears likely to hold for the foreseeable future. For example, Eli Lilly's transparency report noted that the company raised list prices 14 percent on average in 2016;[29] Allergan increased its list prices for 18 medications by 9.5 percent.[30]

These price increases have played a significant role in drug company profits in recent years. For example, the *Wall Street Journal* reported in 2015 that 80 percent of the growth in profits for the 20 largest drug companies were the result of increasing prices on existing drugs, not of new drugs or increased drug sales.[31]

In general, the price rises are most dramatic in a category called "specialty drugs." Neither the industry nor the federal government's Centers for Medicare and Medicaid Services (CMS) has a consistent definition of "specialty drug," but the category tends to include drugs

that are used to treat a rare condition, require special handling, use a limited distribution network, or require ongoing clinical assessment.[32] Some drugs are categorized as "specialty," however, simply because their cost exceeds $10,000 a year.[33] The National Academy of Sciences (NAS) reports that, over the last five years, spending on specialty medicines has nearly doubled, outpacing the consumer price index (CPI) from 2011 and 2013, and composing more than two-thirds of growth in drug spending between 2010 and 2015.[34] The 2016 annual report from Express Scripts PBM projects that 1 percent of all drugs will account for 50 percent of the drug spend because of higher-cost specialty medicines.[35] In other words, more of the drug spend is flowing into the specialty drug category.

List prices, of course, are only the beginning of the story. Drug companies enter into a variety of contracts that provide for rebates from the list price. Although these price concessions are a closely guarded secret, and it is difficult to tease out the actual net price that different entities pay along the drug chain,[36] the net price paid to the drug company is substantially less than the list price.[37] For example, in defending against complaints about rising drug prices, industry group PhRMA reported at a Federal Trade Commission (FTC) roundtable that, after accounting for rebates and discounts, prices grew only 3.5 percent in 2016.[38] Similarly, a leading analysis group estimates that, although list prices increased 13.5 percent in 2014, the net price increase was only 5.5 percent.[39] Even these net price increases, however, outstrip the inflation rate over the last five years, which has ranged from a low of less than 1 percent in 2014 and 2015 to a high of 2 percent for 2016 and 2017, with the same projected for 2018.[40] In other words, even assuming that everyone pays discounted prices, rather than full list prices, the discounted prices are still rising far more rapidly than inflation.

Many people, however, *do* pay the full list price. Private insurance plans often require that patients contribute an amount based on a percentage of the full list price of the drug.[41] Other plans require that patients pay the total price of medications at the list price until patients meet an individual or family deductible.[42] Specifically, nearly 30 percent of those enrolled in employer-sponsored healthcare plans have high-deductible plans in which patients pay 100 percent of their

healthcare costs up to a defined amount.[43] Other plans require substantial deductibles or co-pays, with studies showing dramatic reductions in coverage and increased cost-sharing burdens for higher-priced drugs across time.[44] Even when full Medicare coverage is in place, patients must pay part of the cost of medications, with gaps occurring that can force patients to pay the majority of costs.[45] These amounts are largely based on the list price and not the net price of the medication, thus depriving consumers of the benefit of the rebate price concessions.

In addition, although the number of people with health insurance increased substantially after passage of the Affordable Care Act of 2010,[46] 10 percent of those under the age of 65 in the United States still had no insurance in 2017, and not all of those who had health insurance enjoyed prescription drug coverage.[47] Even with Medicare, 12 percent of beneficiaries are neither enrolled in prescription drug coverage nor covered by another prescription plan such as veteran's benefits.[48] Thus cash-paying consumers who lack sufficient drug benefits also pay the exaggerated list price. And, of course, when prices rise year after year, rebates have less meaning in real dollar terms. A 10 percent rebate on a price that has risen 20 percent in recent years is not much of a bargain. As a result, the total out-of-pocket amount that US consumers are spending on medication continues to rise sharply.[49]

Against this backdrop, drug companies have retained a healthy profit margin. Gross profits on brand drugs are roughly 76 percent.[50] In addition, despite the costs of research and development, drug company profits are rising overall. Eli Lilly, for example, saw a 6 percent increase in revenue and a 14 percent increase in net income between 2015 and 2016.[51]

The pharmacy benefit manager (PBM) industry also enjoys a healthy and rapidly expanding balance sheet. For example, Express Scripts, one of the three major PBMs, reports a steady increase in its net income, climbing from $1,898 million in 2013 to $3,404 million in 2016 – an increase of 79.3 percent.[52] Diluted earnings per share more than doubled over the same period, increasing from $2.31 to $5.39.[53] Similarly, OptumRx reported operating profits of $2.7 billion in 2016, up from $1.7 billion the prior year.[54]