ABSTRACT

Pharmaceutical Price Regulation: Lessons From Europe

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The United States is often cited as both having the world's highest pharmaceutical prices and developing the most new therapeutic drugs, two facts that many in the industry claim to be connected. The United States is unique among developed nations in its lack of price controls on pharmaceuticals. This paper attempts to examine the price controls used in European nations and attempt to determine if an application to the United States would be at all successful. The key issue to be addressed is whether regulation can successfully decrease prices without an overly negative effect on research and development undertaken by profit driven firms. While some decrease in R&D spending is to be expected, this paper seeks for instances of price controls where this effect is relatively mild.

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# PHARMACEUTICAL PRICE REGULATION: LESSONS FROM EUROPE

A Thesis Submitted to the Faculty of

Baylor University

In Partial Fulfillment of the Requirements for the

Honors Program

By

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Waco, Texas

May 2016

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# PREFACE

For as long as I can remember, I have wanted to be a doctor. As a young child, I had an anatomy book that I read cover to cover, over and over. Even when I was growing up, far too young to think seriously about a career outside of being able to answer, "what do you want to be when you grow up?", I always had that sense of direction about where I would end up. Science classes were always my favorite in high school, and as my interests solidified I could look ahead to a future that could actually start to seem a bit real. My senior year, I took my required class in economics, and suddenly I had found another subject that grabbed my attention. While not diverted from my original plans of a career in medicine, I now had another field that I wanted to explore thoroughly, and I am very grateful that the University Scholars Program at Baylor allowed me to do just that.

The economics of health care was a natural intersection of my future in medicine and my interest in economics, and this culminated in the summer of 2015, as I was searching for a thesis topic. I spent a month studying abroad in Great Britain, where I took a course on the healthcare systems of various countries, taught by my future thesis director. I was fascinated by the vastly different approaches that nations took to solve very similar problems, and the different views they had of their results. Certain outcomes, such as long waiting lists for care, that would be widely accepted in the United Kingdom would be quite unpleasant to an American, and vice versa. Despite these differences in evaluation, there is, as with any problem

affecting large groups of people, always some common ground on which to learn from the varying perspectives of others. This becomes even truer as the world shrinks around us, and the problems that once defined a specific group become more and more universal.

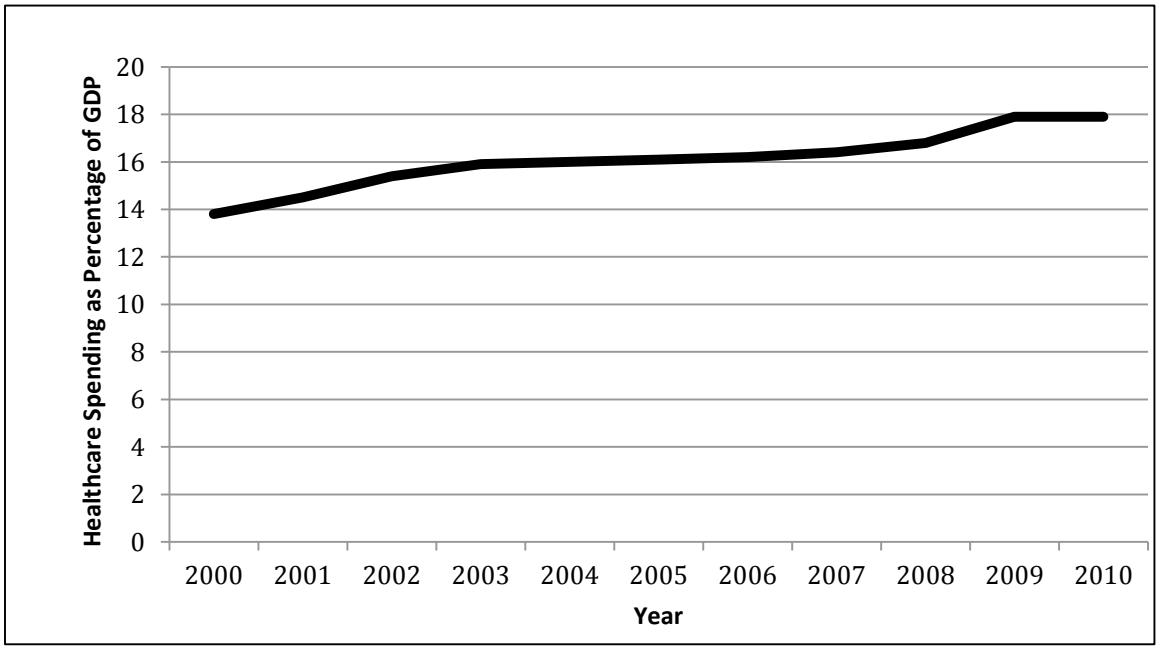
My goal in writing this thesis is to capitalize on this opportunity to learn from both the successes and failures of ourselves and others. By examining the methods, outcomes, and consequences of styles of reform that remain largely alien to the United States, perhaps there are in fact valuable lessons to be learn that will help shape the American vision of healthcare.

CHAPTER ONE

Introduction and Cost Drivers

Across the developed world, pharmaceuticals are becoming a more and more essential, and expensive, part of healthcare. This statement can easily be verified by a quick glance at spending data. Healthcare, as a whole, faces increased spending in every area. According to the Centers for Medicare and Medicaid Services[1], in 2013, healthcare spending in the United States increased by 2.9 percent, followed by even more rapid growth of 5.3 percent the following year. Expenditures rose to three trillion dollars, a little less than $10,000 per person. These expenses outpaced the growth of the US GDP as a whole, rising from 13.8 percent of GDP in 2000 to 17.9 percent in 2010.

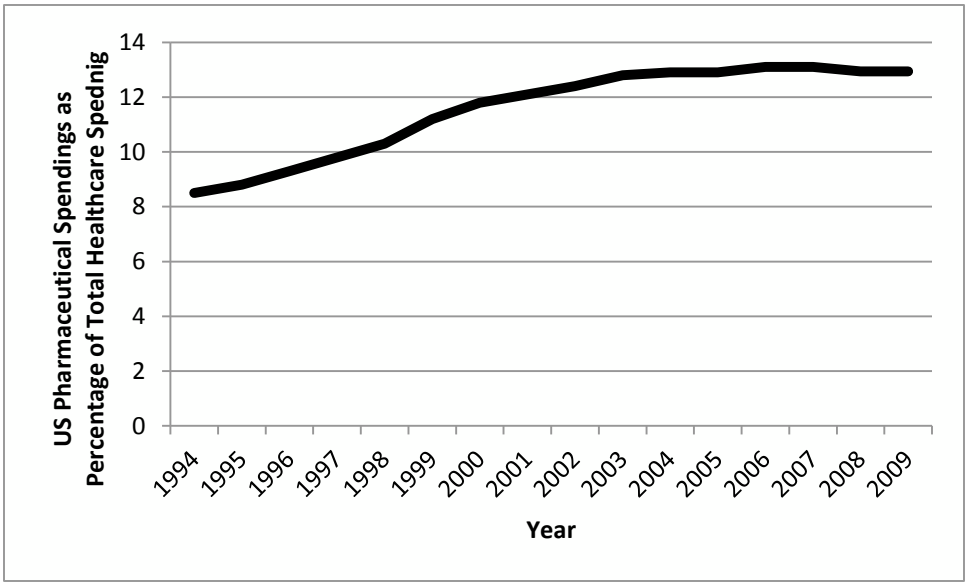
*Figure 1.1: US Healthcare Spending as a Percentage of GPD Over Time*



This is not only a recent trend: in the 1960's, healthcare accounted for only five percent of the GDP.

The United States is spending more each year on healthcare as a whole, but this is especially true for pharmaceuticals. Increases in these expenses easily outpaced growth in general healthcare spending in 2014, with retail prescription drug spending growing by over 12 percent to account for almost ten percent of all health care spending. Pharmaceutical spending in general accounted for 8.5% of healthcare spending in 1994, according to OECD data. By 2004, this figure had risen to 12.9%. This trend of increased pharmaceutical spending growth holds true regardless of the source of the spending, be it Medicare, Medicaid, or private insurance, according to the Centers for Medicare and Medicaid Services.

*Figure 1.2: Pharmaceutical Spending as a Percentage of Total Healthcare Spending in the United States Over Time*




This is not simply a trend in American healthcare: pharmaceuticals have claimed a very important place in European healthcare as well. For example, in the

United Kingdom, healthcare expenditures have increased every year from 1997-2013, both in terms of total and per capita spending, according to data from the Office of National Statistics. Although the public sector in the United Kingdom bears over 80 percent of healthcare expenses, household consumption accounted for over two thirds of private sector spending in 2013. Of this out of pocket spending, 33.8 percent went towards pharmaceuticals, more than any other category of medical products, as well as accounting for a greater share of expenditures than either hospital, medical, or dental services. Other European countries also spend significant amounts on pharmaceuticals as a percentage of total healthcare expenses, including Germany, (14.1 percent), France (15.1 percent), and Italy (18.8 percent), as described in OECD data. This is even more exaggerated in Eastern European countries such as Greece and Hungary, where pharmaceutical expenditures account for more than 30 percent of total healthcare spending. These percentages are all significantly higher than in the United States.

Efforts to expand access to healthcare are taking center stage in the United States, but with this access comes the increased spending of providing these additional services. It is natural to look to pharmaceuticals as one area where some savings can be found, due to the important and expensive place they hold in global healthcare systems. Nations have sought and attempted various methods to reduce these expenditures, and these will be examined in greater detail in later chapters. This paper will attempt to determine in which areas, if any, American policy regarding pharmaceuticals falls short, and which reforms from other nations may be able to successfully fill in this gap. First, this paper will discuss the causes and

consequences of increased spending as well as issues surrounding the innovation of new products. The effectiveness of the strategies pursued both by the United States and others will be evaluated and compared to achieve the primary purpose of this work: determining which, if any methods of pharmaceutical spending controls have a place in the United States.

## *Cost Drivers*

The previously discussed data provides evidence that pharmaceutical spending has been increasing over time. There are a number of factors that are responsible for this: the development of new drugs is becoming more expensive and more risky, competition is often somewhat limited, and generic drugs are not as successful as they could be in lowering prices. Each of these cost drivers will be discussed in turn.

### *Cost of Development*

The regulations concerning the development of new pharmaceuticals vary from nation to nation, but the industry usually follows a fairly consistent process in a broad sense. The initial step is pre-clinical research, including the synthesis of the molecule, often followed by testing on animals for both short-term and long-term effects. Following positive results from this stage, clinical testing can begin, usually going through several stages of human trials. This includes an initial phase with fewer than 100 volunteers designed to determine the safe dosage of a drug, a second phase lasting up to two years involving several hundred people, a third stage

including up to 3000 subjects over four years, and a fourth stage that observes several thousand patients across the country. These final three stages are used to determine the effectiveness of the drug as well as how safe it is, including factors such as side effects and adverse reaction. The final step is a review and approval by the governing body of the applicable nation where the developer is located and proposes to market the drug. It is important to note that at any one of the phases mentioned above, the potential new drug may fail to achieve the desired results, and the developer will incur a significant sunk cost, a cost that more successful products must cover.

Studies over the last several years have found varying success rates for the development of new drugs, with a success being defined as a pharmaceutical product that enters the first stages of clinical testing eventually gaining approval for widespread use. Some found success rates as high as 24 percent (Adams and Brantner 2006), while others determined the rate to be as low as 8 percent (Gilbert et al. 2003), but the general trend seems to be that data taken from more recent times reflects a lower success rate (DiMasi, Grabowski, Hansen 2016). Large molecule drugs also have a better track record at making it through clinical trials than their small molecule counterparts. Studies using data from different time frames also have difficulty agreeing on the average cost of a drug that enters clinical trials. A drug that is removed from development in the early phases of testing will incur less costs than a drug that makes it all the way to market; the probability that a developing product gets far enough into the process to require certain expenses must be taken into account. In the end, studies have found the average cost of a drug

that starts the first stages of clinical testing in the United States to vary from $802 million (DiMasi et al. 2003) to $2.5 billion (DiMasi, Grabowski, Hansen 2016). Despite this apparent lack of consensus, looking at the year that data is collected reveals a similar trend to the change in clinical success rate: over time, the cost of developing a new drug has steeply increased.

*Figure 1.3: Costs of Drug Development Over Time (DiMasi, Grabowski, Hansen 2016)*

| Year of Development | Cost of Development Estimate (Billions) |
|---|---|
| 1983-1994 | $.802 |
| 1985-2001 | $1.2 |
| 1989-2002 | $.868 |
| 1990-2003 | $1.2 |
| 1997-1999 | $1.5 |
| 2000-2002 | $1.7 |
| 2007 | $1.8 |
| 2009 | $2.2 |
| 2012 | $2.5 |

These trends may provide one possible explanation for the increasing share of healthcare expenses claimed by pharmaceuticals, and therefore a potential target for policy that reduces spending.

In order to provide continued incentives for the pharmaceutical industry to develop new and more effective products, these efforts must remain profitable

despite the steep increase in the cost of development. In practice, this has the potential to result in one of two effects: an increase in price which leads to more healthcare spending due to the important place these drugs hold within the system, or a decrease in innovation, an effect that will be further examined later.

*Limited Competition*

It seems that competition among pharmaceuticals can have both positive and negative effects, as limiting competition can provide a powerful incentive for innovation and advances in medical care, but this also gives certain firms in the pharmaceutical industry a very large market share and significant power to negotiate favorable prices with payers. In addition, health insurance in many nations covers the cost of pharmaceuticals, sometimes without a copay, or with a copay charged per item that is constant regardless of the price of the drug in question. This leads to very inelastic demand for pharmaceuticals, as the consumer does not bear the price of the drug charged by the developer. As a result, cheaper products are less able to compete with more recognizable and expensive products, because the price simply does not matter to the consumer. The lack of competition for a specific formula granted by a patent and consumer insensitivity to price gives the pharmaceutical industry a great deal of power to set high prices, leading to rising healthcare expenses.

Efforts to reduce the rapidly rising pharmaceutical expenses made by healthcare systems across the world can therefore be directed towards finding ways

to control the prices of healthcare in the face of a pharmaceutical industry that holds much negotiating power over health insurers. These attempts vary from nation to nation, and can range from placing a simple cap on the price of a drug, laws that requires manufacturers to provide their product at a discount to certain insurers, attempts to develop value-based price ranges, importing cheaper drugs from foreign manufacturers, and setting benchmark prices for drugs that insurers can cover while making up the difference with copayments. This last scheme is known as reference pricing, and it has gained popularity over the last several decades in European nations. The methods discussed here will be a major focus of the following chapters of this paper.

*Brand Loyalty and Delayed Generics*

Despite attempts to lower the prices charged by brand-name pharmaceutical manufacturers, this often does not produce satisfactory results towards lowering drug expenditures. However, generic drugs entering the market after patents expire provide a much cheaper alternative and potentially a great deal of competition that could drive down the price of a name brand drug. Rather than differentiating themselves through their product, generics attempt to appeal to the consumer by offering a cheaper price. The generics manufacturer can offer a cheaper price due to low development costs compared to the innovator, as there is less research and testing required.

The market for pharmaceuticals can be fairly contestable if two conditions are met: there are no patents providing barriers to entry and the sunk costs that

come with developing a competing product is low. Once a patent has expired, the first condition is met. The second condition is usually true due to the reduced amount of research that has to be conducted when developing a generic drug as compared to an innovative name brand drug. Therefore, once patents expire, the market is contestable and generics will enter. This leads to prices that can be anywhere from 20 percent lower to 80 percent lower (Simeon and de Coster 2006). There is also evidence that these lower priced alternatives to name brand drugs do succeed in bringing competition to the marketplace, as the market share owned by the holder of a recently expired patent falls by 50 percent within two years of the expiration date (Berndt and Aitken 2010). However, this also means that a large percentage of consumers and physicians continue to remain loyal to the more expensive option even though generics, offering the same formula at lower prices, would theoretically be far more appealing. This implies that over the period of exclusivity, physicians have developed some level of brand loyalty towards the name brand drug. It could also signify that the consumer lacks the information to determine the relative quality of the drug, or the knowledge that the generic and the name brand pharmaceutical are chemically equivalent.

In addition, there are often delays between the expiration of a patent and the entry of a genetic competitor to the market, resulting in an extended period when the developer of the name brand drug has complete market control. This phenomenon, found across the globe, does contribute to higher pharmaceutical expenditures. This is despite legislation present in both the United States and the European Union that allows generic manufacturers to begin research and

development prior to the expiration of a patent. Because law allows generic drugs to, in theory, be approved and ready for launch the day a patent expires, there must be other reasons behind this expense-inducing delay. This average delay was found to be an average of six months during which consumers were forced to pay higher prices, when there is little reason a cheaper competitor should not be on the market (Hudson 2000). The length of this delay varies with the size of the market and the price of the patented drug. If a patented drug sells at a high price and gains a large sales volume, this gives the developers of generic drugs an incentive to have a competitor ready to take advantage of this profitable market at the earliest opportunity (Hudson 2000, Costa-Font, McGuire, Varol 2014).

For example, in 1999, the name brand drug Claritin had sales reported in excess of $2.6 billion. In 2002, the drug went off patent and by 2004, generic loratadine had a majority of the market share over name brand Claritin. On the other side of the spectrum, Daraprim used in the treatment of HIV has not been protected by a patent since the 1970s, but has no generic competition, due in large part to sales that failed to exceed $1 million in 2010, and only rose to $6.3 million the next year after a price increase from $1 per dose to $13.5.

### *Innovation*

The pharmaceutical industry creates a new product with the expectation that it not only recover the large costs of development previously discussed, but make a profit as well. Members of the industry will often argue that high prices drive

innovation by providing incentives for development. Therefore, this introduction will examine the problems surrounding innovation as well as spending.

The cost of developing new drugs always involves the risk of failure, but this risk is magnified when the drug is a new formula that represents a new mechanism of treatment. These drugs, known as first-in-class drugs, are significantly more expensive to develop and there is much less certainty of creating a marketable product. Trying to discover and take advantage of a new therapeutic mechanism is much more complex and risky than using one that is already known. However, these drugs also can lead to breakthroughs in improved patient care and treatment (Angell 2004), because they explore methods of treatment that were previously unutilized by medicine, and therefore are a highly desirable form of innovation. There is more potential for a leap forward in care in an area that is unknown than one that has been thoroughly explored. However, due to cost barriers, it is logical that pharmaceutical developers may choose to pursue a less risky option, such as creating a competing product that acts along the same mechanism as the first-in-class drug. While patent law in most nations protects the formulas of first-in-class drugs for a certain period of time in an effort to incentivize this innovation, creating a new formula, or a molecular modification, that utilizes the same mechanism of treatment is still significantly cheaper and less risky than creating a new first-in-class drug. These follow-on drugs, derisively known as “me-too” drugs, are often seen as a less desirable allocation of resources by the pharmaceutical industry because they do not move medicine forward the way the drugs they seek to imitate. Some models have shown that a drug company may prefer to devote their limited

resources to a “me-too” drug even though a first-in-class drug is socially optimal, but the industry will never have the incentive to develop a breakthrough drug when follow-on drugs are socially preferred (González et al. 2016). This means that it is far more common for researchers to prefer to compete with first-in-class drugs than to make their own.

Although this trend may seem to be clearly detrimental to progress in health care, there are some who argue that this “incremental innovation” does in fact provide new and valuable options to both patients and physicians. It has been argued that, over time, steady increases in the quality and versatility of a drug can lead to therapeutic benefits greater than those brought about by a breakthrough first-in-class drug (DiMasi and Paquette 2004). For example, these drugs can have slight differences that make them better suited for a particular group of patients, they can have fewer side effects, or they can have fewer safety concerns. These “me-too” drugs actually can allow for a higher degree of specificity when the physician selects a method of treatment for his or her patients, a benefit that would not be obtained if only first-in-class pharmaceuticals were pursued. In addition, similar drugs introduce competition into the marketplace for these drugs, and therefore contribute to lower prices, with follow-on products introduced to the marketplace at prices below that of the breakthrough drug 80 percent of the time, and below the average price of the class 65 percent of the time (Towse and Leighton 1999). It is therefore a matter of some debate in the current literature exactly how detrimental, if at all, this trend of incremental innovation replacing breakthrough drugs is to patients.

It is worth nothing that, in addition to the lower risk and cost associated with the development within an established class of pharmaceutical, other factors may be at play as well. It has been argued that "me-too" drugs in modern times are not attempts to copy a breakthrough made by a competitor but rather the result of simultaneous research that one party finishes before another (DiMasi and Paquette 2004). Evidence offered for this trend includes the fact that a significant majority of subsequent entries into a class were in development at the time of approval for market, and that the average length where a drug enjoys an exclusive hold on a class has dramatically dropped since the 1970s, when the time period of exclusivity was 10.2 years, to the 1990s when this time period was only 1.2 years.

*Summary*

Pharmaceuticals are accounting for a larger and larger share of healthcare expenses, and therefore produce and ideal target when attempting to slow the growth of the cost of providing greater access to care. Currently, there are several factors that could potentially be addressed in an effort to lower healthcare expenditures via focusing on pharmaceuticals. Research costs are rising as time goes on, and the pharmaceutical products they create receive market approval less often. These risks and expenses also discourage efforts to create breakthrough drugs, with the industry instead creating follow-on drugs that aim to indirectly compete with first-in-class drugs by utilizing a similar therapeutic mechanism. Competition should also theoretically come from generic drugs, but these are often delayed in reaching the marketplace. Regardless of the competition a product faces from generic competitors or "me-too" drugs within the same class, it retains a great deal of power

over consumers and insurers when it comes to setting prices. It may be possible that price controls are the answer to cutting the growth pharmaceutical expenditures down to a level more on par with the rest of healthcare.

In Chapter Two, this thesis will examine current attempts within the United States to control pharmaceutical spending, and the issues that these solutions leave unresolved. In Chapter Three, the focus will be on the methods used to control prices in Europe and Canada, such as the reference pricing scheme that is becoming more commonplace in these nations. Chapter Four will conclude the thesis with a discussion of whether the methods examined in Chapter Three will be effective in addressing unresolved problems with the American approach to dealing with high pharmaceutical pricing.

# CHAPTER TWO

## American Solutions

With the passage of the Affordable Care Act, healthcare in the United States is undergoing extensive transformation, aimed at expanding access to healthcare in all its forms, including pharmaceuticals, to a broader socioeconomic spectrum. According to data from the Center for Disease Control, 48.7 percent of American's have taken a prescription drug in the last month, while 67.2 percent of visits to a physician's office involve the administration of therapeutic drugs. With this increased access to and demand for care comes further spending and a potential need to reduce it.

The strength of the American pharmaceutical industry is the volume of new products that it can put on the market every year, more than any other nation in the world. This innovation comes at a price however, as the prices that American consumers pay for drugs are arguably the world's highest. Pharmaceutical policy that can lower prices and spending without slowing down the development of new and innovative drugs would be ideal. The unfortunate reality is that it is the profits of the pharmaceutical industry that incentivize and allow its firms to engage in this innovation, and high profits come with high prices.

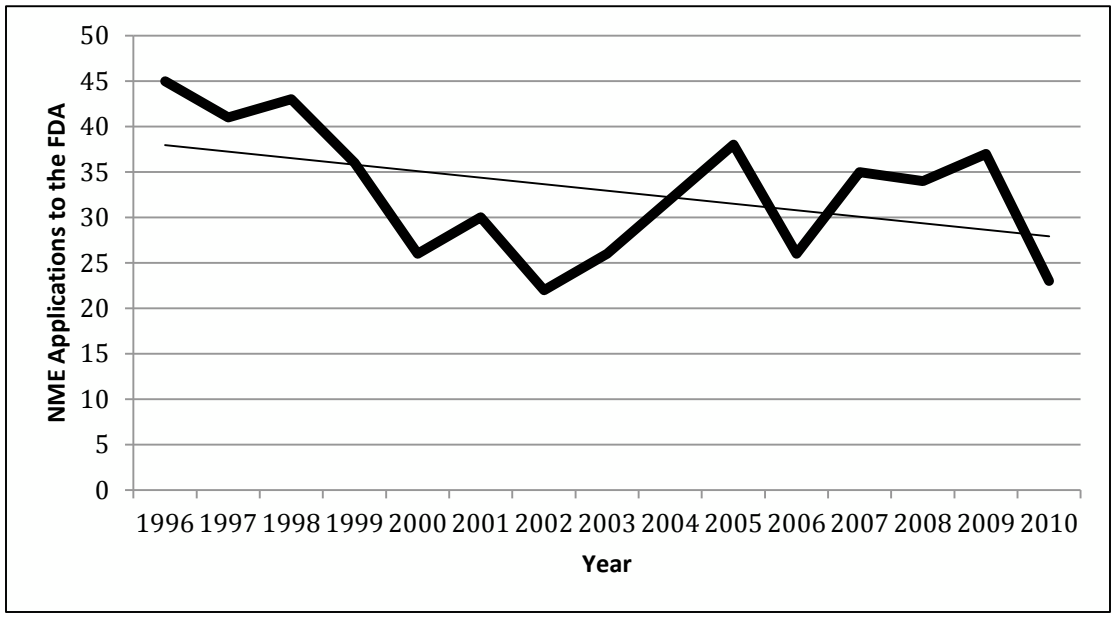
This chapter will examine policy used and proposed for the United States, and its effectiveness in stimulating innovation and lowering spending. The central goal of this chapter is to locate policy areas where the United States might be lacking and can do better. Subsequent chapters will attempt to address these gaps by taking

lessons from successful policies in other nations. Policies regarding pharmaceuticals can be very generally divided into two groups. First, there are policies that focus on encouraging innovation. These policies can, but do not necessarily, lead to higher drug prices. The second category takes the opposite approach and has the primary goal of lowering prices, sometimes at the expense of innovation.

### *Innovation Focused Policy*

In the United States, market and profit based incentives appear to be the primary drivers of pharmaceutical innovation. As the cost of developing new products, the risk involved in attempting development, and competition from generic and follow-on drugs have all trended upward over the years, this incentive has decreased. In 1996, applications for the approval of 45 New Molecular Entities (NMEs) were filed with the FDA. By 2010, this number had decreased to only 23, representing a significant decline in the innovation of these novel drugs.

*Figure 2.1: NME Applications Over Time*

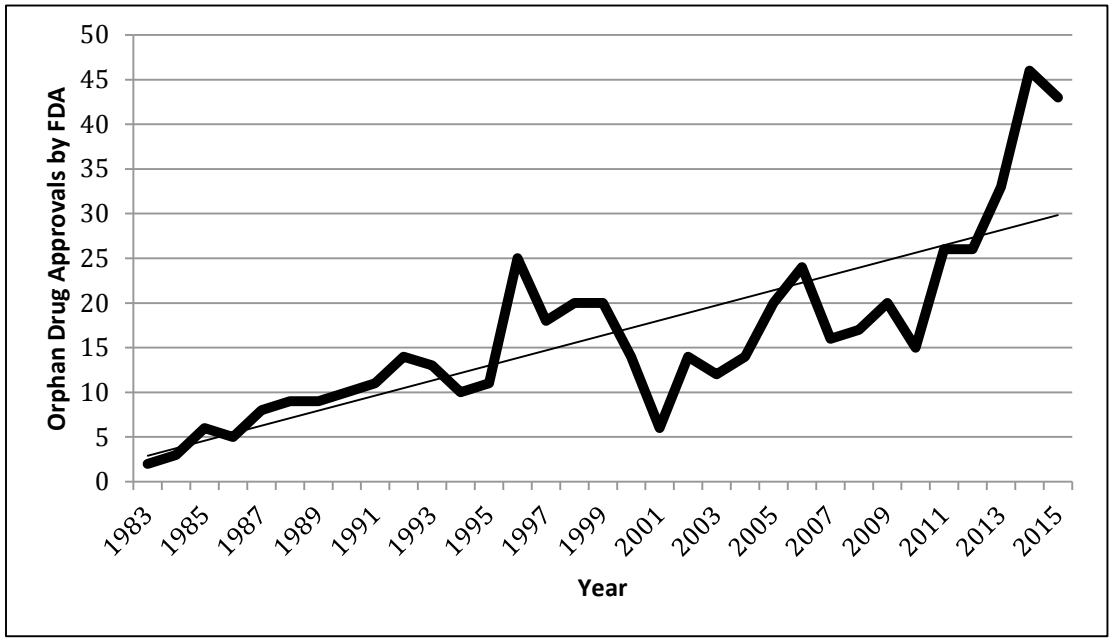


*Innovation for Small Markets*

The lack of market based incentives for drug development is especially problematic for rare diseases that do not promise a large market and the sales that go with it. The monopoly provided by a patent is not a sufficient incentive when the monopolized market is extremely small. The United States has attempted to address the shortcoming of the patent system through legislation. The Orphan Drug Act (ODA), passed in 1983, grants market exclusivity for a period of seven years, which differs from a patent in that the exclusivity period does not begin until the drug is approved, and any competitors developing a differing treatment of the orphan disease must show that their new product has therapeutic benefits greater than those of the exclusive drug. In addition, a variety of tax credits are given to the developer, as well as grants to help fund the research. Therefore, the approach taken by the ODA is twofold: it works to provide the traditional incentive of greater profits by granting control of the market, and it helps offset the cost of research and development by direct and indirect payments to the pharmaceutical firm.

The effect of this legislation on the development of drugs to treat rare diseases is very significant. In 1983, when the law was first passed, only one product was approved under the legislation. By contrast, in 2014, 49 orphan drugs were approved for the market by the FDA, and in the decade leading up to 2014, an average of 24.5 pharmaceuticals were approved each year, a massive increase from the first year of the ODA. This legislation has highly successfully incentivized the innovation of treatments for rare diseases in a way that letting the market run its course simply cannot accomplish.

*Figure 2.2: Orphan Drug Designations Approved for Market*




The ODA is but one example of government spending, funded via taxation, as a method of lowering the costs of pharmaceuticals. Because government subsidies help to offset rising development costs, this leads to lower prices for the consumer. However, because taxation is used to bring about these lower prices, the burden for drug costs is shifted from the sick consumer who purchases the product to a larger group of healthy individuals. The Orphan Drug Act successfully stimulates innovation of products that would remain underexplored without grants, and results in lower prices by expanding the supply side of the market, allowing production at lower costs, and dispersing of the price over a wider range of individuals.

*Research Subsidies*

The success of the ODA naturally raises the question of why government grants are not provided to subsidize more pharmaceutical research. There are a few drawbacks that discourage this widespread implementation of government funded pharmaceutical research. In terms of economic obstacles, the government agencies responsible for funding distribution would likely not have the same knowledge and expertise as the researchers in the pharmaceutical industry, in other words, the problem of asymmetric information. Due to the fact that the researchers have more information about what they will produce, it is possible that funding would be misallocated to innovation that is not necessarily best for society, either due to market size, personal interests of the researchers, or other reasons. There would also be issues regarding the fairly unique political culture of the United States that could prevent a successful mass subsidy program from achieving its goals. In 2014, members of the Pharmaceutical Research and Manufacturers of America (PhRMA) spent and estimated $51.2 billion on research and development. A subsidy pattern that follows the ODA precedent of providing tax credits worth half the costs of development would represent a significant burden on taxpayers that would never use most of the drugs they are indirectly paying for, an idea many in the United States would oppose. In addition, political lobbyists often have a great deal of influence in America, which could further lead to a less than optimal allocation of limited funding.

*Patent Purchases*

It has also been suggested that government funding for research should not be focused on the input, which is the development, but on the output. The commonly cited mechanism for this program is the government buyout of drug patents. This would allow the innovator to keep the full profit of the monopoly they are giving up, provided that they are compensated for the patent at market value, while at the same time eliminating the price distortions that come with such a monopoly. This solution therefore aims to solve the problem of rising pharmaceutical prices imposed on the consumer without having a detrimental effect on innovation. The major problem with this proposal centers on the ability to properly determine the fair value of a patent.

One potential solution involves applying an auction mechanism to pharmaceutical patents, should a member of the industry decide to explore selling one (Kremer 1998). Auctions are a commonly cited way to reveal the hidden value of the object being bid for, as the competitors interested in purchasing the patent would have an incentive to bid their estimated value of the patent. It is very likely that other members of the drug industry would have more information and experience than any government actor necessary to properly determine the value of a patent for a given product. The government could then buy the patent at the value determined via the bids given at auction, which would theoretically be fair compensation for the original developer. Kremer suggests that the government pay at a markup, held constant for the entire process for all patents, to account for the distortions between social and private incentives. Once the government purchases

the patent, it would be put in the public domain, allowing competition to drive down prices and eliminate the deadweight loss that comes with a monopoly. However, in order to provide the entities biding on a patent an incentive to properly value their bids, there must be a chance that they could actually acquire the patent. In order to solve this problem, Kremer proposes implementing a randomization process, where for every patent sold, there is a set percentage that the patent is sold to the highest bidder rather than the government.

This method does have drawbacks, namely that it hinges on the willingness of a patent holder to sell rather than take their chances with the product on the market. This means that a number of products would remain under patent protection and therefore impose monopolies on the market, both due to innovators that elect not to sell and the percentage of patents that are sold at auction to the highest bidder and not the government. The problem of imperfect information also remains, despite the fact that the members of the pharmaceutical industry bidding on the rights to a patented product are better equipped than the government to make an estimate of the true market value. There is still a great deal of room for error. This method therefore leaves room for improvement in regard to deciding the value of a drug and therefore fair compensation. In addition, there is a distributional effect similar to that of government subsidies for research. The costs of healthcare are distributed from the sick to the healthy, similar to the distribution that comes with insurance. Regardless, there is likely a substantial set of the American population that will be opposed to this increased spending by the government, even if the effect of the distribution is beneficial in many ways.

*Alternatives to Patents*

Others have suggested eliminating the patent system completely, turning to alternative methods of encouraging innovation from drug developers. Auctions leading to government purchase, as described above, would aim to accomplish this, but some drugs would remain under patent protection, and monopolies would occasionally remain in place. This leads economists to seek out methods of encouraging innovation without putting the deadweight losses associated with a monopoly in place. One such idea is that of a bounty system, where the pharmaceutical industry is rewarded for their innovations with a payment. This can be awarded on a per-sale payment intended to make up for the fact that the drug would be placed in the public domain, with the per-sale bounty boosting profits despite competition lowering prices. There have been claims that a bounty of 28 percent would be enough to shift all deadweight loss from monopoly to the producer (Grinols and Henderson 2007). The bounty amount would be fully adjustable over time, allowing the government to keep payments at the precise spot it needs to be to keep innovation profitable.

*Valuing Innovation*

When focusing on properly valuing innovation in the pharmaceutical industry, it is important to examine the impact that new drugs have on health and the related spending. A new drug may be more expensive, but if it provides better treatment it may make other medical expenses superfluous and end up reducing

total healthcare spending. Lichtenberg (2001), taking into account the effect on mortality, productivity losses (morbidity), length of hospital stays, and other spending associated with treatment for the condition (hypertension in this case) studied, found that even with and increase in prescription cost of $18, other spending was reduced by $71.09, resulting in clear net savings, even as drug prices rose. The savings resulting from new treatments indicate that an ideal pharmaceutical industry should place a premium on developing new drugs, even at the cost of rising prices, with the expectation that the new drug will pay for itself by reducing other healthcare spending.

However, there have been questions raised about the validity of the model used to reach these conclusions, due to the large number of potentially confounding variables that are difficult to account for, including differences in severity of patient condition, due to factors outside the data set utilized. Other variables include physician preferences for treatment and differences in what treatment methods and drugs are most commonly used in varying regions. In addition, attempts to recreate clinical results with the regression model used in the Lichtenberg study for hypertension generated results that are quite different from what is observed in a clinical setting (Law and Grépin 2010). The empirical results seen here indicate that, in some cases, newer drugs may not pay for themselves and control of pharmaceutical prices remains a significant concern as well as the stimulation of new innovations from the industry.

*Regulation*

The key agent that regulates pharmaceuticals in the market in the United States is the Food and Drug Administration, and the FDA has major impact on innovation and pricing in the United States. This organization reviews every new drug that is developed for use in the United States before approving it for the marketplace. An entity with this level of control over the pharmaceutical industry is ideally positioned to have influence on drugs in health care. One way the FDA uses this influence is to encourage the development of drugs that will have a greater social benefit and a large impact on health care. To this end, the FDA has created a process known as priority review, in which certain drugs undergo an expedited review process that takes around six months, as opposed to the standard ten. A drug that gets to market sooner will be active for more of the time that it is under patent protection, which commonly begins during the review process, a time period when this patent generates no profits. Therefore, priority review aims to deliver larger profits to drugs that will prove most helpful to patients. The FDA can choose to designate any product in development for priority review, and developers can also apply for priority review consideration. The standard for granting priority review is a significant improvement in treatment, diagnosis, or prevention of a condition. According to FDA standards, eliminating negative reactions with other drugs, as well as improved patient safety and compliance, are also factors in obtaining this status. This program should incentivize the development of new improved drugs rather than follower products that do not significantly improve healthcare. The problem here lies with the ability of the FDA to determine which drugs will have the

greatest benefit to the population, but so far it appears that they have been fairly accurate in their discernments. Drugs that are granted priority review status tend to provide more quality adjusted life years than drugs that undergo standard review (Thorat et al 2013), indicating that the FDA is successfully encouraging the development of drugs that provide real improvements to patient care.

## *Price Control Policies*

Up until now, this chapter has focused on how to control drugs costs and innovation by influencing the development process, or innovation-focused controls. Attention will now be turned to market focused controls and the effect they have not only more directly on the prices of drugs, but also indirectly the development of new products. There are two major categories that market-based cost control strategies fall into: price controls and competition. First, price control methods in the United States will be examined.

### *Medicare Part D*

Under the current American healthcare system, there is very little regulation of pharmaceutical prices. Manufacturers set whatever prices they want, and private insurance has little negotiating power, leading to higher prices. Patients covered by Medicare Part D have seen a modest increase in premiums, which have previously remained fairly flat. This is in part due to the rising cost of drugs covered by the plans, as Medicare does not negotiate prices with pharmaceutical companies, allowing them to charge any price and counting on competition to control costs.

This fact presents an easy target for those looking to lower pharmaceutical prices. Proposals include implementing mandatory discounts for Medicare, as is currently in place for Medicaid, as well as simply allowing the government to set the price. It is easy to imagine that this could have a detrimental effect on new development by the pharmaceutical industry, as they could face potentially significant losses. Others have suggested allowing for true negotiations to attempt to reach a price agreement that satisfies both the government and the pharmaceutical industry. The effect that this process would have is far from certain, and depends on the regulatory powers held by the government. A 2007 study by the Congressional Budget Office estimated that, if the government were not given additional regulatory powers over the pharmaceutical industry, savings from being allowed to negotiate would be nonexistent. Even with enhanced enforcement powers, savings estimates are mixed. Some estimate savings of $16 billion yearly, contingent upon providing drugs under Medicare Part D at the same rates as Medicaid (Shih et al 2016), but there is no certainty whatsoever that is can be accomplished, especially without an impact on the rate of development of new drugs.

*Value Based Pricing*

Others support more widespread price controls on pharmaceuticals that go beyond just Medicare, and regulate drug prices on the wider market. One such proposal is value-based pricing, which, as the name implies, assigns a price to a drug based on its value, or how well it works and how much it benefits a patient. This idea has the appeal of truly giving patients what they pay for, but there is a great

deal of difficulty in determining how to fairly value a product's benefits.

Potential proposals involve refunding patients and providers when drugs do not work as intended, or looking at total healthcare spending on one patient as a measure of how well a drug works. Lichtenberg argues that an effective drug will reduce the need for additional treatment and therefore lower total healthcare spending. However, situations are rarely black and white, imposing severe difficulties on these proposals. Patients are often treated by multiple drugs simultaneously, and it is very difficult to find a model that works for every drug in ever situation. A successful drug may actually increase healthcare spending by increasing the lifespan of a patient. This means that despite the fact that a drug is successful, this system would penalize it for driving up costs.

Another proposed strategy involves developing formulas that generate a price for a drug based on how well it treats a patient, but it is very challenging to find a widely agreed-upon definition of what makes a pharmaceutical product valuable. Life years added is often used as a good starting point but fails to account for how those years of life are actually lived. A drug that extends a patient's life for twenty years but leaves them unable to lead an active life is worth less than one that has an identical effect on lifespan but comes without the lifestyle limitations incurred by using the first product. For this reason, quality-adjusted life years are commonly used as a metric when evaluating the success of any healthcare product, but even that might not tell the whole story in a setting where every patient and case is unique. Some tools, such as DrugAbacus[7], attempt to take a multitude of variables into effect, including life years added, toxicity and side effects, novelty of

mechanism, cost of research and development, rarity of disease, and years of life that the population as a whole loses to the disease. Pricing drugs according to their true value would provide a strong incentive to manufacturers and researchers to invest in the creation of new products that truly benefit the population, but there are still large barriers to arriving at a pricing scheme, and there will always be confounding variables that make complete accuracy in this process nearly impossible. To date, widespread price controls and regulation in the United States are largely underutilized, and little experimentation has been done to determine the positive and negative effects that would come with such policy.

*Stimulating Competition*

Attempts to stimulate competition are significantly more commonplace, often taking the form of encouraging the manufacture of generic drugs to compete with brand name drugs at lower prices. One such example of this practice is the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act, passed in 1984 and designed to make the creation of generic drugs easier, in order to bring swift competition to the marketplace. The law achieves this by reducing the number of clinical trials that must be completed when manufacturing a generic drug. Instead, a developer must simply show that their generic product is bioequivalent to the patented name-brand product. As a result, generic drugs enter the market sooner and gain a larger market share in the United States than in most European countries (Costa-Font et al 2014).

Despite the presence of generic drugs, brand-name products still retain a significant market share. Sometimes this is because they lower their price, but often it has more to do with brand loyalty and product differentiation. Brand-name products are known to raise prices after the introduction of generics (Grabowski and Vernon 1992), profiting from customers who assume that the more expensive drugs works better simply because it is more expensive.

In spite of the Hatch-Waxman Act's passage making generic prescription drugs far easier to develop than a new, patented product, there are still a significant number of tests that must be undergone before the FDA will approve the generic drug. These tests are designed to establish bioequivalence, and they vary in their number and stringency from product to product. The bioequivalence tests for pyrimethamine, the active ingredient in Daraprim used in the treatment of HIV positive individuals, are relatively simple The subject of an infamous price hike due to lack of generic competition, the generic requires only two straightforward and simple tests, both observational, one on a fed population, and the other on a fasting population. Rivastigmine, a cognitive enhancer used to treat dementia, also requires only two tests, but they are far more complex and come with a sixteen page document listing detailed specifications for how the test should be conducted, how the population should be selected, several phases of testing involved, and safety information. Ciclesonide, used in the brand-name product Alvesco in the prevention of asthma attacks, requires seven equally detailed bioequivalence tests for approval[8]. Demonstrating bioequivalence is not always simple, and can act as a barrier to the entry of generic drugs.

*Parallel Trading*

Another proposal to increase competition in American pharmaceutical markets involves importing drugs from foreign countries, such as Canada. This would act to reduce prices via the same economic mechanism as an influx of generic drug. Because drug prices are, in general, lower in the rest of the world than the United States, bringing these more affordable products onto the market would not only give consumers a lower-priced alternative but also encourage the developers of more expensive products to lower their prices to remain competitive. Currently, the import of unapproved drugs from foreign countries, even for personal use, is illegal. Although the prospect of bringing cheaper competition into the United States is tempting, it is difficult to discern the safety risks involved with many unapproved drugs, even those that appear to come from legitimate sources. There are exceptions for cases of a serious condition where an effective treatment does not exist in the United States, but this has little effect on the market as a whole.

The idea of importing pharmaceuticals is heavily opposed by the pharmaceutical industry. Legalizing such trade was originally part of the Affordable Care Act, but was dropped after facing harsh challenges from the industry. They argue that the safety of patients is put at risk when unapproved chemicals are brought into the country, and that there is no way to know the true source of drugs. Of course, pharmaceutical companies in the United States also stand to lose significant profits if cheaper versions of their product flood the American market, which likely explains as much of their opposition as safety concerns.

*Chapter Discussion*

This chapter has discussed a variety of American policies surrounding pharmaceutical pricing and innovation. A large amount of this policy is centered on promoting innovation, occasionally at the expense of raised prices. Promising reform in this area includes changes to the patent system, with systems such as patent purchases and bounty payments by the government seeking to eliminate the deadweight loss of monopoly, manifested in the decreased access to the drugs by those who can't afford the higher prices. These proposals also avoid upsetting the balance between robust innovation and affordable pricing. In doing so, the large payments made by the sick who use drugs are reduced, with the differences being distributed to and paid for by taxpayers as a whole. This effect is a potential point of political contention, due to the individualistic culture more prevalent in the United States than European nations where healthcare is a more public and social than private concern. Overall, policy in the United States has allowed innovation and the pharmaceutical industry to thrive, and there is likely little need to adopt from other nations in this area.

On the market side, the United States has found more success than others in stimulating healthy competition from generic drugs, but more direct control over pricing schemes remains highly unexplored. Legislation such as the Hatch-Waxman Act has given the generics industry in the United States the highest market penetration in the world. On the other hand, there is no American policy in place that controls price. While such controls would lower prices, they would also negatively impact the pharmaceutical industry, and likely decrease innovation that

is currently the real strength of the  pharmaceutical system in the United States. For better or worse, this presents an opportunity for investigation, and a target for the introduction of a successful European system, if any are to be found that would lower prices and spending without severely decreasing the creation of new therapeutic drugs. The potential for success for such a system will be addressed in following chapters.

# CHAPTER THREE

## European Solutions

Nations other than the United States are fundamentally different in their underlying ideas regarding how healthcare delivery should be organized. While the United States encourages individuals and employers to take responsibility for healthcare and purchase private insurance for themselves and their dependents, many countries in Europe take a more centralized approach by providing health care coverage at a national level. If healthcare is not a socialized entitlement in these countries, the government is much involved in controlling and regulating the practices that members of the pharmaceutical industry undertake. In the United States, the focus of pharmaceutical reform generally takes the form of finding ways to stimulate innovation without taking away the profits that drive development of new products. In Europe, price controls lie at the center of government influence over the pharmaceutical industry, even at the risk of lowering profits and deterring new innovation, which is far less important to these nations.

This reflects the relative status of the pharmaceutical industry in these nations: the United States is home to developers that create more new drugs than the rest of the world (Daemmrich 2009), and wants to protect that industry in order to allow the development of more beneficial therapies. Europe is less dependent on domestic development, and is therefore primarily concerned with making sure that their citizens can afford the healthcare they need. Europe also takes different routes

to introducing competition into the market. The United States aims for a strong generics market, while Europe prefers to stimulate competition between all developers. Europe borrows a few ideas from the United States, especially in the area of directing innovation to areas that the market cannot, but the pricing schemes they use are quiet different and worth examining. The purpose of this chapter is to examine and discuss policies related to pharmaceuticals in developed nations other than the United States. Policies used in other countries that have a positive impact will be further evaluated in the final chapter.

### *Innovation*

Some European countries are willing to implement strategies to encourage pharmaceutical innovation similar to those seen in the United States. One example of this is the introduction of a priority review style process by the European Medicines Agency (EMA). The goal of this system, known as PRIME (PRIority MEdicines) is to encourage socially optimal development of new drugs by offering incentives that the private market does not. There is little incentive in terms of profit for the development of drugs for rare diseases, or diseases mainly prevalent in developing nations that do not offer a lucrative healthcare market. The PRIME program offers an accelerated review process for products designed to meet a healthcare need that is generally neglected by the industry. In addition to the accelerated review and approval, the EMA also provides scientific aid to the developers, an endeavor attempting to make the creation of such drugs both faster and easier for the pharmaceutical industry. This begins much earlier in the process

than the FDA priority review process, with the EMA becoming involved as early as preclinical trials to assist with the design of clinical trials. The EMA, not a regulatory body itself, will also help with applications to the individual European regulators in order to expedite approval of the product. Even though this priority review process has not yet been adopted by the regulatory agencies, the third-party EMA has taken this idea and attempted to apply it across Europe.

The program has only just launched in 2016, so there is currently too little data to judge the success of the program. If it has similar results to its American counterpart, it could encourage the development of new products for small markets and rare diseases.

Other proposals along similar lines include the introduction of priority review vouchers, which allow a company that develops a product to treat a neglected disease to send a second product of their choice through a priority review process to increase the profit incentive for making an effort to treat rare diseases. Additionally, European countries generally regulate their pharmaceutical pricing much more than the United States. A priority review style process would move these drugs to the front of the line for pricing decisions, further decreasing their time spent in development before market (Ridley and Sanchez 2010). The success of priority review in the United State has offered other nations an idea of how to improve their own innovation.

*Generic Competition*

Another area where the United States has enjoyed more success than its European counterparts is the increased competition that comes from generic products. Part of this may be due to the fact that United States uses tiered copays, where the cost of purchasing generic drugs is lower for consumers. This cost sharing encourages consumers, especially those who are more sensitive to price, to purchase cheaper drugs, allowing generics to compete with brand-name products. This mechanism is not used in most European nations. The result is that consumers have less of a reason to choose a generic drug over a brand name that they recognize. As a result, generic drugs have a market penetration rate of 88 percent in the United States, 67 percent in Canada, and only 41 percent in 19 European OECD countries. In the case of Spain, even with cost-sharing of around 40% of the price of a prescription, around 10 percent of the population still remains loyal to a brand-name drug, resisting the prescription of a generic alternative from a physician (Costa-Font et al 2014). This suggests that the problem with the European generics market lies not completely with the lack of cost sharing, but with the perceived inferiority of a generic product, despite the fact that these drugs are required to be bioequivalent to their name brand counterparts before regulatory bodies will approve them. Education programs explaining that there is no medical difference between the products, despite the higher price of the original, may help to alleviate this problem. European pricing schemes that price drugs based on the cheapest version available could also increase generic uptake. The implementation of

American policy for generic drugs, which has produced highly successful results as previously discussed, may provide yet another option.

### *Price Controls*

One area where European policy makers have focused far more attention than Americans is pricing schemes. By showing a willingness to take a more direct role in pricing pharmaceuticals, European governments hope to keep prices affordable for their citizens without hampering the development of beneficial new products. This policy, if applied universally, would very likely result in fewer innovative developments

The simplest pricing scheme used in Europe is a price cap, wherein the government does nothing more than place an upper boundary on prices, and all price changes require government approval. This is the system used in France, and it necessitates negotiation between developers and the government to arrive at an acceptable price. This often results in a form of a negotiated value based pricing scheme.

#### *Value Based Pricing*

A previously discussed method of price regulation is value based pricing, and this idea has its advocates in Europe as well. There is no consensus on the best method of determining the value of a given drug. Assessing the value of a new product is already practiced by government agencies in certain nations, such as the

National Center for Health and Clinical Excellence (NICE) in the United Kingdom, for the purpose of determining whether a treatment is worth covering. Other countries attempt to regulate prices by setting a maximum reimbursement level for providers. In Europe, it is far more common to attempt to determine if a drug is actually cost-effective at a given price. These practices have elements of value-based pricing, even though they do not go as far as directly setting the price of a drug. An OECD report (Paris and Belloni 2013) made several conclusions about how the value of a drug is commonly determined in Europe, and it is quite possible that the United States may find parts of these methods worth considering. A common feature of all these efforts to assess value is scientific evaluation by a third party. In a few countries, the assessment agency doubles as the regulatory agency that can authorize the drug for use in the market, but it is more common that they are separate bodies.

While the criteria used by each nation varies, they almost always include clinical outcomes, such as life-years saved hospital readmission rates. Nations also give varying weight to the utility that patients gain from a drug, such as quality of life gain or loss that comes from treatment. Countries also vary in the stringency of data and trials that they require when considering the value that a drug brings to the healthcare system. Some only consider large randomized control trials, while others merely need observational studies. The cost of a drug is also an obvious factor when determining if a drug is cost-effective, especially when working within an overall national budget. The innovativeness of a drug also tends to matter to many nations. In addition, a product tends to be valued more if it is used to treat a

severe condition or a rare disease that does not often see new innovative treatments.

As one might expect, the inconsistency of factors and the weight given to them used to evaluate drugs leads to a similarly inconsistent assessment of a drug's value. This indicates that if the United States were to undertake value based pricing, there would not be a hard and fast right or wrong way to determine these prices.

*Reference Pricing*

A commonly used pricing scheme in European nations is reference pricing, in which drugs are grouped into categories based on their medical use. The process originated in Germany, then spread to many other nations, including Denmark, Sweden, Spain, and Italy. A reference price is set based on the price of a cheaper drug in the category, and insurance will not cover any cost above this price. Instead, patients must pay the difference between the charged price and the reference price, encouraging them to select a cheaper product. When cost sharing is not common, consumers tend to be fairly insensitive to price, which leaves producers with little incentive to compete via low prices. By requiring consumers to share the cost of more expensive drugs, price sensitivity, and therefore competition, increases. Categories are either formed by active ingredient, pairing generic drugs with their name brand counterparts, or by their intended therapeutic effect. Some studies show that clustering drugs by therapeutic effect has the greatest success in creating competition, but only if new patented drugs can make a profit by entering the market (Brekke et al 2007). Under these conditions, clustering by active ingredient

distorts patient choices away from what is optimal for their health. If new drugs are not willing to enter the market, reference pricing using these broad clusters fails to achieve its goals.

A case study involving Denmark (Kaiser et al 2014) documented several positive effects on the pharmaceutical market involving reference pricing reform. Prices as a whole dropped by 20 percent, while generic prices fell by 40 percent. Demand for drugs rose, especially generics, while demand for brand name products fell. Overall, generic drugs saw an increase in revenues, while name brand developers saw their revenues decrease. This is indicative that reference pricing has successfully aided generic products in competing as a cheaper alternative by increasing cost sharing, and as a result overall prices fell. However, a loss in profits for name brand developers, who are the members of the industry responsible for creating new drugs, may not bode well for future innovation.

The above studies present evidence that cost sharing in the form of reference pricing increases price sensitivity and allows drugs that have less name recognition and brand loyalty to compete due to their lower cost. However, there are some concerns that generics put a great deal of pressure on the system, often reallocating gains from the system away from society to retailers. Results from this study show that a competitive generics market is necessary for a successful reference pricing scheme that avoids this fate.

Even when generics do manage to compete with other generics, the issue of how to determine the reference price remains a question. The Ghislandi study argues that a reference price based on the prices charged by branded products is

always higher, regardless of how competitive the generics market is. This can lead to the welfare transfer problem, as well as less cost shifting to the consumer and reduced price sensitivity and savings associated with it. One proposed solution to this issue is to freeze prices for a given time period after setting a reference price, allowing the market to react properly before making necessary changes to the set price. As a reference price must be otherwise dynamic, in order to adjust to new drugs, especially the cheap generics, entering the market this scheme allows a ever changing system that is difficult to keep updated in an optimal way to retain more degree of stability when the market, for one reason or another, is not trusted to do so.

Collusion is also an issue in markets that employ reference pricing. Part of this results from the ability for prices to change in response to a new reference price. This provides another incentive for a temporary price freeze after the introduction of this new reference price. The set price offers a convenient point for generics producers to converge, thereby eliminating the competition vital to the overall success of this scheme. Firms often can not gain from breaking away from this implicit collusion by undercutting their competitors (Ghislandi 2011). This effect is due to the lack of price sensitivity below the reference price for consumers. Frequent updates to the reference price, combined with less dynamic pricing from generic firms, may lead to a more successful and competitive market for generics.

*Substitution Scheme*

Another example of price reform that acts along a similar mechanism to reference pricing is the substitution scheme. In Sweden, 2002 reforms required doctors to offer their patients prescriptions of cheap generic alternatives, rather than a name brand product. There are exceptions if the physician has doubts about the quality of a cheaper treatment. Under no circumstances should a physician compromise the health of a patient in an effort to save money. The patient is free to refuse the generic prescription and instead choose a name brand product, but they have to pay a copayment. This scheme is therefore simply a more aggressive form of reference pricing. The generic price is set as the reference price and, physicians should offer this reference drug before an expensive alternative. By giving the consumer more information about cheaper alternatives by a physician, they will be more likely to see it as a viable option. The reform's main goal is to induce competition by making consumers more cost sensitive through the introduction of cost sharing in instances of name brand drug use. The hope is that competition will lower the prices of all products, decreasing pharmaceutical costs. One effort to determine the effect of decreased prices found that the price of both generic drugs and name brand drugs forced to compete against generics fell by four percent (Granlund and Rudholm 2007).

Other studies found a more significant effect, including a price decrease of 10 percent on average for all pharmaceuticals over the period from the introduction of reform in 2002 until 2007, with brand name products facing a more dramatic decrease in prices than generics. The reform at least partly closed the gap in price

between name brand and generic drug (Granlund 2010). The fall of prices was reported to be fairly gradual, which may account for the disparity between the results of studies over Swedish substitution reform. Similar substitution programs have been used in other OECD nations, which were estimated to have a lesser effect than in Sweden (Buzzelli et al 2006). This may be because fewer name brand developers are headquartered in Sweden than other nations, which means that a reduced desire to protect name brand drugs may make it easier for the generics to compete and drive down prices (Granlund 2010). This must be taken into consideration when evaluating the utility of this program in the United States, home to many name brand developers. The reduced success of name brand drugs in the market also has the potential to reduce incentives for innovation.

*Canada and Price Approval*

Many nations that do not have large domestic industries for producing pharmaceuticals still face the same issue of rising prices, but often take to different approaches due to their increased reliance on imports over domestic production. Though all nations sell drugs developed in other countries, nations with less of a pharmaceutical industry are forced to depend more on foreign products. One example of this is the Canadian pharmaceutical industry, which only accounts for two percent of the world pharmaceutical market. Canada formerly took advantage of this by using a compulsory licensing scheme, in which patent products that were deemed essential to the public could be placed in the public domain by the government, thereby opening development to generics manufacturers, with

compensation given to the former patent holder. This has a similar goal to the proposed auction plan in the United States, namely preventing monopoly pricing, with the exception that selling the patent is not optional, and auctions do not take place, as to not leave a chance of the patent being transferred to a different holder rather than being put in the public domain. International pressure during trade talks held from 1986-1994 (GATT Uruguay Round) led to this practice being abandoned. In addition, the pharmaceutical industry in Canada was stifled and grew little, meaning that this method would not be beneficial to an innovation-heavy country such as the United States. Now, Canadian price regulation takes the form of multi-level price regulation, with both federal and provincial government exerting some influence on the process. Provinces set their own reimbursement schedules and regulations based on the cost effectiveness of the drug, while at the national level, the government works to ensure that the market as a whole remains competitive (Anis and Wen 1998).

Canada attempts to balance innovation and pricing by allowing developers to have a significant period of market exclusivity but regulates the prices that they charge rather than allowing them to set monopoly prices. Brand developers have a 20 year period of market exclusivity, a practice that normally leads to high monopoly prices and associated deadweight losses. To counter this, a review board has been established to determine which pricing practices are excessive and which are acceptable. There is some evidence that these principles may lead to lower prices rather than simply allowing the market to run its course, without harming innovation as much as the old compulsory licensing scheme did.

*The United Kingdom: Indirect Price Controls*

In contrast to the methods discussed so far, the United Kingdom takes a relatively indirect approach to price controls. Rather than limiting a price that a company can charge, the government, via the National Health Service, limits the profit that the company can make off of a drug. This profit ceiling is negotiated with the company prior to release of the drug. After the negotiation of a ceiling, the company is free to charge whatever price they wish, as long as it does not result in profits exceeding the negotiated limit. In this way, the government does exert a considerable amount of control over price without actually setting an exact limit on them or setting the prices directly. As with other price control schemes, this system works best if the value of a drug, both to society and to the developer, can be accurately determined before the product goes on the marketplace.

*Copayments and Cost-Sharing*

The healthcare system in the United States is fairly unique among the international community in that it imposes higher levels of cost sharing upon consumers, and this is true for pharmaceuticals as well. As discussed previously, cost sharing is often used to increase competition and lower costs via the introduction of price sensitivity. Another reason to introduce cost sharing to the market is to combat the potential overuse of drugs, which is more likely to occur when this overuse does not place a financial burden on the consumer. In France, Germany, the United Kingdom, and Sweden, the share of payment that must be made by the consumer has increased since the 1990s in an effort to both create

competition for lower prices and to prevent moral hazard, in which patients have no incentive to carefully manage how much of a product they buy (Gross et al 1994). If government sponsored health insurance pays the full cost of health care, as is the case for many citizens in the United Kingdom, and if these people overuse or misuse the healthcare options presented to them, they incur very little financial burden themselves. Meanwhile, government spending is forced to rise to cover these costs.

The higher copayments that are becoming more common serve to alleviate this issue. The United Kingdom also give its physicians prescription budgets to attempt to reduce the overuse of pharmaceuticals from a second angle. By limiting the number of drugs that a physician can prescribe to patients, it is more important for them to be conscious of the actual need that a given patient may have for the drug. If other, cheaper treatments are available, the physician will consider the alternative option instead. The drawback is that a physician trying to not exceed the recommended budget may give a patient inferior treatment. The system attempts to prevent this by making the budget guidelines rather than hard caps, and closely monitors the practices of those who exceed them, in some cases penalizing the physician when the spending is not defensible.

*Parallel Imports*

Nations also increase competition by using the practice of parallel imports. Under this practice, it is legal to import patented products into a nation, where they can be sold for cheaper prices without the consent of the patent holder. As might be expected, manufacturers are opposed to parallel imports, because they would lose a

great deal of sales when these cheaper products are brought in to compete against them. One estimate of European pharmaceutical losses claims that annual sales of domestic manufacturers have dropped by $3 million annually due to the practice of parallel imports (Ganslandt and Maskus 2004).

In the case of Sweden, 16 percent of pharmaceutical sales came from parallel imports over the period from 1995-1998, even though this practice was concentrated in a few specific products rather than widely dispersed throughout the market. This indicates that the products originally present in the market retain a good amount of market share, but competition does occur, with the potential for prices to fall accordingly. In fact, this does seem to occur. The price of products originally present on the market before parallel imports began fell by nineteen percent, and even the imported products themselves became cheaper, falling by four percent (Ganslandt and Maskus 2004). This reveals that this strategy, despite objections from manufacturers, does create competition and achieves its goal of lower prices. The United States passed bills in 2000 and 2007 allowing the parallel import of pharmaceuticals from Canada, but Presidents Clinton and Bush both vetoed this legislation. Currently, some presidential candidates are in favor of implementing such a policy to lower rising American drugs prices. The arguments against such a policy were discussed in the previous chapter.

*Discussion*

Outside of the United States, reform involving pricing structures and regulations has been much more heavily utilized and explored. While the United

States already has successful programs in place to stimulate innovation, such as the Orphan Drug Act and the priority review process, and a strong generics market, due to reform such as the Hatch-Waxman Act, price regulation is one area that remains less utilized. Regulation has proved in its varying forms, from reference pricing to substitution reform to profit caps, to make drugs more affordable for consumers, but this may come with a decrease in profits that American pharmaceutical companies would be unwilling to pay. European countries simply do not have the same level of domestic innovation. This means that they are less concerned with the effect that reforms have on the pharmaceutical industry and the development of new treatments, because to a great extent they can free-ride off of foreign production and imports. This is not the case in the United States, where reformers must be conscious not only of the effect they are having on affordability, but also on innovation.

The area where the United States struggles the most is in lowering prices. European solutions to this include parallel imports and price controls. Price controls that have shown themselves to be successful in making drugs more affordable include reference pricing, generic substitutions, and profit limits as seen in the United Kingdom. The final chapter will focus on these solutions to rising prices, and attempt to evaluate if they have a place in the United States, or the harm to the pharmaceutical industry, and therefore innovation, is too great.

# CHAPTER FOUR

## Lessons

### *Introduction*

This paper has presented evidence that schemes such as reference pricing and other regulations lead to more competition and more affordable pharmaceuticals in many European countries. However, this does not mean that these solutions would be strictly beneficial in the United States. The American healthcare system in general struggles to find the correct balance between providing both high quality care to its patients and freedom for physicians to treat using their desired methods, and making healthcare affordable and accessible for more of the population. This is true for pharmaceuticals as well: there is a need for balance between giving the pharmaceutical industry incentives to develop new and better treatments by allowing them to make a profit, and keeping prices low enough for people to actually be able to afford these new drugs.

This chapter attempts to determine what effects the regulation of the pharmaceutical industry in Europe has on this balance, to show if the benefits would outweigh the costs if similar regulation were applied in the United States. To achieve this purpose, this chapter will compare pricing in the United States and Europe, as well as the location of the innovation of new molecular entities, examining data from the United States and European countries that use either reference pricing or alternative price controls. By comparing this data, a picture will emerge of the

effects that pharmaceutical regulation has on the balance between affordability and innovation.

### *Price Differences*

Comparing drug prices among different nations is not a straightforward process. Due to the significant regulation by government bodies regarding which products are available on the market, nations often offer different drugs that have different active ingredients, mechanisms, and therapeutic outcomes for the same condition. Therefore, it is difficult to determine how prices really compare once all these variables are taken into account. Some comparison can be made by looking at the price of a drug that is available in a variety of countries using data from the International Federation of Health Plans.

*Figure 4.1: Drug Prices by Country (2013)*

| | United States | Canada | New Zealand | Netherlands | Spain | England | Switzerland |
|---|---|---|---|---|---|---|---|
| Enbrel | $2,255 | $1,646 | $1,563 | $1,509 | $1,386 | $1,117 | $1,017 |
| Gleevec | $6,214 | $1,141 | $989 | $3,321 | $3,348 | $2,697 | $3,633 |
| Humira | $2,246 | $1,950 | $1,491 | $1,498 | $1,498 | $1,102 | $881 |
| Copaxone | $3,903 | - | $898 | $1,190 | $1,191 | $862 | $1,357 |
| Gilenya | $5,473 | $2,541 | - | $2,428 | $2,287 | $2,299 | $2,499 |
| Celebrex | $225 | $51 | - | $112 | $164 | $112 | $138 |
| Cymbalta | $194 | $110 | - | $52 | $71 | $46 | $76 |
| Nexium | $215 | - | - | $23 | $58 | $42 | $60 |

*Figure 4.2: American Price as a Percentage of Prices in Other Nations*

| | American Price | Average in Other Nations | American Price as % of Average |
|---|---|---|---|
| Enbrel | $2,255 | $1,373 | 164.24% |
| Gleevec | $6,412 | $2,521.50 | 254.29% |
| Humira | $2,246 | $1,403.33 | 160.09% |
| Copaxone | $3,903 | $1,099 | 355.14% |
| Gilenya | $5,473 | $2,410.80 | 227.02% |
| Celebrex | $225 | $115.40 | 194.97% |
| Cymbalta | $194 | $71 | 273.24% |
| Nexium | $215 | $45.75 | 469.95% |

On average among the eight drug prices examined in the above tables, the price of a drug in the United States is 262.37% of the average price in the other nations included in this survey. This sample size is quite limited, however, so it is worth looking at studies that have taken a broader view of drug prices. Two studies by the US Accounting Office found the price of American drugs to be 32 percent higher than those in Canada (1992) and 70 percent higher than those in the United Kingdom (1994). The United States House of Representatives found the price of American drugs to be 70 percent higher than the price of Canadian equivalents (1998). The fact that studies conducted only six years apart found vastly different results regarding the American and Canadian price differential suggests the

difficulty in accurately conducting such a study. However, it appears fairly well agreed upon that prices in the United States are generally higher than those in other developed countries. There is some literature that takes the opposite stance, however, citing small sample sizes and failure to weigh drugs properly (Danzon 2000). According to these studies, price differences between the United States and the rest of the world are exaggerated. This results would mean that the United States is experiencing more innovation than the rest of the world without overpricing the resulting products: a very good result.

It is also useful to examine the price differences between countries that do and do not use reference pricing schemes. Of the nations included in the above tables, Spain and the Netherlands use reference pricing schemes, while Canada and England do not. Switzerland has recently moved towards reference pricing, but at the time the 2013 price data was collected, this method of price regulation had not been implemented.

In many cases, the nations that regulated prices using methods other than reference pricing achieved lower price than nations than did use this method. This provides evidence that prices can be effectively controlled by other methods, such as the profit caps imposed by the United Kingdom, price review boards in Canada, and the Swiss method of refusing reimbursement for drugs that are priced excessively.

*Figure 4.3: Reference Pricing vs. Non-Reference Pricing*

| | Reference Pricing (Netherlands/Spain) | Other (Canada/UK/Switzerland) |
|---|---|---|
| Enbrel | $1,447.50 | $1,260 |
| Gleevec | $3,334.50 | $2,490.33 |
| Humira | $1,498 | $1,311 |
| Copaxone | $1,190.50 | $1,109.50 |
| Gilenya | $2,357.50 | $2,446.33 |
| Celebrex | $138 | $100.33 |
| Cymbalta | $61.50 | $77.33 |
| Nexium | $40.50 | $51 |

*Pharmaceutical Industry Revenues*

The profitability of pharmaceutical industries is often believed to be the primary driving force of innovation. If the nations that produce the most new products also allow their industries to make the most profits, this will lend credence to this theory. To measure the profitability of the pharmaceutical industry of a nation, the average profit margin of the three largest firms in each nation is reported below.

*Figure 4.4: Profit Margin by Nation*

| Country | Profit Margin |
|---|---|
| Switzerland | 14.38% |
| United States | 31% |
| United Kingdom | 17.26% |
| France | 12.13% |
| Germany | 8.27% |

Large American pharmaceutical companies have vastly larger profit margins than their international counterparts, which is logical considering the much higher prices charged by the companies in the United States, as demonstrated above.

The pharmaceutical industries in the Netherlands, Spain, and Canada produce largely generic drugs, and even then account for a small percentage of the market. None of the ten companies that make the most revenue in the Netherlands are headquartered there, while only one in Canada, Apotex, fits this category. It is then useful to examine the profit margins in nations that have large market share These numbers will be more useful for correlating innovation and profit than the margins in Spain or the Netherlands.

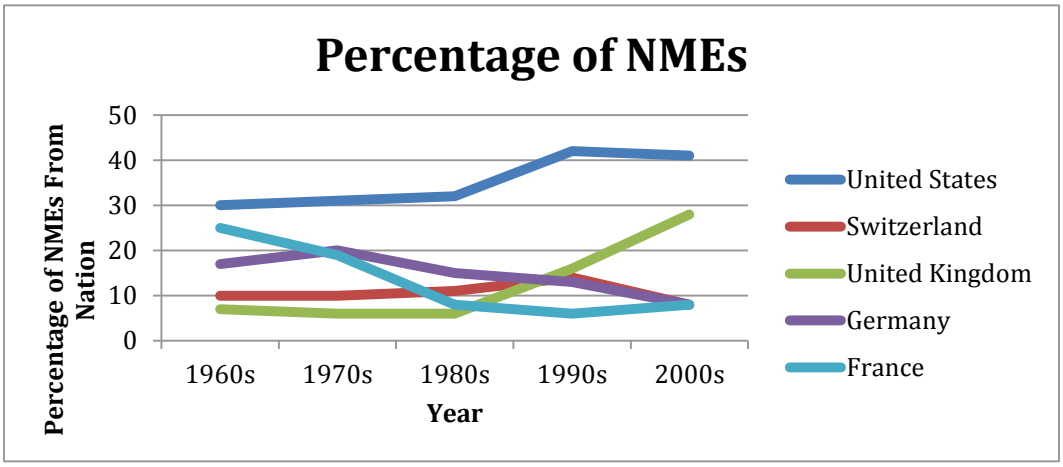
*Figure 4.5: US Revenue Percentage*

| Country | Percentage of Sales Revenue in United States |
|---|---|
| Switzerland | 43.1% |
| United States | 61.5% |
| United Kingdom | 37.3% |
| France | 32.8% |
| Germany | 40.1% |

*Innovation*

In this section, this paper will attempt to evaluate the effectiveness of the pharmaceutical industry in each surveyed country at producing new therapeutic molecules. New molecular entities (NMEs) are the chosen measure of innovation for this study, because they represent more novel innovation than a simple follow-on drug. This paper will examine the trends in innovation over time, and how these trends compare with pharmaceutical reform in European nations. The Netherlands, Canada, and Spain all account for less than 2% of NMEs, and are therefor not included here.

*Figure 4.6: Innovation by Country*




Over the past decades, the United States and the United Kingdom have produced a larger share of the world's NMEs, while other European countries, such as France and Germany, have been less innovative over time (Daemmrich 2007). France and Germany are known for their strict regulation of pharmaceutical prices, while the United States has very few price controls, and the United Kingdom is less stringent than other European nations. The United States, which produces the most NMEs makes almost no efforts to control pharmaceuticals. In second place, and rapidly producing more and more, is the United Kingdom, which tries to control profits rather than directly limiting prices. Switzerland, which does take some steps to control excessive pricing, has remained fairly constant in its production. Germany uses reference pricing, and has seen a steady drop in its innovation since the 1980s, the same decade this scheme was introduced. France directly caps the allowed price of pharmaceuticals and has seen the sharpest decrease in NME development of all the nations included in the survey.

*Innovation and Profit*

A comparison of the innovation percentage and the profit margins determined in previous sections will either lend or deny credence to claims made by supporters of the pharmaceutical industry and opponents of price controls that high profits are necessary for innovation.

There does in fact appear to be a correlation between the profits that a pharmaceutical firm can make and the innovation that they are responsible for (Figure 4.6). For a nation such as the United States that has historically favored proposals that protect innovation over price, this is a point against increased control of prices.

*Figure 4.7: US Sales Percentage vs. Innovation*

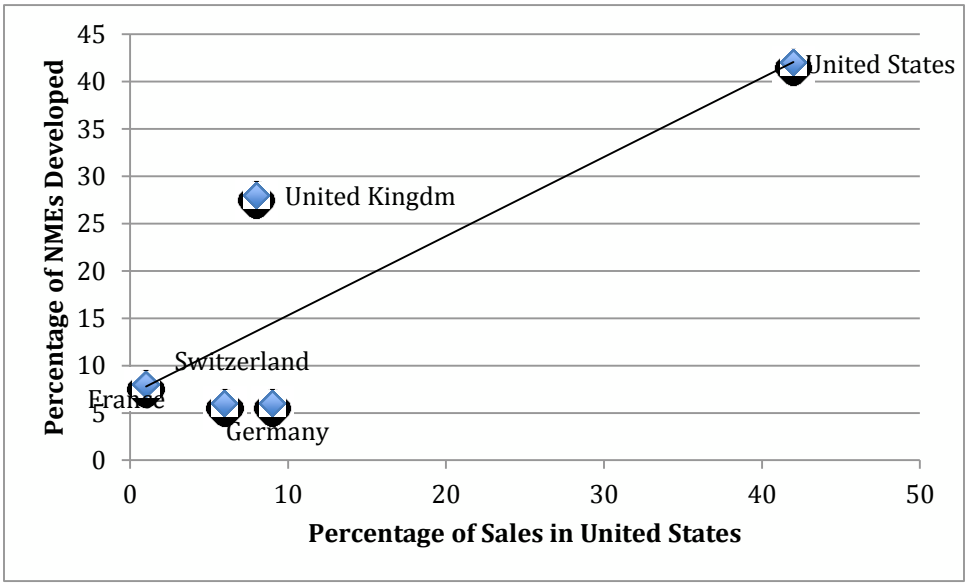
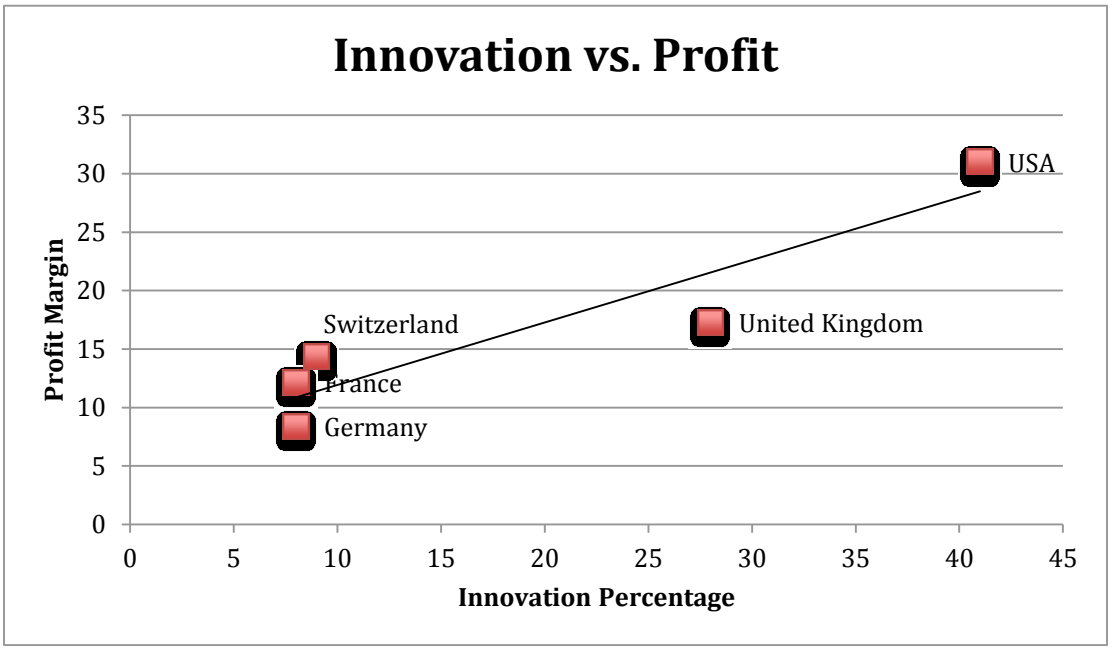


*Figure 4.8: Innovation vs. Profit Margin*

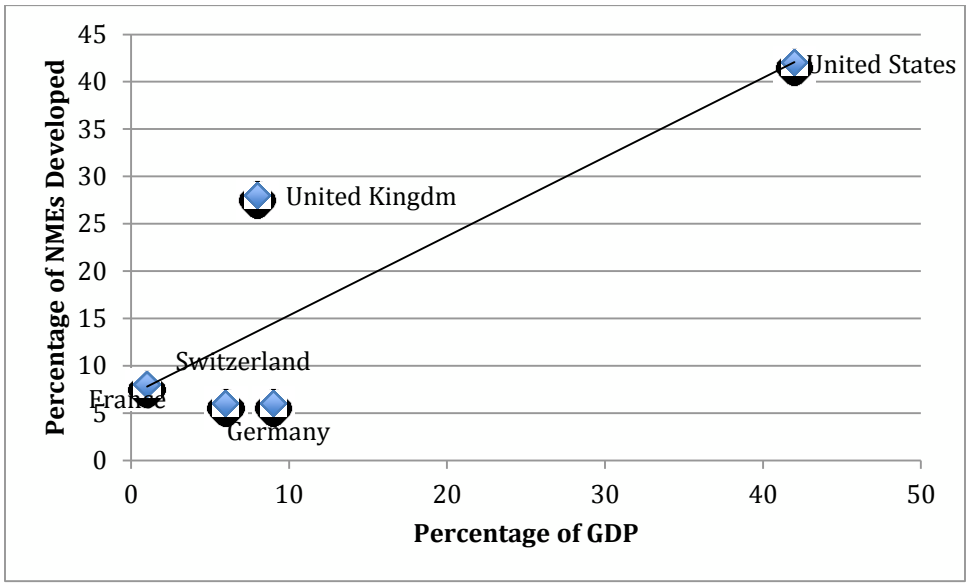



However, looking at the raw data in regard to the number of new drugs that come out of a country does not capture all the factors that go into innovation. A country with more capital and resources that spends more on healthcare is likely to be able to innovate more even if the firms are less profitable. A country that innovates at a lower per capita rate can still out-produce other nations through sheer volume of spending and the size of the industry.

To this end, comparing the GDP and the total drug spending within a country to its innovation is one method of attempting to account for these variables. The United States, for example, accounts for 40% of the GDP of all countries that innovate new NMEs, as well as 42% of all prescription drug spending, and contributes about 42% of NMEs (Figure 4.9). Therefore, innovation in the United States is fairly proportional to the nation's overall wealth and drug spending. The United Kingdom and Switzerland exceed the United States in this metric, while

others such as Canada and Italy lag behind (Keyhani et al 2010). By this measure, the high profits available to firms in the United States does not drive innovation all that far ahead of international competition.

*Figure 4.9: Innovation vs. GDP*




Using the data and methods from the Keyhani study, comparing GDP to innovation, the United States appears fairly average, while the United Kingdom has excellent innovation compared to the overall wealth of the country. The evidence from this chart corroborates the evidence from the raw percentages of NMEs discussed previously: Germany and France, the nations with stricter price regulation, both struggle compared to other innovating nations.

### *Concluding Discussion*

The evidence for the costs and benefits of European price regulation does not clearly point in one direction or the other. Judging from the trends of innovation

over time, the implementation of price regulation, especially stricter programs such has those found in France, does have detrimental effects on the development of new treatments. If the drop in innovation found in France or Germany was replicated in the United States with the introduction of reference pricing or price caps, the effect on the international industry would be even more substantial due to the massive contribution the United States makes to the development of NMEs. At the same time, nations such as the United Kingdom have been able to foster a successful pharmaceutical industry that not only develops more than its share of new products based on GDP, but also provides them to consumers at more affordable prices than those found in the United States.

There are a multitude of reasons for rising pharmaceutical prices, ranging from slow generic entry, to increased cost and decreased success of clinical trials and development, to lack of negotiation power among payers. Reform in the United States has been more successful than most nations at introducing competitive generics into the market quickly, and many laws and proposals focus on making innovation easier and cheaper for the pharmaceutical industry. Europe, meanwhile, focuses on making drugs affordable rather than making drugs. This is truer in some nations than others, as the methods and stringencies of regulation vary, but they all take more steps to control prices than the United States. In some cases, such as France and Germany, this has had detrimental long term effects on the development of new products. In other cases innovation and somewhat regulated prices, often limited indirectly rater than directly, managed to coexists.

In any aspect of healthcare, including pharmaceuticals, there will always be a conflict between affordable care available to everyone and high quality new treatments available only to those who can pay. In the case of therapeutic drugs, this is encapsulated in the trade-off between rapid innovation of new and better treatments bought at high prices and incremental increases in new therapeutic options and affordable prices that do not place as heavy a burden on the sick. Given the role the United States currently holds in the creation of NMEs, a shift to the other side of the trade off is unlikely in the near future, but the success that the United Kingdom and Switzerland have in achieving disproportionately large innovation relative to their GDP while keeping prices low shows that there is room for improvement in the American pharmaceutical system. While this does not need to come in the form of strict price caps or reference pricing that correlate with reduced innovation in some nations, softer regulations, such as the ability to negotiate with the pharmaceutical industry and profit caps that reduce margins slightly, have been shown to lower prices without catastrophic effects on innovation in Europe.

This paper has shown the United States to successfully encourage the innovation of new products for large and small markets, as well as allow generic competition to thrive and lower prices. Where the United States has little experience is in the area of price controls. Looking to Europe, price controls come in the form of strict limits on pricing, reference or substitution pricing, and indirect regulation. While nations using the stricter methods of regulation struggle to keep pace in terms of innovation, nations using the third category, indirect price controls, had few issues. If the United States is to adopt price controls, any system that falls into

the stricter categories has some correlation with a decrease in innovation, and therefore would be a significant risk for the world's leading pharmaceutical producer. A decrease in new beneficial treatments would, to many, not be worth the cheaper prices. On the other hand, there are success stories such as the United Kingdom, which has implemented price controls, albeit indirectly, and still maintained a fairly strong pharmaceutical industry. If the United States is to use a form of price regulation, there is evidence that it must remain indirect and not compromise the ability of the pharmaceutical industry to make profits. The United States holds a unique place in the world due to the proportion of new drugs developed by its pharmaceutical industry, and therefore must take steps to ensure that this development is not halted, for the benefit of patients for years to come. Price controls should not be completely taken off the table, but they should not deny the industry its opportunity to profit.

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