AFFORDABILITY vs. INNOVATION: THE EFFECTS OF REDUCING PATENT LENGTHS OF MEDICATIONS FOR CHRONIC ILLNESSES ON PRODUCERS AND CONSUMERS

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Isaac Zachem

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Isaac Zachem

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Abstract

This thesis examines the delicate balance of satisfying the needs of both producers and consumers of prescription pharmaceutical drugs. An analysis of the factors which influence a drug's lifetime revenue is performed through executing an Ordinary Least-Squares linear regression. In addition, the cumulative lifetime revenues of the drugs were manipulated to determine the effects of reducing the length of a pharmaceutical patent to simulate a shorter period of exclusivity and an accelerated time of possible entry for generics into the market. The results of these experiments find that market size, defined as the prevalence of the disease the medication treats in the US, and years active on the market possess the strongest association with lifetime cumulative revenue, while the type of illness being treated, either chronic or acute, has a positive but weak association. The expected revenues of the drugs with patent lives reduced to 10 and 15 years suggest that the changes would be too extreme for producers at the 10 year patent life but beneficial to both sides at the 15 year patent life.

KEYWORDS: (patent life, incentive to innovate, market competition)

JEL CODES: *O38, O31, L11*

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ON MY HONOR, I HAVE NEITHER GIVEN NOR RECEIVED UNAUTHORIZED AID ON THIS THESIS

Isaac Zachem

Signature

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I. Introduction

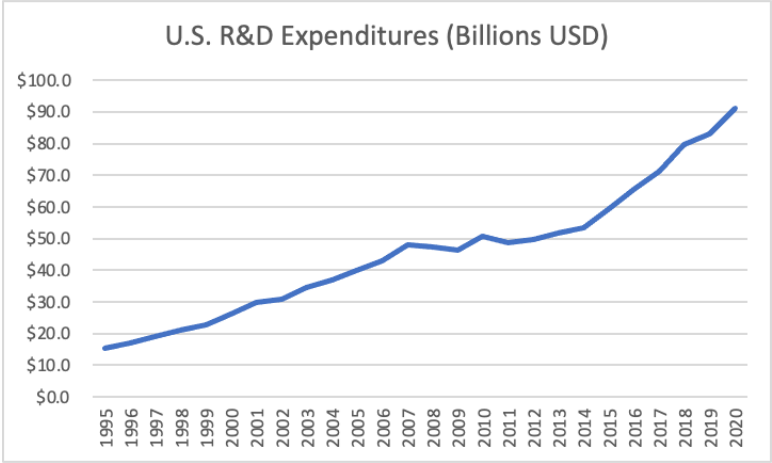
Value-based pricing stems from the principle that prices should reflect both the benefit an added drug provides patients, in terms of either quality of life or longer life, the healthcare system, and even broader society as a whole, as well as reward successful innovation and promote further research and development[1]. The pharmaceutical industry has often received criticism for disrupting this balance and taking advantage of market power to charge prices above what is justifiable. This is especially prevalent due to the lack of alternatives for many drugs. As a result, studies have shown that one in four people in the United States has difficulty covering the costs of their prescription medications[2]. In response to these outcries from the American people, the federal government has begun to take action to take some of this burden off of consumers. H.R.3, The Elijah E. Cummings Lower Drug Costs Now Act, has been passed with the intent of making prescription drugs more affordable, which is often not the case for those who need them most[3].

However, pharmaceutical companies still require incentive to continue pursuing the discovery and production of new medications, which is a massively expensive process. According to the Congressional Budget Office, the expected cost of developing a new drug in 2021, including capital costs and expenditures of drugs that fail to reach the market, has been estimated to range from one billion dollars to greater than two billion[4]. In the U.S., pharmaceutical research and development expenditures have skyrocketed since 1995, as the total

[1] Santiago G. Moreno, David Epstein, "The price of innovation - the role of drug pricing in financing pharmaceutical innovation. A conceptual framework", (NCBI, 2019)
[2] Chaarushena Deb, Gregory Curfman, "Relentless Prescription Drug Price Increases", (JAMA Network, 2020)
[3] Nicole Rapfogel, Emily Gee, Maura Calsyn, "H.R. 3 Could Save Patients Thousands of Dollars on Prescription Drugs", (The Center for American Progress, 2021)
[4] David Austin, Tamara Hayford, "Research and Development in the Pharmaceutical Industry", (Congressional Budget Office, 2021)

expenditure of PhRMA member companies is about six times greater than it was twenty five years ago[5]. These values have been adjusted for inflation and are measured in real dollars.

Figure 1. United States Research and Development Expenditures (1995-2020)



Expenditures on R & D are influenced by three main factors; the anticipated lifetime global revenues of a new drug, the expected costs to develop a new drug, and policies and programs that influence the supply and demand for prescription drugs.

Costs can be a disincentive and often present a messy dilemma; how are prescription drugs made more affordable while providing sufficient incentives for pharmaceutical companies to be innovative in the pursuit of developing new medications? This question is especially difficult to answer due to the nature of capitalist America, as maximal profits are able to be made, but many argue this is not worth the moral injustice of diminishing the pockets of those who need medication to be treated. Policy changes to allow government funding of clinical trials have been proposed to reduce costs, prices, and direct research, but in turn will likely result in greater taxation of the population, an argument to be had in its own right[6].

[5] Matej Mikulic, "Research and development expenditure of total U.S. pharmaceutical industry from 1995 to 2020", (Statista, 2021)
[6] Arjun Dayajev, Joseph Stiglitz, "Two Ideas to Increase Innovation and Reduce Pharmaceutical Costs and Prices", (Health Affairs, 2008)

The suppliers are not the only group under criticism, though, as more capable payers are also accused of taking advantage of their "monopsonistic purchasing power by extracting unilateral discounts from the industry" that may not apply to the greater population[7]. This in turn can distort the value-based pricing system, diminish trust between manufacturers and consumers, and cause patients to lose out.

To best analyze this problem, a closer look must be taken at the financial factors going into investing, researching, and developing these drugs, the policy changes made in recent years to combat the burden these costs can put on consumers, and the morality of excluding millions of Americans from medication they may need to survive.

For change to be made, there must be compromise. Pharmaceutical companies must be willing to lose some revenue, but consumers may need to temper expectations. Though costs of research and development can be quite high, the revenues some drug companies can bring in from their treatment dwarfs any expenditures. For drugs that treat chronic conditions, the revenue seemingly can extend forever. Patents protect the exclusivity of these medications, and if there is a monopoly, someone suffering from a chronic illness will have to pay extreme prices for a seemingly endless future. Recent studies have even shown that up to a third of patients suffering from chronic illnesses may delay filling a prescription out of a lack of ability to afford their treatment[8].

Seeing as drugs for chronic illnesses would logically be the most profitable of a pharmaceutical company's products due to their extensive nature, they are likely the most valuable assets to a firm. Reducing exclusivity periods on these medications would likely

[7] Santiago G. Moreno, David Epstein, "The price of innovation - the role of drug pricing in financing pharmaceutical innovation. A conceptual framework", (NCBI, 2019)
[8] John D. Piette, Ann Marie Rosland, Maria J. Silveira, Rodney Hayward, Colleen A. McHorney, "Medication cost problems among chronically ill adults in the US: did the financial crisis make a bad situation even worse?", (NCBI, 2011)

diminish a company's revenue substantially. However, this would not cripple their returns. Rather, reducing a patent on a drug for a chronic illness should prove to be a fair compromise. Pharmaceutical companies would still maintain exclusivity for a period, the market would grow when generics are introduced, and substitutes should allow consumers to find more fair prices in their combat with a disease.

This thesis will examine what factors influence a firm's incentive to innovate, the revenue they earn for their product, as well as how significant adjusting a medication's patent life would be on it's current cumulative revenue.

II. Literature Review

The process of innovating a new prescription drug is both financially and time consuming. The approval process is long and winding, as there are four steps to getting a new medication approved; discovery and development, preclinical research, clinical research, and FDA review[9]. Even within the drug being tested in clinical trials, there are four phases to pass[10]. These help determine if the drug is safe for humans and how it is distributed throughout the body, the effectiveness of the treatment and correct dosage, if the treatment can benefit a wide variety of people, and how the public responds once on the market, respectively. This process takes, on average, 10.5 years in the U.S., with most prospective medications not even reaching clinical trials[11]. Of the drugs that have reached clinical trials in the last decade, there is just a 7.9 percent likelihood of approval (LOA).

II. 1. Patent Framework

The process of getting a new treatment on the market can be extended by the attempt to patent the medication, allowing the manufacturer exclusive rights to the design, production and distribution of the invention in a designated period of time in exchange for a complete disclosure of said invention. In addition to the time cost of getting a drug approved, pharmaceutical companies may spend up to 2.6 billion dollars (in 2013 dollars)[12]. This immense investment in turn yields highly valuable intellectual property that can bring revenue to the producer for long

[9] U.S. Food and Drug Administration, "The Drug Development Process", (2018)
[10] BrightFocus Foundation, "Phases of Clinical Trials", (2021)
[11] J.P. Carroll, "How long does it take to get a drug approved?", (Biotechnology Innovation Organization, 2021)
[12] Jan Berger, Jeffrey D. Dunn, Margaret M. Johnson, Kurt R. Karst, W. Chad Shear, "How Drug Life-Cycle Management Patent Strategies May Impact Formulary Management", (AJMC, 2017)

periods of time. Because of this, pharmaceutical companies will typically apply for a patent through the Patent and Trademark Office (PTO) prior to submitting a New Drug Application (NDA) to the FDA[13]. By securing a patent on a new medication, companies will be able to exclusively collect revenue for the period of time given, which by statute is 20 years from the time of patent filing. AbbVie's Humira, the highest-revenue prescription drug of all-time, is set to lose exclusivity in 2023, opening a door for other pharmaceutical companies to produce and distribute biosimilars, for example. Due to the immensity of the pharmaceutical market, which as of the end of 2020 was about 1.27 trillion U.S. dollars globally, these patents are massively important for profiting in this industry[14].

II. 2. Legislation

Prescription drug pricing is governed by multiple pieces of legislation, with some even on the way. The Federal Food, Drug, and Cosmetic Act (FDCA) of 1938 allows the FDA complete regulatory control over the pharmaceutical industry[15]. This act was then amended in 1962 with the Kefauver Harris Amendment, the goal being to strengthen the inspection of drugs submitted to the FDA through NDA's and legitimize the efficacy of new treatments[16]. This resulted in a lack of innovation due to the difficulty of getting a new drug approved through an already lengthy process, causing the U.S. congress to take action by easing up the approval process, to an extent. In 1984, the Hatch-Waxman Act was passed, which amended the FDCA and created the modern U.S. generic drug industry[17]. This established the submission of Abbreviated New Drug

[13] Jessica Eisenburg, "Biotech patents: looking backward while moving forward", (Nature Biotechnology, Vol. 24, Issue 3, 2006)
[14] Matej Mikulic, "Revenue of the Worldwide Pharmaceutical Market from 2001-2020", (Statista, 2021)
[15] 21 U.S. Code 355
[16] Leo E. Hollister, "The FDA ten years after the Kefauver-Harris Amendments", (Perspectives in Biology and Medicine, Vol. 17, Number 2, 1974)
[17] Garth Boehm, Lixin Yao, Liang Han, Qiang Zheng, ""Development of the generic drug industry in the U.S. after the Hatch-Waxman Act of 1984", (Acta Pharmaceutica Sinica B, 2013)

Applications (ANDA's), allowing generic drugs that were similar to products already on the market to be approved on the basis of bioequivalence, as well as restoring much of the time spent in the NDA review period. Following this act, the incentive for innovation increased, resulting in more extensive market exclusivity periods for pharmaceutical companies, shorter approval periods, and greater market innovation as a whole[18].

II. 3. Cost-Effectiveness

At the heart of debates about drug prices is the question of how to assess what is fair and acceptable. Unlike most other markets, many of which set their own prices, the prescription drug market presents numerous conditions that make it difficult for consumers to accurately judge the value they may receive from a medication. There are many supporters of beginning to perform cost-effectiveness analyses in which a therapy's costs are weighed against its health benefits, such as improved quality of life and extended life expectancy[19]. Though many protest this way of thought, arguing that life-expectancy gains and overall health should not be attached to numeric values. Some also believe this technique discriminates against older adults or people with disabilities, as they are already being placed at a disadvantage in determining how the treatment in question may be beneficial. However, implementing an established process for the U.S. healthcare system in which analyses are conducted would be a great improvement. Using cost-effectiveness analysis would seem to present a fair solution. The issue stems from the inability to make this a universally equal estimate of the benefits of a drug. For example, should the determined value of the analysis vary by subpopulation or condition? The NEJM, concurrent

[18] H Grabowski, J Vernon, "Longer Patents for increased generic competition in the U.S. The Hatch-Waxman Act after one decade", (doi: 10.2165/00019053-199600102-00017, 1996)
[19] Peter J. Neuman, Sc.D., Joshua T. Cohen, Ph. D., Daniel A. Ollendorf, Ph. D., "Drug-Pricing Debate Redux - Should Cost-Effectiveness Analysis Be Used Now to Price Pharmaceuticals?", (New England Journal of Medicine, 2021)

with the recommendations of the Second Panel on Cost-Effectiveness in Health and Medicine, suggests a compromise may be for analysts to conduct studies using traditional, conventional methods while also incorporating sensitivity analyses which add considerations that may be different between evaluations.

II.4. Revenue

A major piece of innovation incentive for pharmaceutical producers is expected revenue. This guarantee of revenue from innovation is driven in large part by the generous insurance coverage of new drugs approved by the FDA[20]. Insurance coverage is called into question as an incentive to innovate, though, in that companies may opt to invest in well-known areas of treatment rather than push the boundaries and explore the efficacies and values of new therapies. Knowing they are backed by Medicare D in some clinical areas, there is understandable reason for producers to invest in these covered areas with little risk of losing their money. Since 2006, coverage and reimbursement have varied considerably for new and expensive therapies by therapeutic class and payer. For example, while Medicaid Part D and commercial insurers have provided access to treatments for Hepatitis C, only about 10 percent of those eligible for treatment and covered by state Medicaid programs have received treatment[21].

II.5. Models of Pharmaceutical Innovation

Acemoglu and Linn (2004). In 2004, Daron Acemoglu and Joshua Linn constructed a simple model examining the link between innovation rates to current and future market sizes.

[20] Rena M. Conti, Frank S. David, "Rebalancing High Prescription Drug Prices with Innovation Incentives", (Health Affairs, 2019)
[21] National Academies of Science, Engineering, and Medicine, "Making Medicines Affordable; A National Imperative", (National Academies of Science, Engineering, and Medicine, 2018)

Their findings exploit changes in the market size for different drug categories based on United States demographic trends, and reveal highly significant economic effects of markets size on pharmaceutical innovation[22]. This study is not without flaws, as it is stated within the paper that the difficulty with any evaluation of the impact of market size on is the endogeneity of market size; simply, better products will attract a greater market.

To evaluate the effects in question, Acomoglu and Linn estimated market size and innovation through creating age profiles based on demographic as well as income trends in the U.S. and using the FDA's approval of new drugs, respectively. They recognize that while many non-U.S. markets may be relevant in this analysis, the U.S. pharmaceutical market is disproportionately important, as it constitutes just over 40 percent of the revenue generated globally, both at the time of this study as well as of 2018[23]. The results of this analysis show that as the baby-boom generation aged, the markets for drugs primarily consumed by young individuals declined while those for drugs consumed by middle-aged people increased.

Throughout this study, there are some difficulties that arise. While similar results were obtained when controlling for expected advances in biotechnology, Acomoglu and Linn acknowledge the dilemma of determining whether, past, present, or future market size is correct in evaluating the effect on innovation. It would make sense that future market size could be the heaviest influence on innovation, as adjustments in demographics can be anticipated. However, due to the intensity of the duration of drug review and approval (typically a 10-15 year process[24]), an argument could be made that entry may be most influenced by past market size.

[22] Daron Acemoglu, Joshua Linn, "Market Size in Innovation: Theory and Evidence from the Pharmaceutical Industry", (The Quarterly Journal of Economics, 2004)
[23] Matej Mikulic, "U.S. Pharmaceutical Industry - Statistics and Facts", (Statista, 2021)
[24] Christopher Ty Williams, "Food and Drug Administration Drug Approval Process", (Pharmacology Updates, 2016)

Acomoglu and Linn conclude from their findings, though, that new molecular entities and generic drugs respond to anticipated changes in market size, with a lead of ten to twenty years.

Grootendorst and Di Matteo (2007) The approach of this study was to analyze the effects of new patent policies on pharmaceutical innovation in Canada. Their approach was to analyze the "inputs" of pharmaceutical R & D rather than the health "outputs," choosing instead to look into the effects of the 1987 patent extension in Canada on Canadian pharmaceutical research and development expenditures[25]. In this study, Grootendorst and Di Matteo define the impact of patent term extension of pharmaceutical R & D as the difference between what R & D would have been lacking the patent extension and actual R & D expenditures (with patents extended).

II. 5. Advertising

Brand-name producers have two ways of influencing the shape of the market when generic entry is possible: price and advertising. Price is a clear advantage; companies that were the first to produce a biochemical medication may drop prices when generic competitors are considering entering the market, thus possibly deterring these competitors seeing as they would have to offer even lower prices to gain a share of the market. This may not prove to be profitable enough to justify the fixed costs to be incurred upon entry. However, upon patent expiration, companies may not have the liberty to be able to do this. Rather, companies will choose to advertise with the intention of catching the attention of physicians who prescribe their medications[26]. Recent studies have found that advertising can have both an advantageous and

[25] Paul Grootendorst, Livio Di Matteo, "The Effect of Pharmaceutical Patent Length on Research and Development and Drug Expenditures in Canada", (NCBI, 2007)
[26] Fiona M. Scott Morton, "Barriers to entry, brand advertising, and generic entry in the US pharmaceutical industry", (International Journal of Industrial Organization, 2000)

adverse effect on entry by generics into the market. On one hand, advertising by brand names can expand the market by making physicians aware of therapies that may benefit their patients, suggesting this market may be profitable in the future and encouraging producers of biosimilars to invest in researching and developing medications of similar makeups to their more popular counterparts. On the other hand, existing advertising may build switching costs with doctors and reduce possible profits for generic competitors, making entering the market unappealing. In this way, advertising has an association with the price elasticity of drugs. The more a product is advertised, the less elastic it becomes, as it will likely be more referred to patients by doctors the advertisements are catered to.

III. Theory

A pharmaceutical firm's ability to generate revenue and earn a profit is directly associated with it's incentives to innovate. As a result, a firm's greatest incentives for investment in innovation stem not from markets that possess the greatest demand for treatments, but rather markets that promote exclusivity and do not require extensive research periods, thus limiting costs. The problem stems from the basis that pharmaceutical firms are incentivized to execute research and development with a reward once the product is on the market, but as the R & D timeline grows, the incentives remain constant or even diminish[27]. This, in turn, results in shorter timelines for R & D. While leading to significantly lower costs for the firms to produce the treatment, shorter clinical trials and FDA review periods can result in ineffective and unsafe treatments long-term.

The last forty years have seen both the costs of R & D and revenues for pharmaceutical firms rise dramatically. In 1980, the annual domestic revenue for pharmaceutical member firms was 32.21 billion dollars[28]. As of 2018, that value had ballooned to 286.34 billion dollars generated domestically. With the rise in revenue came an increase in research and development costs, though, as pharmaceutical firms spent 83.00 billion dollars on R & D in 2019 compared to 7.64 billion (in 2019 dollars) in 1984. This massive boost has been reflected in the percentage of research and development costs for pharmaceuticals among all industries. The Congressional Budget Office's 2021 report on R & D looked at the average research and development intensities of publicly traded U.S. companies by industry, in which pharmaceuticals accounted for 25.66 percent of all intensities in 2019.

[27] Erika Lietzan, "The Drug Innovation Paradox", (SSRN, 2017)
[28] David Austin, Tamara Hayford, "Research and Development in the Pharmaceutical Industry", (Congressional Budget Office, 2021)

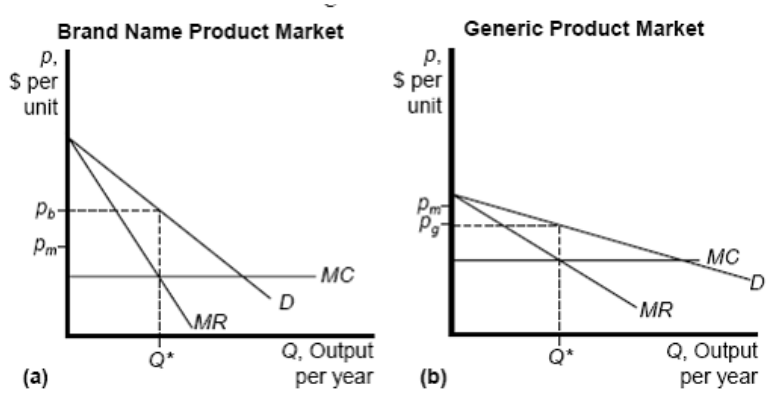
Patents are essential to a producer's profit as well in that they provide exclusivity, thus preventing the risk of competitors sharing the market. A 2007 study shows that market prices decrease significantly following the introduction of generic competitors to the market, as firms are no longer able to monopolize and charge high prices with the presence of alternatives following the end of a patent[29]. Pharmaceutical patents also reflect the value of the treatment, as new molecular entities (NMEs) with the greatest market size retain exclusivity for longer periods of time[30]. This allows pharmaceutical companies to charge the highest prices for drugs that have the greatest population in need for them.

III.1. Demand

Demand in the pharmaceutical industry is determined primarily by the size of the population needing a specific treatment. In addition, a drug that has lost exclusivity, thus allowing competitors and biosimilars to enter the market, has a much more elastic demand than a drug that merely has substitutes, meaning the chemical makeup of two treatments may be different but both can treat the same illness[31]. This, in turn, causes significant differences in price sensitivity between generics and exclusive medications with imperfect substitutes. The following presents an example of the differences in demand elasticity between brand-name products and generic products.

[29] Henry G Grabowski, Margaret Kyle, "Generic Competition and Market Exclusivity Periods in Pharmaceuticals", (Wiley InterScience, 2007)
[30] Henry G Grabowski, Margaret Kyle, "Generic Competition and Market Exclusivity Periods in Pharmaceuticals", (Wiley InterScience, 2007)
[31] Sara Fisher Elison, Iain Cockburn, Zvi Griliches, Jerry Hausman, "Characteristics of Demand for Pharmaceutical Products: An Examination of Four Cephalosporins", (RAND Journal of Economics, 1997)

Figure 2. Demand Curves for Exclusive and Generic Products



[32]http://www.uvm.edu/~awoolf/classes/fall2007/ec172/hwch12solution.htm

Market size and disease prevalence also factor heavily into a firm's incentives to innovate, as treatments that benefit a smaller population affected by a rare, less prevalent condition may prove to cost more and return less profit[33]. Because there is a small population of people with a rare condition, demand may be high from a small market. The 1983 Orphan Drug Act (ODA) was signed into law with the intent of providing incentives to target these rare diseases for R & D, including firms being able to earn tax credits, improved patent protections, fast-track development and approval, and subsidies for clinical research to compensate for the reduced market size. However, firms have found this to be an opportunity for market exclusivity, and there may be too great of incentives for focus on producing orphan drugs. Approximately 250 new rare diseases are described annually, thus calling into question whether the ODA needs to be amended[34]. Nonetheless, incentives for a firm to innovate have proven to be the greatest in markets which promote exclusivity, thus limiting competitors, allow less costs for drugs to be produced, and grant the ability to monopolize and charge high prices. This reality presents a

[32] University of Vermont, Economics 172, (uvm.edu, 2007)
[33] Frank R. Lichtenberg, Joel Waldfogel, "Does Misery Love Company? Evidence from pharmaceutical markets before and after the Orphan Drug Act", (NBER, 2003)
[34] Olivier Wellman-Labadie, Youwen Zhou, "The US Orphan Drug Act: Rare disease research stimulator or commercial opportunity?", (ScienceDirect, 2009)

dilemma in the way pharmaceutical companies are motivated; firms are more likely to innovate in a market in which they benefit greatly, rather than a market with the greatest need for treatment.

An easy solution would be to pass price regulations into law, possibly preventing pharmaceutical firms from pricing their products themselves. However, numerous economic studies have found that by cutting the return pharmaceutical companies receive through the sale of their products, the result could reduce the number of drugs being brought to the market. A study by NBER, taking into account the uncertainty of R & D costs, the success rates for drug development, and the financial returns to those products which are successfully launched into market, found that regulating prices by 40 to 50 percent could lead to 30 to 60 fewer research and development projects being undertaken annually[35]. Thus, this benefit for consumers in the short-run could yield negative outcomes long-term.

III.2. Acute vs. Chronic Illness

When examining the price of a prescription drug, two main factors need to be accounted for; the prevalence of the disease the treatment is designed to mend, but also the duration of the disease. In the United States, the term of a new patent lasts 20 years from when the new drug application was issued, regardless of how long the term of treatment may be. A new approach to making prescription drugs more accessible may be hiding in plain sight; by reducing the patent length for drugs that treat acute diseases (those which may be treated or even cured), while allowing patent length to remain the same for treatments of chronic illnesses, the problem of accessibility will at least be lessened. While both acute and chronic illnesses can be very challenging to treat, the manner in which they need to be treated is often vastly different; acute

[35] David R. Francis, "The Effect of Price Controls on Pharmaceutical Research", (NBER, 2005)

illnesses tend to develop suddenly and last a shorter period of time, while chronic illnesses tend to develop slowly and worsen over an extended period of time[36].

The value of a treatment of an acute disease is hard to measure. Through a monetary scope, a pharmaceutical company may be able to charge as much as they want to for a drug, as it will treat the disease in an explicit timeframe. While there may be some opposition to this from consumers, there is an argument to be made that if this treatment can cure a disease, isn't that as valuable a drug as one can have? While the cost of treatment may remain high, the value of the reduction in the burden of the disease as well as a decrease in transmission as a result of treatment must be factored into the cost, though monetarily this may seem abstract. For example, treatment for Hepatitis C has been found to be almost 90 percent effective. As a result, studies have found that this treatment, despite its monetary cost, is in fact cost-effective especially when started earlier in the onset of the illness due to the quality-adjusted life-years added[37].

Due to the nature of chronic vs. acute illnesses, economic theory would suggest that pharmaceutical companies would lean towards producing treatments that will remain in demand. Acute illness treatments may have a significantly lower quantity being demanded, as they are not being provided recurrently, thus firms may set a higher price for a single unit when compared to their chronic counterparts. Acute treatments will also be more elastic in their demand, as treatment will be shorter in length, thus a lower priced drug that has the same effect with few uses will be as appealing as a higher priced alternative. However, because treatments for chronic illnesses are a recurrent event for consumers, a significantly greater quantity will be demanded. Thus, over time, even if at a lower price, chronic illness medications would prove to be more

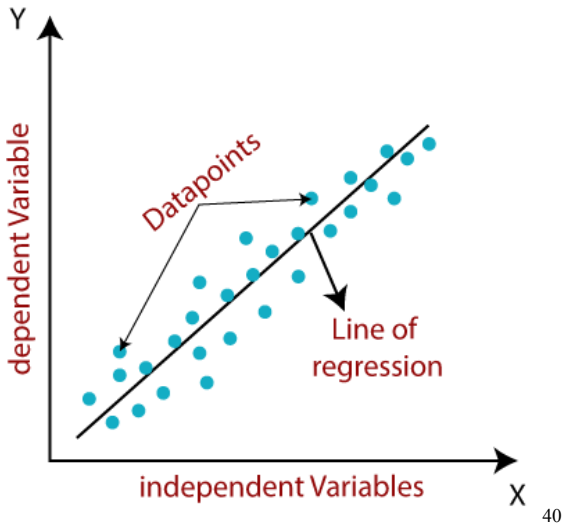
[36] "Chronic vs. Acute Medical Conditions: What's the difference?", (NCOA, 2020)
[37] Andrew J. Leidner, Harrell W. Chesson, Fujie Xu, John W. Ward, Philip R. Spradling, Scott D. Holmberg, "Cost-effectiveness of Hepatitis C treatment for patients in early stages of liver disease", (AASLD, 2015)

profitable[38]. With the additional greater market size (as acute treatments aid in the reduction of transfer of a disease), pharmaceutical companies are much more incentivized to innovate drugs that treat patients suffering chronically, both financially and ethically.

III.3. Determining Correlation

Correlation can be determined by executing a linear regression, in which the coefficients of the equation reveal whether an independent variable has a positive or negative relationship with the dependent variable. More accurately, linear regression is the method of statistically calculating a straight line that demonstrates the relationship between two variables[39].

Figure 3. Example of Linear Regression



[40]

[38] Hans Duvefelt, MD, "Chronic Disease Drugs are Big Business, Antibiotics are Not", (THCB, 2020)
[39] Peter Grant, "Understanding the Fundamentals of Linear Regression", (Towards Data Science, 2019)
[40] "Linear Regression in Machine Learning", (Java T Point)

By examining the distance of the line from the data points it is fit through, the strength of the relationship of association between the two variables can be determined. It is important to understand that this relationship looks at association, not causation, meaning one variable being examined may affect the dependent variable, but not be the full reason of it happening[41]. For example, a high ACT score may not cause a high GPA, but they may be associated.

The most common use of a linear regression is the ordinary least-squares (OLS) method. This entails calculating the line of best fit by minimizing the squares of the vertical distances of each data point from the line.

Figure 4. OLS Regression Line Example Equation

$$Y = a + bX$$

The above equation is for a linear regression line broken down into its simplest form. In this equation, "Y" is the dependent variable, "X" is the independent variable, "a" is the constant, and "b" is the slope of the line. This thesis will use this method to explain the correlation between the independent variables and the dependent variable used in this study.

[41] "Linear Regression", (Stat.Yale.Edu, 1998)

IV. Data

To best analyze how drug pricing regulations will impact incentivization for pharmaceutical companies, this paper will examine how shortening patent lengths will affect an individual drug's revenue. Because reducing the period of a patent being in effect will allow for the entry of competitors into the market, a logical expectation would be for revenues to fall for a specific drug. Using a dataset published by Knowledge Ecology International's Drug Database[42], the patent lengths of twenty five individual pharmaceutical drugs were manipulated to determine how their cumulative lifetime revenues would be affected. The following figures show these treatments and their length on the market as well as cumulative revenues, respectively:

Figure 4. Years since each drug's first FDA Approval (Lifetime on Market)

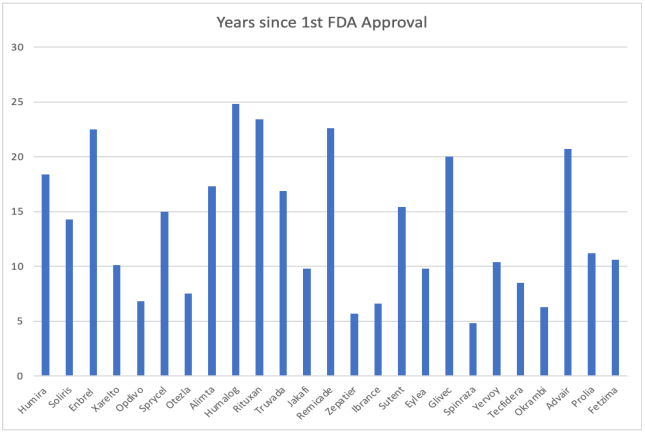
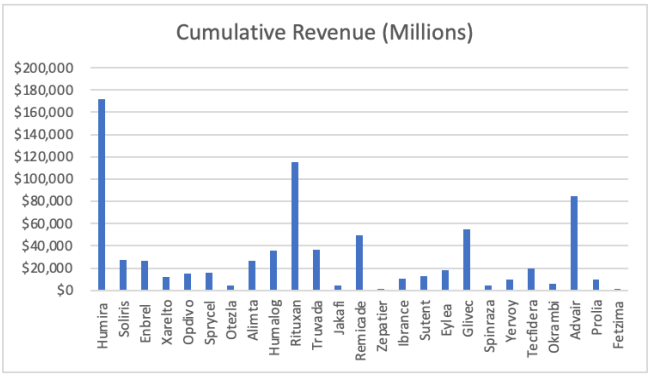


Figure 5. Lifetime Revenue of Each Drug



[42] Knowledge Ecology International, "Drug Database"

The data includes the indication each drug treats, thus determining whether the medication is for an acute or chronic illness as well as the prevalence of the illness. In addition, the amount of time each drug has been on the market is included.

IV.1. Methods

The effects of putting the proposition of different patent lengths into law is measured by examining the revenue differences when adjusting the time of exclusivity. A linear regression taking into account market size and type of illness (acute or chronic) will present how these differing patent lengths could affect a pharmaceutical manufacturer's ability to profit. Market size is measured by taking the prevalence of the disease as the estimated population of those with an illness in the U.S. Prevalence statistics were used from the National Institute of Health's statistics database[43]. To determine profit, an average cost of research and development of 3.1 billion dollars, as inflation has raised the 2.6 billion dollar average from 2013. The loss of revenue due to exclusivity and competition entering the market is an expectation of 80 percent less according to the Congressional Research Service[44].

To determine whether a medication treats a chronic or acute disease, a binary value has been assigned; in this case, a 1 if a chronic illness is being treated, and a 0 if an acute illness is being treated. The following summarizes our dependent variable of cumulative lifetime revenue and our independent variables of years since first FDA approval, market size in the U.S., and whether the treatment is for a chronic or acute illness.

[43] National Institute of Health, "Health Statistics", (NIH, 2021)
[44] Congressional Research Service, "Drug Patent Expirations: Potential Effects on Pharmaceutical Innovation", (CRS, 2012)

Table 1. Summary Statistics for Variables Used in Regression (n=25)

Variable	Obs	Mean	Std. dev.	Min	Max
Cumulative~s	25	30963.49	39892.86	1267	171993
Yearssince~l	25	13.576	6.271914	4.8	24.8
Acute0vsCh~1	25	.68	.4760952	0	1
Prevalence~s	25	13197.58	39427.33	4.11875	197700

The expectation going into this process is that drugs for chronic illnesses, drugs that treat illnesses affecting a greater amount of the population, and drugs that have been active on the market the longest will prove to be most correlated with lifetime revenue.

Figure 6. Regression Equation

$$Revenue = c + b(prevalence) + a(yearsactive) + d(typeofillness)$$

This regression equation, in which "R" is revenue, "p" is prevalence, "y" is years active on market, and "t" is type of illness treated (chronic/acute), should confirm or refute this hypothesis. By examining the resulting coefficients, in this case "b", "a", and "d", as well as the p-values that are returned, correlation of these three variables to the revenue earned of each drug. The "c" in this equation is the constant.

While examining the strength of the relationships of the three independent variables with the dependent variable will be valuable in understanding the factors of earning revenue in the pharmaceutical industry, this thesis will also attempt to quantify the effects of possibly shortening the patents of chronic medications to 10 or 15 years. Both differences will be examined.

Figure 7. Expected Revenue with Length of Exclusivity Adjustments Equation

$$ER = (CR \times (T/Y)) + ((CR \times ((Y - T)/Y)) \times .2)$$

In this equation, "ER" is expected revenue following patent length adjustments and the dependent variable. "CR" stands for cumulative revenue and is the value of the revenue solved for in the given regression equation, where the variables values are the mean values found in the summary and the coefficients found from the solved regression. "T" stands for patent time, and is either 10 or 15. "Y" stands for the years each drug has been active. Because the Congressional Research Service estimates the entry of generics into the market by way of loss of exclusivity to be an 80% reduction in revenue, the value of the years of revenue after the hypothetical expiration of the patent will be reduced to 20% of it's value. This method will not be applicable to all the drugs in the dataset, but those that have been active long enough will reflect the extent of the effects these patent length manipulations will have on cumulative lifetime revenue.

V. Results

Figure 8. Results of Linear Regression

Source	SS	df	MS	Number of obs	=	25
				F(3, 21)	=	24.77
Model	2.9779e+10	3	9.9265e+09	Prob > F	=	0.0000
Residual	8.4151e+09	21	400719257	R-squared	=	0.7797
				Adj R-squared	=	0.7482
Total	3.8195e+10	24	1.5914e+09	Root MSE	=	20018

CumulativeR~s	Coefficient	Std. err.	t	P>|t|	[95% conf.	interval]
Yearssince1~l	3137.137	680.9623	4.61	0.000	1720.998	4553.275
Acute0vsChr~1	12551.24	8749.421	1.43	0.166	-5644.179	30746.65
PrevalenceI~s	.619551	.1076272	5.76	0.000	.395728	.843374
_cons	-28337.69	12205.04	-2.32	0.030	-53719.45	-2955.923

V. 1. Trends in Market Size

Despite greater market sizes having a theoretically significantly greater demand for treatment, prevalence of the disease each medication is meant to treat did not correlate greatly with the lifetime revenue of each drug. The coefficient of .619 does mean there is a positive relationship between an illness's prevalence and the revenue of the drug meant to treat it. However, a p-value of 0.00 does imply that disease prevalence is statistically significant.

V. 2. Lifetime Activity

As hypothesized, the duration of a drug's presence on the market correlates strongly with the revenue it earns. The large coefficient value shows a strong positive relationship with revenue earned, and a p-value of zero reveals this variable to be statistically significant. This makes much logical sense, as the longer a drug is available, the more time it has to be prescribed, especially if for a prevalent disease.

V. 3. Acute vs. Chronic

Reading the coefficient of the “acute vs. chronic” variable is somewhat misleading in determining its correlation with revenue. The coefficient is quite large, suggesting a strong positive relationship between this independent variable and the dependent variable. However, the resulting p-value of 0.166 implies that this is significant at the 83.4th percentile, thus it is not a fully trustworthy factor. This comes as somewhat of a surprise, as the aforementioned theory that chronic medications should see more lifetime revenue as a product of their continual use appears disproved.

V. 4. Expected Revenue

Using the results from the linear regression, the below equation predicts an accurate value of each drug's cumulative revenue based on the three independent variables used in this thesis.

Figure 9. Regression Equation solving for Expected Revenue of Each Drug

$$\underline{PREDREV} = .61955(prevalence) + 3{,}137.137(yearsactive) + 12{,}551.24(typeofillness) - 28{,}337.69$$

With the predicted cumulative revenue value then plugged into the revenue equation in which the patent length is diminished and the years after exclusivity are 20% of their value with exclusivity, the resulting revenues for 10 and 15 year patent lengths appear as follows:

Table 1. Predicted Revenues of Drugs for Chronic Illnesses active 10+ Years with Exclusivity lost after 10 Years

Drug	Cumulative Revenue using Regression Coefficients (Millions USD)	Expected Cumulative Revenue With 10 Year Patent Life (Millions USD)
Humira	$164,422	$104,372
Soliris	$29,077	$22,082
Sprycel	$31,276	$22,935
Alimta	$38,632	$25,590
Rituxan	$58,082	$31,474
Sutent	$32,572	$23,435
Yervoy	$17,642	$17,099
Advair	$64,663	$37,923
Prolia	$25,657	$23,458
Fetzima	$29,486	$28,151
Glivec	$46,994	$28,196

Of the 25 therapies included in this study, just 11 treat chronic illnesses and have been active long enough to have their patent lengths adjusted to last 10 years.

The expected revenue with the patent length adjusted to last ten years saw an average of 73.4 percent of the real revenue returned. The drugs with the longest activity on the market saw the greatest hits to their revenue, as they have had more, in some cases twice as much, time on the market to accrue money for their product.

Table 2. Real and Expected Revenues of Drugs for Chronic Illnesses active 15+ Years with Exclusivity lost after 15 Years

Drug	Cumulative Revenue using Regression Coefficients (Millions USD)	Expected Cumulative Revenue With 15 Year Patent Life (Millions USD)
Humira	$164,422	$140,116
Sprycel	$31,276	$31,276
Alimta	$38,632	$35,523
Rituxan	$58,082	$41,402
Sutent	$32,572	$31,895
Advair	$64,663	$50,418
Glivec	$46,994	$37,595

Of the eleven drugs that matched the criteria needed for the 10 year patent length experiment, seven met the requirements to be included in the model of adjusting patent length to 15 years.

The expected revenue with the patent length adjusted to last 15 years saw an average of 86.9 percent of the real revenue returned. This is a bit skewed, as Sprycel and Sutent have been active for 15 years and 15.4 years, respectively, thus their values are hardly affected by the loss of revenue when exclusivity expires at the moment of this data being recorded. Nonetheless, an average return of 86.9 percent results in each medication still seeing significant profits despite an average cost of research and development 3.1 billion dollars.

V.5. Limitations of the Study

While this thesis intends to offer an accurate and comprehensive quantification of the factors that affect a drug's revenue, there are some shortcomings in this process. While twenty

five observations provides sufficient variance for this study, to be as accurate as possible, a larger sample size would be used. In addition, some other variables could provide clarity into further factors that determine pharmaceutical revenue. Some possible additions that would be of interest include FDA Orphan Indications as well as QALYs (Quality Adjusted Life-Years) added by each of the drugs. This could help cost-effectiveness be analyzed as well. Finally, a quantifiable measurement could be applied to determining whether a treatment is chronic or acute. An exact timeframe (i.e. a month on medication) would be a helpful addition to distinguishing this variable.

VI. Conclusions

VI. Interpreting Results

Using revenue data of 25 prescription drugs as of 2020, provided by Knowledge Ecology International's Drug Database, an examination of the strength of the association between three main factors and cumulative revenue was performed. In addition, a calculation of the predicted revenue earned by treatments for chronic illnesses with a shorter patent length was executed with the intent of providing a look at how much the producers of these medications would lose. The purpose of this exercise was to balance the need of a reduction in price for consumers, which was accomplished by the theoretical earlier entry of generic medications into the market through shorter patent lengths, and the incentives for pharmaceutical companies to still receive a return on their investment, which was done through still maintaining exclusivity for a duration of time. The reasoning behind focusing on the patent lengths of medications of chronic illnesses was the timeframe of being on the therapy; chronic illnesses require consistent treatment for a much longer duration that acute illnesses, which may be recovered from quickly.

The findings of this thesis suggest that reducing the patent lengths of prescription medications for chronic illnesses would benefit consumers while meeting the needs of producers. The regression analysis performed finds that the years since the drug was introduced to the market and the prevalence of the disease it treats are the two biggest factors in a drug's lifetime revenue. This makes much intuitive sense, as the drugs with a longer active shelflife have more time to be prescribed and the drugs with the largest market size will be consumed the most. There is an association between a drug treating a chronic or acute illness, but it is not strongly significant.

The calculated expected revenue using the regression equation as well as adjusting for a shorter period of exclusivity provides interesting conclusions. When patent lengths are reduced from twenty to ten years, the diminishments in revenue prove to be too great to justify this type of policy change to pharmaceutical producers. Due to the investment made in the research and development of these medications, receiving just under three quarters of what they have earned seems too extreme. Adjusting the patent length to fifteen years for chronic therapies, though, proves that producers still make more than enough of a return while generics are allowed to enter the market earlier. This introduction of competition to the market should significantly benefit consumers, as the presence of alternatives will prevent prices from rising to an unaffordable level.

With an average cost of production of 3.1 billion dollars, each medication still should see significant returns for their producer. The earlier addition of competition into the market should significantly benefit patients suffering from chronic diseases, thus satisfying consumers more. If pharmaceutical companies can reconcile this lessened return on their product that in most cases is not a steep decline, both parties will have reached a point of satisfaction. While patent lengths of twenty years provide greater lengths of time to earn profit while a pharmaceutical company's product maintains exclusivity, reducing this period to allow competition at an earlier date should still provide sufficient time to make back the investments of research, development, and advertising, earn a profit in addition, and enable consumers to use lower priced alternatives with biosimilars available.

VI. Further Research

While this thesis serves as a comprehensive analysis on pharmaceutical patent length and how it impacts drug pricing, there is more research to be done in a variety of sectors covered in this paper. Further cost-effectiveness analysis could assist in possible price regulation, as differing patent lengths based on whether a medication is acute or chronic could assist in quantifying how the therapy will add benefits to a patient's life following diagnosis. Research could be done on the coronavirus pandemic and how patents were distributed for companies researching and developing vaccines, as well as the cost-effectiveness for the producers in this case, as their product is in high demand but there is not a promise of profit to be made on their investment. Finally, examining how government subsidies of pharmaceutical R & D impact pricing could present some clarity into how to prevent price gouging, as the costs of producing a medication are the driving factor behind charging high prices for consumers.

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