# The Effects of Patent Expiration on Prescription Rates of Different Branded and Generic Drugs

A Senior Thesis

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Saksham Goel

Advisor: Professor Frank Limbrock

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**Abstract**

This paper examines the impact brought upon by the introduction of generic alternatives, after a drug loses its patent exclusivity, on prescription rates of certain branded drugs, their generics and their therapeutic substitutes. The study uses provider level prescription data from Medicare Part D Prescriber Datasets to focus on 10 highly profitable drugs whose patents expired between the years 2014-2017. This research provides evidence that the generic share of prescriptions one year post-patent expiration of a branded drug has continued to increase in the US. Using a regular cross-section regression model, the paper finds that there is no correlation between the change in prescription behavior of physicians and the per capita income of the zip codes in which they practice medicine. Also, the study shows that any potential effects of business stealing from therapeutic substitutes, upon the introduction of a generic version of a leading molecule, are offset by other external factors affecting the entire drug class.

## 1. Introduction

Healthcare expenditure in the United States has been consistently increasing since 1960. As per the Organization for Economic Cooperation and Development (OECD) Healthcare Data, the United States spent 16.9% of its GDP – more than any other OECD country – on healthcare related expenditures in 2018. According to the National Center for Health Statistics, approximately 9.2% of this healthcare expenditure in 2018 can be attributed to prescription drugs ("Health Expenditures"). A main reason behind this is high costs and utilization of branded drugs. The United States is one of the only two countries in the world that allows for direct to consumer advertising (DTCA) of prescription drugs (Morton and Kyle, 769). In addition, pharmaceutical companies also spend a large sum of money on 'detailing' where they send their sales representatives to clinics. These employees directly advertise their firm's branded drugs to prescribing physicians in an attempt to induce increased prescriptions of branded drug formulations.

Moreover, according to the Handbook of Health Economics, advances in low-cost production of generics of off-patent branded drugs has had a significant impact on the market structure of the pharmaceutical industry (Morton and Kyle, 764). For instance, the move to generic alternatives leads to lower drug prices and increased accessibility, thereby creating a gain in social welfare. The growth in development and production of generic alternatives was made possible by the enactment of the Hatch-Waxman Act in 1984 which established the abbreviated new drug application (ANDA) process for generics. As a result of ANDA, the introduction of generic alternatives in the market, after the loss of a drug's patent exclusivity, became very rapid. One of the reasons behind rapid introduction of generics into the market was an incentive referred to as the 180-days exclusivity period under which the first applicant granted ANDA

would enjoy an effective monopoly in the generic market for the branded drug that just lost its patent exclusivity (Rumore).

When a drug nears loss of patent exclusivity, pharmaceutical firms sometimes rebrand the small-molecule drug in its extended-release form and divert their resources from the branded drug to aggressively market this extended-release version which is also protected by a patent (Gupta et al., 4). This strategy of investing in incremental innovation allows pharmaceutical companies to maintain their monopoly in the market for a specific drug. On the other hand, large-molecule drugs or biologics (as they are commonly referred to) are more complex drugs with higher manufacturing costs. These large-molecule drugs usually don't have generics in the market as pharmaceutical firms develop biosimilar drugs to retain market exclusivity upon a molecule's patent expiration. As the name suggests, these biosimilar drugs are very similar in their composition to their corresponding biologics.

This research aims to study the degree to which a patent expiration leads to business expansion (new patients getting prescriptions to a molecule formulation they wouldn't have been prescribed before its patent expiration) versus business stealing (patients who used to or would have gotten a different drug now getting the new generic drug). To do so, the thesis focuses on three main research sub-questions. The first is to explore how the generic share of providers' prescriptions change for a given drug. The second is to determine the effect per capita income has on total volume of the molecule (branded and generic combined) prescribed after patent expiration. The third is to study the effect of patent expiration on therapeutic substitution for a given drug class.

For my research, I have focused on the case study of 10 highly profitable smaller-

molecule drugs, 2 of which lost their patents in 2014, 4 lost their patents in 2015, 2 in 2016 and 2 expired in 2017. The information on these drugs, their active ingredients and their year of patent expiry is listed below in Table 1. In addition, information on the respective drug class and therapeutic substitutes for these drugs can be found below in Table 2. To analyze the change in prescription behavior of physicians between one year pre-patent expiration and one year post-patent expiration, the master data file used contains provider-level prescription data for the years 2013-2018.

Furthermore, I have primarily used Medicare Part D prescriber data to conduct my study. Centers of Medicare and Medicaid Services (CMS) only included prescription drug coverage for Medicare beneficiaries through the introduction of Medicare Part D in 2006. This was possible due to Congress' approval of the 'Medicare Prescription Drug, Improvement, and Modernization Act of 2003' ("Part D/ Prescription Drug Benefits").

| Drug Name | Active Ingredient | Patent Expiry |
|---|---|---|
| Celebrex | Celecoxib | 2014 |
| Evista | Raloxifene HCL | 2014 |
| Clarinex | Desloratadine | 2015 |
| Avodart | Dutasteride | 2015 |
| Focalin XR | Dexmethylphenidate HCL | 2015 |
| Abilify | Aripiprazole | 2015 |
| Crestor | Rosuvastatin Calcium | 2016 |
| Benicar | Olmesartan Medoxomil | 2016 |
| Reyataz | Atazanavir Sulfate | 2017 |
| Cubicin | Daptomycin | 2017 |

**Table 1: List of Branded Drugs with Patent Expiry**

*Source: Pharmacy Purchasing and Products*

| Drug Name | Drug Class | Therapeutic Substitutes |
|---|---|---|
| Celebrex | Non-steroidal Anti-inflammatory drugs (NSAIDs) | No branded alternative |
| Evista | Selective Estrogen Receptor Modulators | Fareston (Toremifene Citrate), Tamoxifen Citrate |
| Clarinex | 2nd Generation Histamine H1 Antagonist | No branded alternative (only OTC options) |
| Avodart | 5-Alpha-Reductase Inhibitors | Jalyn, Tamsulosin HCL, Proscar, Finasteride |
| Focalin XR | Stimulants; ADHD Agents (Long-acting) | Daytarna (Methylphenidate), Vyvanse (Lisdexamfetamine Dimesylate), Strattera (Atomoxetine HCL), Concerta, Methylphenidate HCL, Adderall XR, Dextroamphetamine-Amphetamine, Metadate CD, Ritalin LA |
| Abilify | Atypical Antipsychotics | Saphris (Asenapine Maleate), Fanapt (Iloperidone), Latuda (Lurasidone), Invega (Paliperidone), Clozaril, Clozapine, Zyprexa, Olanzapine, Seroquel, Quetiapine Fumarate, Risperdal, Risperidone, Geodon, Ziprasidone HCL |
| Crestor | HMG-CoA Reductase Inhibitors (Statins) | Livalo (Pitavastatin Calcium), Lipitor, Atorvastatin Calcium, Lescol, Fluvastatin Sodium, Lovastatin, Pravachol, Pravastatin Sodium, and Zocor, Simvastatin |
| Benicar | Angiotensin II Receptor Blocker (ARB) | Edarbi (Azilsartan), Cozaar, Losartan Potassium, Atacand, Candesartan Cilexetil, Avapro, Irbesartan, Diovan, Valsartan, Micardis, Telmisartan |
| Reyataz | HIV Protease Inhibitor | Prezista (Darunavir Ethanolate), Crixivan (Indinavir Sulfate), Kaletra (Lopinavir, Ritonavir), Viracept (Nelfinavir Mesylate), Lexiva, Fosamprenavir Calcium, Norvir, Ritonavir, Invirase |
| Cubicin | Cyclic Lipopeptide Antibiotic | No substitute found |

**Table 2: Information on Drug Class and Therapeutic Substitutes**

*Source: U.S. Food and Drug Administration, Cleveland Clinic*

## 2. Literature Review

This paper is inspired by two categories of research that have been done in this field. The first set of literature studies the impact of changes in market structure, as a result of patent expiration of branded drugs, on drug prices, drug utilization and other non-price factors such as advertising. While the focus of most of the existing research is to understand the relationship between the aforementioned factors, the studies mainly differ in the datasets (each study looks at different set of drugs in different time periods) used and the empirical strategies employed.

Lakdawalla and Philipson (2007) in their paper analyze IMS Health data on 101 unique molecules with patent expirations dated between 1990 and 2003. The aim of their study is to understand the welfare effects of patent expiration. The authors use a 3SLS model where 'timing of patent expiration' is used as an instrumental variable to conclude that there are two effects of loss of market exclusivity on drug utilization. While a reduction in prices has a positive effect on utilization, this change is more than offset by the negative effect of reduction in marketing. As a result, the study concludes that patent expirations reduce both drug utilization and consumer welfare in the short-run.

This conclusion is further strengthened by the work of Huckfeldt and Knittel (2011). They run a time series regression using a dataset of 35 therapeutic drugs whose patents expired between 1996 and 2007 to find a similar decrease in drug utilization levels in the short-run. Through their empirical analysis, Huckfeldt and Knittel (2011) conclude that total molecule use (branded and generic drugs combined) falls by almost 20 percent in two years after generic entry. They also find that this decrease in total molecule use coincides with increased utilization of branded reformulations of molecules going off patent.

Another key paper in this field is by Duflos and Lichtenberg (2011). They employ the differences-in-differences model to study the effect of competition on drug utilization. In contrast to the past research, this paper uses 'number of years since first launch of the drug' as the instrumental variable for estimating changes in market structure and advertising. Additionally, it uses the data for almost all prescription drugs sold in the US between 2000-04 to again find that generic entry leads to a decrease in both prices and advertising of these drugs. While a reduction in prices has a positive effect on utilization, this change is completely offset by the negative effect of reduction in marketing. As a result, contrary to the claims made by other existing literature, the study finds that the net effect of patent expiration on drug utilization is zero.

Overall, majority of the existing literature explores the impact of intellectual property protection for innovative drugs and the entry of generic substitutes on drug utilization at a patient level. However, my analyses differ from past research in that I study the impact of patent expiration on prescription rates of drugs at a physician level. Through my empirical analysis, I intend to explore whether the trends identified in past research hold when studied using providers' prescription data. In specific, I not only look at the effect of patent expiration on total utilization of the molecule (branded and generic drugs combined), but also examine the impact on the quantity prescribed of its therapeutic substitutes.

Apart from this, the second set of literature relevant to my research analyzes the impact of various factors (such as variation in levels of cost information available to the prescriber) on the prescribing behavior of physicians. This type of research is relevant to my paper as I aim to assess the role different provider characteristics play in influencing the prescribing behavior of providers. In other words, my paper will examine whether characteristics such as time since

graduation from medical school, gender and education level affect how different providers respond to change in information. For instance, some changes in information in the case of patent expiration include uniform price reduction, significant decrease in advertising and entry of generic substitutes.

The paper by Carrera, Goldman and Joyce (2013) employs a conditional logit regression model to study the responses of physicians and patients to variations in the cost of drugs. The authors use the patent expiration of Zocor (a statin drug) as a price shock to analyze the change in prescription rates for various branded statin drugs. They conclude that, after patent expiration, there was a significant increase in prescriptions for Zocor for low-income patients. They also hypothesize that this change in prescription behavior of physicians is only seen as a result of a large and uniform change in price. Building on this in my thesis, I intend to examine the extent to which prescribing behavior of physicians, in response to patent expiration of drugs (that leads to these large and uniform price changes), is also influenced by the physicians' characteristics.

In the end, my research will contribute to the existing literature by analyzing a more recent, highly-detailed dataset. I will use prescription data from the Centers of Medicare and Medicaid Services (CMS) Part D Prescriber Datasets for 2013-2018 where I will focus on 10 highly profitable drugs whose patents expired in that time period. In addition, I will use the provider demographic data from the Physician Compare National Dataset and the provider geographic data from the Medicare Provider Utilization and Payment Datasets to match each unique National Provider Identifier (NPI) to the unique characteristics of that provider.

## 3. Hypotheses

Before conducting the data analyses, I had three main hypotheses, one corresponding to each of the three research sub-questions.

**H1:** The patent expiration of a branded drug and the resulting introduction of its generic alternative should lead to a clear progression in the generic share of providers' prescriptions. One could expect to see a change from all physicians having a generic share of 0 (when only the branded drug is prescribed) in the year pre-patent expiration to a large number of physicians having a generic share closer to 1 (when mostly only the generic alternative of the branded drug is prescribed) in the year post-patent expiration.

**H2:** For zip codes with relatively lower per capita income, the introduction of the generic alternative should lead to an increase in the total volume of the molecule (branded and generic drug combined) being prescribed. This is the case as most Medicare Part D coverage plans include a deductible, and a co-payment or a co-insurance requirement due to which Medicare Part D beneficiaries are still assumed to be sensitive to changes in prescription costs.

**H3:** The introduction of a generic medicine in a given drug class should steal business away from the other available therapeutic substitutes and therefore, should, on average, lead to a decline in the total volume of therapeutic substitutes being prescribed by each physician. This is because the generic alternative for one branded drug in a given drug class serves as indirect competition to other branded drugs in that drug class.

## 4. Data Collection and Processing

To study the effect of patent expiration on prescription rates of certain branded drugs, their generics and their therapeutic substitutes, I used the Medicare Part D Prescriber Datasets from the Centers of Medicare and Medicaid Services (CMS) for the years 2013-2018. I decided to use the Medicare Part D data for my research as the CMS database was the only publicly available data source with provider level prescription information. These datasets provided information on the prescription behavior (the drugs prescribed, the total volume of each drug prescribed, the total number of unique beneficiaries for each drug prescribed, and the total Medicare Part D claim count for each drug) of physicians. Additionally, the physicians were labelled using unique National Provider Identifier (NPI) numbers corresponding to each different physician. Using NPI as the key variable, I then merged provider demographic data (including gender, credentials and graduation year) from the Physician Compare National Dataset with the Medicare Part D Prescriber Dataset for each of the years. Again, using NPI as the key variable, I merged provider geographic data (the zip code in which each physician was practicing medicine in that specific year) taken from the Medicare Provider Utilization and Payment Datasets for years 2013-2018. These datasets were publicly available on the Centers of Medicare and Medicaid Services (CMS) database.

After including provider demographic and geographic data, I appended the datasets for years 2013-2018 to create one master data file containing prescription information for 385,414 different physicians across the six-year period. I then merged the data on Median Household Income (in 2019 dollars) at a zip code level from the American Community Survey (ACS) available on the Census Bureau Website. I used the median household income as an indicator of the per-capita income of the zip code a physician was practicing medicine in to determine the

average affluence of each provider's zip code.

I used the total_30_day_fill_count variable (which contains information on the aggregate number of Medicare Part D standardized 30-day fills by each physician for a particular drug) provided in the Part D Prescriber Datasets as an indicator for the total volume of a specific drug prescribed by a physician in a given year. Working with the variable allowed me to calculate the total volume of a molecule (branded and generic drug combined) prescribed by each physician in a given year. I defined this new variable as drug_brandgen_vol. Similarly, using the total_30_day_fill_count variable, I also calculated the total volume of a molecule's therapeutic substitutes prescribed by each physician in a given year. This variable was defined as drug_sub_vol.

Finally, I used the *reshape* function on Stata to reshape the data from long to wide with each row now being an entry for a unique NPI. I also replaced all missing values for the total volume of therapeutic substitutes prescribed variable (drug_sub_vol) with 0. The Medicare Part D Prescriber Dataset only records entries for drugs that are actually prescribed by a given physician and therefore, a missing value for the sub_vol_final variable indicates that the physician did not prescribe any therapeutic substitutes for the given branded drug.

## 5. Research Methodology

### *5.1: Physicians' Generic Share of Prescriptions for a Particular Drug*

To calculate a physician's generic share of prescriptions for a particular drug, I divided the value of the total_30_day_fill_count variable for the generic alternative prescribed by a physician by the drug_brandgen_vol value computed for that physician for the relevant pair of

branded and generic drugs. I then defined this new variable as drug_gen_share. The value of drug_gen_share variable ranges between 0 to 1, with 0 meaning that 100 percent of the physician's prescriptions are for the branded drug and with 1 meaning that 100 percent of the physician's prescriptions are for the generic alternative of that molecule.

*5.2: Regular Cross-Section Regression Model*

Given the data was structured on physician level outcomes annually, to test the second hypothesis, I conducted a regular cross-section regression using the following mathematical model:

$$\mathbf{drug\_diff\_brandgen_i = B_0 + B_1\ ln\_Median\_HI_{zipcode} + e\ \ if\ zipcode_{pre} = zipcode_{post}}$$

where,

$drug\_diff\_brandgen = (drug\_brandgen\_vol_{post} - drug\_brandgen\_vol_{pre})/\ drug\_brandgen\_vol_{pre}$

ln_Median_HI = ln(Median_HI_2019)

Here, the dependent variable is diff_brandgen which refers to the percent change in total volume of the active ingredient prescribed between one year pre-patent expiration and one year post-patent expiration. It is calculated on the individual physician level. The independent variable is ln_Median_HI which refers to the natural log of the median household income for the zip code in which the physician practices medicine. As a result, ln_Median_HI varies on the zip code level. The regression analysis was conducted only for a set of physicians that remained in the same zip code in the concerned three-year period. As the data is on a provider-level and the analysis is separately performed for each branded drug, I decided not to include any physician or

molecule fixed effects. Also, as the diff_brandgen variable represents a percentage change in total volume prescribed a year before and after patent expiration, I decided not to include any time fixed effect or an instrumental variable for patent expiry.

*5.3: The 'Difference Regression' Model*

In order to study whether the introduction of a generic version of a leading molecule upon expiry of the branded drug's patent leads to business stealing, I conducted a 'difference regression' using the following regression model:

$$\mathbf{drug\_diff\_sub_i = B_0 + B_1\ drug\_diff\_brandgen_i + e}$$

where,

$drug\_diff\_brandgen = (drug\_brandgen\_vol_{post} - drug\_brandgen\_vol_{pre})/\ drug\_brandgen\_vol_{pre}$

$drug\_diff\_sub = (drug\_sub\_vol_{post} - drug\_sub\_vol_{pre})/\ drug\_sub\_vol_{pre}$

Here, the dependent variable is diff_sub which refers to the percent change in total volume of therapeutic substitutes for a given drug class prescribed between one year pre-patent expiration and one year post-patent expiration. It is calculated on the individual physician level. Similarly, for the aforementioned reasons, I have decided not to include any time, molecule or provider fixed effects. The chosen econometrics model allows me to estimate the effect brought upon by a change in total molecule use (both branded and generic drug combined) on the total volume of the drug's therapeutic substitutes prescribed between one year pre-patent expiration and one year post-patent expiration.

## 6. Results and Discussion

*6.1: Analysis of Change in Drug Utilization Levels*

**reg drug_diff_brandgen**

| Drug Name | Constant |
|---|---|
| Celebrex | 0.0593 *** |
| Evista | 0.0373 *** |
| Clarinex | 0.2063 *** |
| Avodart | -0.0946 *** |
| Focalin XR | 0.0141 |
| Abilify | 0.2139 *** |
| Crestor | 0.45 *** |
| Benicar | -0.0744 *** |
| Reyataz | -0.2748 *** |
| Cubicin | 0.3945 *** |

**Table 3: Performing Sanity Check**

This set of regression was performed to confirm whether drug utilization decreased immediately post patent expiration, as suggested by various findings of existing literature reviewed in the thesis. However, we find that once drugs lost their patent exclusivity and generic alternatives became available, total molecule use (branded and generic drug combined) increased. The positive coefficients for most of the 10 drugs, as shown in Table 3, indicate that the loss of patent exclusivity leads to higher drug utilization. For example, loss of Celebrex's patent exclusivity leads to a 6 percent increase in total volume of the molecule prescribed between one year before and after patent expiration.

A possible explanation for this unexpected result is that unlike the findings of other papers, the positive effect of reduction in prices of drugs might actually more than completely offset the negative effect of reduction in advertising. This significant increase in prescription

rates due to reduction in drug prices can be partly attributed to the presence of formulary tier structures in Medicare Part D insurance plans. Also, the higher drug utilization might be a direct consequence of increased drug spending in the US over the previous few years. Lastly, the "changes in the form of cost sharing between insurer and insuree have amplified the incentives that insurance provides to increase use of prescription drugs" (Berndt, 50), which in turn may lead to the aforementioned results.

*6.2: Analysis of Generic Shares of Prescriptions*

| Drug Name | Average Generic Share One Year Post Patent Expiration |
|---|---|
| Celebrex | 98% |
| Evista | 98% |
| Clarinex | 97.3% |
| Avodart | 96.2% |
| Focalin XR | 77.4% |
| Abilify | 98.8% |
| Crestor | 97.5% |
| Benicar | 87.5% |
| Reyataz | 79.8% |
| Cubicin | 93.1% |

**Table 4: Average Generic Share of Prescriptions for Various Drug Molecules**

The average generic share of prescriptions for various drug molecules one year post patent expiration in Table 4 shows that an immediate, complete switch to the generic alternative occurs. The results in the table are fascinating as generic fill rates have historically never been so high. To elaborate, before the passage of the Hatch-Waxman Act in 1984, only a mere 19% of prescriptions in the US were filled with generics (Morton and Kyle, 795). However, once the Act was passed, as the process of developing and commercializing generic drugs became more streamlined and efficient, we noticed a steady increase in the generic fill rate over time. For

instance, the generic share of prescriptions in the US increased to 74.5% in 2009 (Berndt and Aitken, 1). The average generic fill rate for the chosen 10 drugs is 92% across the years 2014-2018, highlighting the continued increase in process efficiency. Moreover, it shows that when there is a generic version of a molecule available, a near full switch to the generic takes place within a very short period of time. This speed of transition is also noteworthy since it can have significant policy implications. To elaborate, if we similarly see an immediate and complete switch to the generic version of drugs that are losing patent exclusivity over the next five years, a social welfare gain worth billions could be generated. This is because the prices of generic drugs tend to be less than 25 percent of their branded counterparts once multiple generic competitors have entered the market (Morton and Kyle, 774).

As stated in Hypothesis 1, we would expect a more gradual rate of switch to the available generic alternatives. However, a potential reason for the observed quick switch to generics is that the analysis conducted uses filled prescription data where pharmacies might have substituted the generic alternative for the branded drug at the point of sale due to restrictions created by generic substitution state laws. Also, as we are only analyzing the prescription data of physicians prescribing drugs to patients covered by Medicare Part D insurance coverage, any maintenance changes to the Part D formulary by the CMS would have also contributed to the acceleration in switch to generics ("Part D/Prescription Drug Benefits").

*6.3: Analysis of Prescriber Characteristics*

Furthermore, to examine whether any characteristic differences such as time since graduation from medical school, gender and education level affect how different providers respond to patent expiration, I first identify prescribers that fall in the bottom 3 percentile of

generic share of prescriptions. I only conduct this analysis for five specific drugs – Celebrex, Evista, Abilify, Avodart, Crestor – as the third percentile is significant (generic share is between 0 and 1) for all these drugs. We find that 10,058 unique prescribers fall in the bottom 3 percentile of at least one of the five aforementioned drugs. In specific, Table 5 below shows that if a physician is in the lowest 3 percentile of prescribers for one drug, then that physician is also more likely to be in the lowest 3 percentile for another drug. This is the case as the likelihood that a physician is in the bottom 3 percentile of both drugs is greater than 0.09% for 9 out of ten drug combinations. The threshold to establish the pattern is 0.09% as a prescriber has a 3% chance to be in the bottom 3 percentile for one drug and similarly, a 3% chance to be in the bottom 3 percentile for the other drug.

| **Drugs** | **Number of Physicians in Bottom 3 Percentile of Both Drugs** | **Total Number of Physicians Who Prescribe Both Drugs** | **Likelihood that a Physician is in Bottom 3 Percentile of Both Drugs** |
|---|---|---|---|
| Celebrex + Evista | 69 | 21404 | 0.0032 |
| Celebrex + Abilify | 26 | 15015 | 0.0017 |
| Celebrex + Avodart | 43 | 12009 | 0.0036 |
| Celebrex + Crestor | 169 | 52489 | 0.0032 |
| Evista + Abilify | 5 | 7541 | **0.0007** |
| Evista + Avodart | 16 | 6780 | 0.0024 |
| Evista + Crestor | 64 | 27663 | 0.0023 |
| Abilify + Avodart | 13 | 5216 | 0.0025 |
| Abilify + Crestor | 29 | 20373 | 0.0014 |
| Avodart + Crestor | 64 | 15869 | 0.004 |

**Table 5: Distribution of Physicians in Bottom 3 Percentile of Certain Combination of Drugs**

To further understand what is particular about the set of prescribers who do not completely switch to generic after loss of patent exclusivity, I analyze the demographic characteristics of physicians in the bottom 3 percentile of these five drugs. Tables 6 and 7 show the demographic comparisons between all physicians who prescribe a certain drug or a combination of drugs and those who specifically fall in the bottom 3 percentile (in terms of generic share of prescriptions) for a certain drug or a combination of drugs.

| **Drugs** | **Average Number of Years After Graduation (For All Physicians Who Prescribe the Drug)** | **Average Number of Years After Graduation (For Prescribers in the Bottom 3 Percentile)** | **Share of Males (Among All Physicians Who Prescribe the Drug)** | **Share of Males (Among Prescribers in the Bottom 3 Percentile)** | **Share of M.D. (Among All Physicians Who Prescribe the Drug)** | **Share of M.D. (Among Prescribers in the Bottom 3 Percentile)** |
|---|---|---|---|---|---|---|
| Celebrex | 29.2 | 31.6 | 55.8% | 57.6% | 34.7% | 38.2% |
| Evista | 31.3 | 33.2 | 50.9% | 52.8% | 38.1% | 42.8% |
| Abilify | 27.7 | 30.3 | 43.6% | 44% | 34% | 39.1% |
| Avodart | 31 | 31.8 | 70.2% | **64.6%** | 39.3% | 40% |
| Crestor | 26.8 | 29.8 | 50.4% | 51.4% | 33% | 37% |

**Table 6: Demographic Characteristics Comparison Between All Prescribers for a Certain Drug and those that Fall in the Bottom 3 Percentile for that Drug**

| Drugs | Average Number of Years After Graduation (For All Physicians Who Prescribe the Drug) | Average Number of Years After Graduation (For Prescribers in the Bottom 3 Percentile) | Share of Males (Among All Physicians Who Prescribe the Drug) | Share of Males (Among Prescribers in the Bottom 3 Percentile) | Share of M.D. (Among All Physicians Who Prescribe the Drug) | Share of M.D. (Among Prescribers in the Bottom 3 Percentile) |
|---|---|---|---|---|---|---|
| Celebrex & Evista | 31.5 | 34.5 | 59.2% | 63.8% | 38.7% | 52.2% |
| Celebrex & Abilify | 30 | 33.2 | 63.2% | 69.2% | 36.4% | 46.2% |
| Celebrex & Avodart | 32 | 33.3 | 73.1% | **72.1%** | 39.6% | 55.8% |
| Celebrex & Crestor | 30.1 | 34.3 | 59.5% | 59.8% | 36% | 45% |
| Evista & Abilify | 31.1 | 31.2 | 63.7% | 80% | 38.4% | 60% |
| Evista & Avodart | 32.6 | 34.1 | 73% | 87.5% | 41.7% | **37.5%** |
| Evista & Crestor | 31.3 | 36 | 58.2% | 59.4% | 39% | 50% |
| Abilify & Avodart | 31.4 | 33.8 | 73% | 100% | 39.1% | 38.5% |
| Abilify & Crestor | 28.9 | 31.5 | 60% | 69% | 34.8% | **27.6%** |
| Avodart & Crestor | 31.5 | 34.1 | 72% | **59.4%** | 39.1% | 43.8% |

**Table 7: Demographic Characteristics Comparison Between All Prescribers for a Certain Combination of Drugs and those that Fall in the Bottom 3 Percentile for that Set of Drugs**

According to Tables 6 and 7, prescribers in the bottom 3 percentile for generic share of prescriptions on average tend to have graduated from medical school before all other prescribers for a certain drug or a combination of drugs. In specific, in Table 6, the average time since graduation from medical school for prescribers in the bottom 3 percentile for a drug is higher by 2.14 years. Similarly, in Table 7, the average time since graduation from medical school for prescribers in the bottom 3 percentile for a combination of drugs is higher by 2.56 years. This finding matches our assumption that prescriber who have spent more number of years practicing medicine (and who might also be older in age) are slower to make the complete switch to the generic alternative. To elaborate, prescribers who have more recently graduated from medical school are more likely to be up to date with the developments in the generic drugs space given there is a higher chance that they are using an electronic drug reference database at the point of care (Mattina). This is because a new study on 'The Impact of Information Technology on the Diffusion of New Pharmaceuticals' found that physicians using "the reference [database] have a significantly greater propensity to prescribe generic drugs [and] are faster to prescribe new generics" (Arrow et al.). At the same time, prescribers who have spent more time practicing medicine after medical school might be relatively more accustomed to prescribing branded drugs. Also, it is possible that the more experienced physicians might have a longer standing relationship with detailing representatives from certain pharmaceutical companies which in turn incentivizes these physicians to continue prescribing the branded drugs.

In terms of gender distribution, it is interesting to note that both in Tables 6 and 7, the percentage of male prescribers in the bottom 3 percentile for generic share of prescriptions is higher. In the case of individual drugs, we observe a 1 percentage point increase on average (when excluding the entry for Avodart as it is an outlier) in the number of male prescribers in the

bottom 3 percentile. Whereas, in the case of a combination of drugs, we observe a significantly higher 6.53 percentage points increase in the number of male prescribers in the bottom 3 percentile.

Lastly, in terms of education level and credentials, given their knowledge, we would expect a Doctor of Medicine (M.D.) to make the switch to the generic alternative due to its affordability and increased population accessibility once it is available. However, contrary to our assumption, in Tables 6 and 7 we find that the percentage of M.D. credited practitioners in the bottom 3 percentile for generic share of prescriptions is higher. In specific, for individual drugs, the number of M.D. prescribers in the bottom 3 percentile increases by 3.6 percentage points on average. Similarly, we see an even higher average increase of 7.38 percentage points in the number of M.D. credited prescribers in the bottom 3 percentile for a combination of drugs. This might be the case as the more qualified physicians feel less pressure to be cost effective. Also, as they are potentially more confident in their area of expertise, these physicians might be slower to change their preferred form of drug (from branded to generic).

*6.4: Analysis of Income Regression*

**reg drug_diff_brandgen ln_Median_HI if $zipcode_{pre} = zipcode_{post}$**

| Drug Name | Constant | Ln_Median_HI |
|---|---|---|
| Celebrex | -0.1402 | 0.0181 * |
| Evista | 0.0681 | -0.0028 |
| Clarinex | 0.2966 | -0.0091 |
| Avodart | -0.0671 | -0.0025 |
| Focalin XR | -0.6946 | 0.0644 |
| Abilify | 0.1352 | 0.007 |
| Crestor | 0.3677 *** | 0.0074 |
| Benicar | -0.6895 *** | 0.0555 *** |
| Reyataz | -0.4678 | 0.0177 |
| Cubicin | 0.1734 | 0.0209 |

**Table 8: Income Regression Results**

As stated in Hypothesis 2, we would expect the coefficient for the log of median household income variable to be negative as a zip code with lower per capita income should see an increase in the total molecule (both branded and generic drugs combined) being prescribed. To illustrate, Abe Dunn in his paper, 'Drug Innovations and Welfare Measures Computed from Market Demand: The Case of Anti-Cholesterol Drugs', found that "even patients with insurance coverage are sensitive to price, with an estimated elasticity of 1.81" (Morton and Kyle, 788). Given the effect of price elasticity of demand for drugs is magnified for individuals in lower-income brackets, we would expect a reduction in price of prescription drugs and associated copayment rates to result in a larger increase in total volume of the active ingredient prescribed in lower per capita income zip codes.

However, as seen in Table 8, the regression for all the 10 respective drugs only yields coefficients of almost 0 for the key variable of interest (ln_Median_HI). This shows that there is no correlation between the change in prescription behavior of a physician and the per capita

income of the zip code in which the physician is practicing medicine. A possible explanation of the above result is the cost sharing mechanisms in place. In contradiction to what the standard economic theory proposes, due to **"**consumers directly footing an ever-smaller marginal share of prescription drug costs, and insurers bearing the ever-larger residual share" (Berndt, 50), the income level of patients does not have a significant effect on their utilization of prescription drugs. In specific, a physician's prescription behavior might also be influenced by the system of tiered cost sharing employed by alternative and enhanced Medicare Part D coverage plans ("Part D/Prescription Drug Benefits"). For instance, if the branded drug being prescribed before patent expiration was originally in a higher tier of the formulary – the co-payment was lower – then the introduction of its generic substitute wouldn't necessarily have a substantial effect on the beneficiaries' prescription costs.

Furthermore, Medicare Part D beneficiaries can also qualify for Low Income Subsidy, also known as "Extra Help," which is administered by the Social Security Administration ("Part D/Prescription Drug Benefits"). This program helps eligible individuals "pay their Part D expenses, including monthly premiums, co-payments and co-insurance" by providing either full or partial subsidy depending on individuals' respective income and asset levels ("Part D/Prescription Drug Benefits"). Additional co-payment assistance is also provided through the State Pharmacy Assistance Programs (SPAPs). Therefore, given these programs for individuals in lower income groups, the introduction of a cheaper, generic alternative does not always differently impact the prescription behavior of physicians in lower income zip codes.

Still, it is important to note that, unfortunately, most of these results come out to be statistically insignificant even at the 95% confidence level. Therefore, we cannot generalize our findings or conclude with certainty that there is no relationship between the physician's

prescribing behavior and the per capita income of the zip code in which a physician is practicing medicine.

*6.5: Analysis of Therapeutic Substitution Regression*

**reg drug_diff_sub drug_diff_brandgen**

| Drug Name | Constant | diff_brandgen |
|---|---|---|
| Evista | -0.323 *** | 0.2142 *** |
| Focalin XR | 2.19 *** | 1.23 |
| Abilify | 0.1656 *** | 0.785 *** |
| Avodart | 0.433 *** | 0.378 *** |
| Crestor | 0.1322 *** | 0.3512 *** |
| Benicar | 0.3933 *** | 0.2521 |
| Reyataz | -0.0494 ** | 0.7483 *** |

**Table 9: Therapeutic Substitution Regression Results**

Only seven out of the ten branded drugs had therapeutic substitutes during their loss of patent exclusivity. As stated in Hypothesis 3, we would expect the coefficient on the change in total volume of the active ingredient prescribed (diff_brandgen) to be negative as an increase in diff_brandgen should come at the expense of the total volume of the therapeutic substitutes being prescribed (diff_sub). To explain, in the case of competitive markets, we would expect the active ingredient of the leading molecule to steal business from other therapeutic substitutes in the drug class once it becomes available in its generic version. However, contrary to our hypothesis, as seen in Table 9, we notice an increase in diff_brandgen has a strong positive effect of on diff_sub. For instance, a 1% increase in the total volume of Evista and its generic Raloxifene HCL prescribed between one-year pre-patent expiration and one-year post patent expiration leads to a 21.42% increase in the total volume of the therapeutic substitutes prescribed between the same time period. Also, almost all of the coefficients are statistically significant at the 99%

confidence level. This finding shows that the whole market size for the drug class increases around the time of patent expiry of the relevant branded drug. Although counterintuitive, this set of regression results might be explained by other external factors affecting the entire drug class.

According to the results of David Ridley's paper, 'Payments, Promotions, and the Purple Pill', "when co-payments for all competitors move together (the co-payment for a formulary tier change but the treatments remain in the same tiers), demand appears relatively insensitive to price" (Morton and Kyle, 789). Therefore, if the recently introduced generic version of the branded drug is in the same formulary tier as other generic substitutes and the branded drug that has gone off-patent is in the same formulary tier as other branded substitutes, then the demand for therapeutic substitutes does not necessarily decrease after the patent expiration of the branded drug.

Another potential reason for this set of results might be the moral hazard problem. To elaborate, "since patients with insurance coverage do not face the full price of the treatment," the patient demand for pharmaceutical drugs has recently increased over the years (Morton and Kyle, 788). The possibility of this being a reason behind business expansion is confirmed by Danzon and Pauly (2002), in their paper titled 'Health Insurance and the Growth in Pharmaceutical Expenditures', where they conclude that "moral hazard may account for one-fourth to one-half of growth in drug spending" (Morton and Kyle, 788). Additionally, even Ernst Berndt in his paper, 'Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price', argues that such an increase in drug utilization is a function of "increased drug insurance benefit coverage and enhanced marketing efforts, including in particular direct-to-consumer marketing" (Berndt, 49). In his paper that he had published in 2002, Berndt had predicted that once prescription drug insurance coverage was expanded to Medicare beneficiaries, we would see a

"substantial insurance induced growth in prescription drug utilization" (Berndt, 54). Hence, any potential effects of business stealing might have been partially offset by the increase in drug spending in the US. However, this increase in drug spending is solely not enough to explain the regression results.

## 7. Limitations

There are some key limitations in the publicly available prescriber level Medicare Part D datasets that directly undermine the strength of this paper's findings. First, the data on drugs prescribed by the physicians is aggregated on an annual level. The research would have been more impactful if the same analyses was run on quarter-level datasets. Information on the prescription behavior of physicians broken down by quarters – could have provided results that depicted a more gradual progression in the generic share of prescriptions rather than seeing an almost complete switch to generic prescriptions for the branded drugs that lost patent exclusivity.

Second, the results of all three sets of analyses conducted in this paper might be skewed given that the Medicare Part D Prescriber Datasets used in the research drop entries of prescribed drugs with less than 11 total claim counts for every physician in the data file. Consequently, the data used to perform the analyses is not completely reflective of physicians' true prescription behavior. This limitation can be extremely problematic as the research pertains to the rate of generic and therapeutic substitution, and having entries dropped if a given provider prescribes a certain drug under less than 11 Medicare Part D claims (that is if a provider prescribes low volume of a certain drug) might lead to the generation of incorrect values for the change in volume variables. Therefore, future research pertaining to similar questions and hypotheses should use quarter-level data where no entries are excluded. Doing so might generate to more

useful insights in this topic area.

Lastly, the Medicare Part D Prescriber Dataset contains prescription information which is ultimately influenced by two stakeholders – the prescribing physician and the dispensing pharmacy. This is the case as the dataset only records the 'filled prescription' which is the medication actually dispensed to the patient after the pharmacist's review of the original prescription written by the physician. Given that many states in the US "require the pharmacist to fill a prescription with a generic version if one is available" to encourage the use of generic drugs, the current dataset might not be truly reflective of physicians' prescribing behavior (Morton and Kyle, 769).

## 8. Conclusion

This study shows that the generic share of prescriptions in the US has continued to increase since the Hatch-Waxman Act was passed in 1984. For the 10 drugs analyzed in this paper, with patents expiring between 2014-2017, analyzed in this paper, we find an average generic fill rate of 92%. The research provides evidence that most providers almost immediately make the full switch to the generic alternative. This higher than expected rate of switch is potentially due to the presence of generic substitution state laws and maintenance changes to Part D formulary by the Centers for Medicare and Medicaid Services (CMS). We also conclude that if a physician is in the lowest 3 percentile of prescribers (in terms of generic share of prescriptions) for one drug, then that physician is also more likely to be in the lowest 3 percentile for another drug. Additionally, our analysis highlights that there is a higher percentage of male and M.D. credited prescribers in the bottom 3 percentile of prescribers for certain individual or combination of drugs. Also, the prescribers in the bottom 3 percentile tend to have on average

graduated from medical school before other physicians who make complete switch to generic alternatives.

Based on the regression results, I do not find any evidence indicating that per capita income of the zip code that the physician practices medicine has an effect on the total volume of the molecule (branded drug and generic combined) prescribed. As discussed, this finding is possibly due to the cost-sharing mechanisms of the Medicare Part D insurance coverage plans. In addition, co-payment assistance programs such as Low-Income Subsidy (LIS) and State Pharmacy Assistance Programs (SPAPs) work to ensure that income does not serve as a constraint when gaining access to prescription drugs. Furthermore, based on the analyses conducted, contrary to Hypothesis 3, I find that the increase in the total volume of the molecule being prescribed leads to an increase in the total volume of the therapeutic substitutes being prescribed. In this case, the expected effects of business stealing are more than offset by the market expansion of prescription drugs taking place in the US. Moreover, some of these results in our income and therapeutic substitution analyses might be explained by Frank and Salkever's finding that the generic drug's price is approximately 70% that of the branded drug's price at launch which is not significantly lower (Morton and Kyle, 792).

While the findings of this paper are intriguing given the initial hypotheses, these surprising results might be due to the structure of the Medicare Part D Prescriber Dataset as alluded to in the limitations section. I therefore recommend other researchers in this field to conduct similar analyses using other sources of provider-level prescription data. In addition, as in the United States, the responsibility of prescribing and dispensing drugs is often separated, I think it will be useful to examine both written and filled prescription data when conducting future research (Morton and Kyle, 769). Lastly, special emphasis should be laid on studying

whether the prescribing behavior of physicians who administer drugs in their offices differs from those physicians who do not fill their prescriptions.

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