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The Impact Of The 340B Drug Pricing Program On Post-Launch Drug Prices

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by

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July 26, 2017

This thesis, submitted by Bryan Temples Miller in partial fulfillment of the requirements for the degree of Master of Science in Applied Economics from the University of North Dakota, has been read by the Faculty Advisory Committee under whom the work has been done and is hereby approved.

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ABSTRACT

Government mandated drug-pricing policies are an understudied—but potentially significant—factor in the price of drugs. The 340B program is one of the more controversial government-mandated prescription drug discount programs. Proponents argue that the program helps health care systems cover the cost of care they provide for low-income patients. Critics argue that the program unfairly benefits certain health care systems by assuring them lower drug prices, drives consolidation and reduces competition in the health care market, and drives up the cost of drugs. Despite this last claim, there is very little evidence that the 340B program actually impacts post-launch drug prices (i.e., the price of drugs once they are on the market).

This project uses regression analysis to explore how growth in the 340B program—specifically, growth in 340B hospitals that have 340B status because they serve a large number of low-income patients—impacts the cost of drugs administered in the outpatient setting (physician-administered drugs). The project's findings reveal that growth in this subset of 340B hospitals (DSH-340B sites) between 2008 and 2017 is associated with an increase in the price of physician-administered drugs that were either on patent or had not been off-patent for more than four time periods (i.e., 24 months). These findings serve as evidence that should be used to inform policy decisions regarding the future of the 340B program.

CHAPTER 1

INTRODUCTION

The US has some of the highest prescription drug prices in the world (Langreth et al., 2015). For example, 12 of the 13 drugs approved for cancer in 2012 cost more than $100,000 per year (Light and Kantarjian, 2013), and a month supply of Gilenya, a drug for multiple sclerosis, costs more than $5,400. These high prices have unintended consequences such as 1) increasing the taxes individuals pay to fund Medicare, 2) increasing the cost of insurance premiums, and 3) negatively impacting health outcomes.[1]

A number of factors have been identified as contributors to high and rising drug costs including research and development, marketing and advertising,[2] exclusivity rights in the form of patents, and consumer price insensitivity due to third party (i.e., health insurer) payment for drugs. Government mandated drug-pricing policies are a less well-studied—but potentially significant—factor in the price of drugs.

This project explores how the 340B program, a government-mandated prescription drug discount program, affects the post-launch price of drugs administered in the outpatient clinic setting (physician-administered drugs). My hypothesis is that growth in a subset of 340B organizations—namely, health care facilities that have 340B status because they are classified as

[1] A 2013 study by Zafar et al. found that roughly 20% of insured cancer patients failed to adhere to medication instructions because of the high out-of-pocket costs they would have incurred.

[2] In 1998 the pharmaceutical industry spent $12.7 billion on various marketing schemes such as advertisements in medical journals, consumer ads, and free-samples securing it the 34th place in marketing expenditures (Pew, 2013). By 2012, advertising costs had increased to $28 billion, 10 percent of the overall amount spent on prescription drugs that year (Pew, 2013). In 2013, the world's ten largest pharmaceutical companies spent more on marketing and advertising than R&D (Anderson, 2014).

disproportionate share hospital sites (DSH)[3]—has caused the price of physician-administered drugs to rise. The aim of the project is to produce evidence that can be used to inform policy decisions regarding the future of the 340B program.

The paper proceeds as follows. I start by explaining the 340B program and how it can impact drug prices (chapter 2). I then situate my project within the current debate about the impact of the 340B program on health care spending (chapter 3). Next, I discuss the data with which I will be working (chapter 4). I then report the results of several descriptive and statistical analyses of the data (chapter 5). I conclude by discussing the relevance of these findings to the debate about how the 340B program impacts consumers and healthcare spending (chapter 6). The conclusion also reviews several limitations of the project and lays out potential next steps.

[3] Disproportionate Share Hospitals are hospitals that serve a disproportionate number of low-income patients (i.e., 11.75% of their patient population are low-income).

CHAPTER 2

THE 340B PROGRAM

The 340B program was created by the US government in 1992 as a way to ensure that "covered entities" (i.e., certain types of hospitals) could provide care for uninsured and underinsured patients (MedPAC, 2015).[4] Covered entities are organizations that provide significant amounts of care to poor individuals (e.g., disproportionate share hospitals—DSHs) or organizations that meet a specific social need (e.g., rural referral centers, children's hospitals, critical access hospitals, etc.). The program requires drug manufacturers to give covered entities deep discounts on drugs in order for the drugs to be included on the Medicaid formulary. The discounted price allows the covered entities to realize greater profit margins on these drugs because their purchase prices are substantially lower than the prices they are reimbursed by both public and private payers. Covered entities are supposed to use the enhanced profit margin to help cover the cost of care they provide to their low-income, uninsured/underinsured patient populations. To fully appreciate how the 340B program benefits covered entities, it is important to understand how Medicare and commercial insurance companies pay for drugs.

Drug Payment

There are two basic types of drugs—self-administered and physician-administered—and two ways that Medicare and other insurers pay for them—the medical benefit and the pharmacy benefit.

[4] At present, covered entities include public or non-profit disproportionate share hospitals, critical access hospitals, children's hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospitals.

Table 1: Two Types of Drugs

	Self-Administered Drugs	Physician-Administered Drugs
Examples	Anti-depressants, antibiotics, oral anti-cancer drugs, etc.	Infused drugs (e.g., chemotherapy), certain injections, blood transfusions, etc.
Medicare Coverage	Medicare Part D	Medicare Part B
Commercial Payer Coverage (including Medicare Advantage)	Pharmacy benefit	Medical benefit

Most small molecule drugs that are self-administered and prescribed in the outpatient setting are covered by a pharmacy benefit. A pharmacy benefit is an insurance plan that covers outpatient prescription drug costs. The pharmacy benefit works as follows: The clinician prescribes the drug, the patient gets the prescription filled at a pharmacy, and the pharmacy benefit pays the pharmacy for the drug. The pharmacy purchases the drugs they sell from either drug manufacturers or wholesalers and are able to make a profit by charging payers a price above the acquisition cost (see figure 1). Many commercial insurers bundle the pharmacy benefit into patients' basic insurance plans though it is often administered through a pharmacy benefit manager (PBM) such as ExpressScripts or CVS Health. Medicare patients must purchase part D coverage in order to have a pharmacy benefit and the benefit they purchase is usually one that is administered by a PBM.

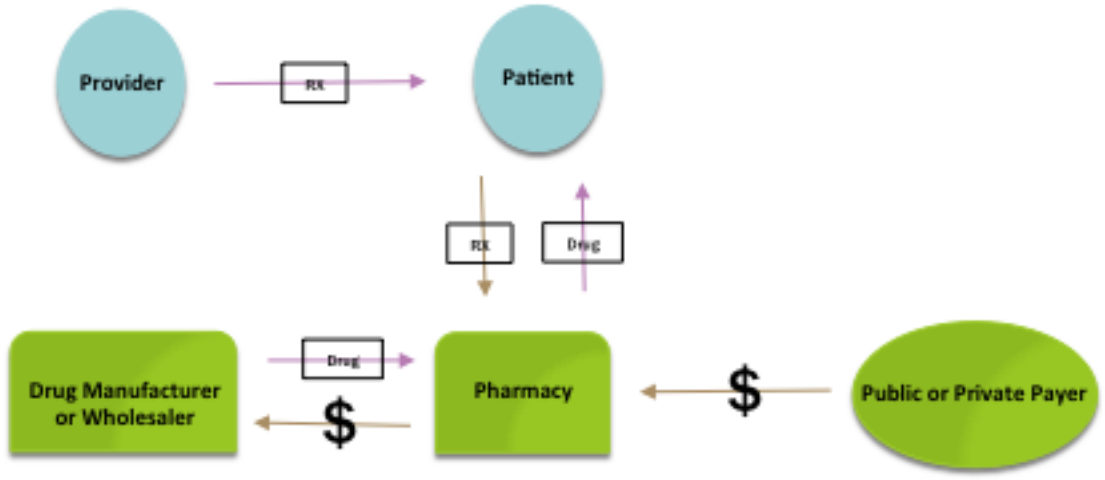

Figure 1. Payment for Self-Administered Drugs Through the Pharmacy Benefit. The provider prescribes the patient a drug and the patient goes to a pharmacy to get the prescription filled. The pharmacy fills the prescription with a drug they have purchased from the drug manufacturer or a

wholesaler. The pharmacy then bills the patient's insurer through the patient's pharmacy benefit manager. The insurer pays the pharmacy benefit manager to conduct all of the negotiating and payment processes for the drug.

Large molecule drugs such as biologics as well as other drugs that are administered in the outpatient clinic setting are generally paid for by a patient's medical benefit.[5] For most privately insured patients, the medical benefit pays for inpatient and outpatient medical services including the medical equipment and drugs administered in these settings. Medicare pays for services provided and drugs administered in the inpatient setting through their part A benefit, and they pay for services provided and drugs administered in the outpatient setting (i.e., physician-administered drugs) through their part B benefit. The medical benefit works as follows: The clinician provides a service or administers a drug, they bill the insurer for the service or administered drug, and the insurer pays the clinician for the rendered service or administered drug. When it comes to physician-administered drugs, this practice is referred to as the "buy-and-bill" method (see figure 2) because the provider buys the drug from the manufacturer or wholesaler, administers it to the patient, and then bills the patient's payer for the drug.

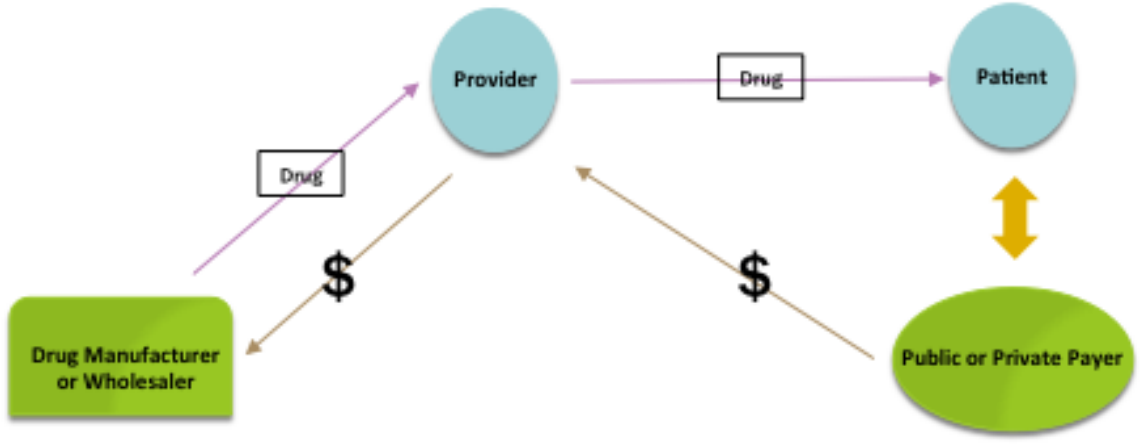

Figure 2. The Buy-and-Bill Method. The provider purchases the drug from the drug manufacturer or wholesaler. The provider then administers the drug to a patient and bills the patient's insurer (i.e., the public or private payer) for the cost of administering the drug and the cost of the drug. Because

[5] Most physician-administered drugs are infused or injected.

payers do not know the amount providers pay for these drugs, they will often negotiate with the provider to reimburse them at a fixed percentage of the average sales price of the drug.

The 340B Benefit

Providers with 340B status benefit because they are guaranteed a reduced price when acquiring 340B eligible drugs. A 2015 MedPAC report, for instance, found that the minimum discount covered entities receive is 22.5% of the drug's average sale price (ASP). Thus, a drug that has an average sales price of $1,000 would only cost a 340B program $775 to acquire.

Because providers do not sell self-administered drugs directly to patients (and do not receive payment for these drugs from the insurer), they must pursue another route to realize the benefit of the price reduction on these drugs. The solution is that they contract with a pharmacy. There are several ways that contract pharmacies can operate. The following is a basic model: the provider purchases the drugs at the reduced 340B price from the manufacturer or wholesaler and has them delivered to the contract pharmacy. After the pharmacy sells the drug to the patient and is paid by the insurer, the pharmacy reimburses the provider the retail sale price of the drug minus an order management fee that the pharmacy keeps.

Providers with 340B benefit from physician-administered drugs in a slightly different, but more straight forward, manner. As already mentioned, for physician-administered drugs, the provider engages in the buy-and-bill process—i.e., the provider purchases the drug from either the manufacturer or a distributor, and then, after administering the drug to the patient, the provider bills the patient's insurer, who pays for the drug. Providers with 340B benefit because they get the physician-administered drugs at a lower price, but insurers reimburse them at the normal, fixed rate. For example, assuming the minimum discount covered entities receive is 22.5% of the drug's average sale price (ASP), a provider with 340B status who is reimbursed for physician-administered drugs at ASP + 6%, the amount Medicare generally reimburses at, will have a profit margin of at least 28.5% on these drugs.

CHAPTER 3

SITUATING THE CURRENT PROJECT

In recent years, there has been increasing scrutiny of the 340B program. While there is some evidence that the 340B program improves care for some low-income patient populations (Castellon et al., 2014), opponents and skeptics argue that it introduces incentives that conflict with providing optimal patient care at the lowest cost. And there is some evidence that it has, in fact, contributed to the rise in overall health care spending and inappropriate drug use.

A 2015 Government Accountability Office (GAO) study, for instance, found that spending at 340B hospitals (i.e., hospitals that receive 340B pricing) was substantially higher and that these hospitals prescribe "more drugs or more expensive drugs" than non-340B hospitals. Importantly, the GAO notes that the difference in spending was not explained by differences in patients' health—i.e., it was not because 340B hospitals were treating sicker patients.[6] The study concluded that the 340B program incentivizes greater drug use and/or the use of more expensive drugs. Another study by Conti and Bach (2014) found that 340B organizations registered after 2004 were more likely to be located in wealthier communities with better payer mixes (i.e., higher rates of privately insured individuals) than those registered prior to 2004, a finding that is seemingly inconsistent with the program's original intent to help impoverished patients. Finally, research sponsored by the Community Oncology Alliance and the Berkeley Research Group used several data sets including CMS Medicare Outpatient Claims data and data on 340B sales from several drug manufacturers to identify the 340B program as a major driver of consolidation in the health care provider market,

[6] The study did not look at the connection between spending and health outcomes so it is possible that the increase in spending led to better health outcomes.

especially hospital acquisition of private oncology practices (Vandervelde, 2014).[7] Many believe that increased consolidation causes health care costs to rise because care provided in the hospital setting is more expensive than that provided in private practices (Gaynor and Town, 2012).

Other critics of the program argue it plays a role in driving up drug prices. The idea behind this line of criticism is that drug manufacturers simply shift the cost of the 340B program by increasing the price they charge for drugs. Because the 340B program has been rapidly growing, these skeptics argue that the impact of the program on drug prices is also rapidly increasing.

Given the interest in drug prices and the intuitive reasoning for how growth in the 340B program could impact prices, it is surprising that relatively little work has been done in this area. It is even more surprising given that previous research showed that government mandated drug discount programs likely lead to higher drug prices. For example, a 1996 study by the Congressional Budget Office (CBO) found that drug manufacturers increased the best price they offered purchasers by almost 17% to offset a drug rebate they were required to provide state Medicaid programs. The one paper that discusses the impact of the 340B program on drug prices did not conduct an analysis to identify the program's impact on post-launch drug prices. Rather, Howard et al. (2015) used least squares regression to show that a 10% annual increase in the launch price of anti-cancer drugs is not attributable to common drug characteristics, and they suggested that the 340B program may be partially responsible for the increase as it may encourage drug manufacturers to raise launch prices to help cover revenue losses they expect to incur from the 340B discounts.[8]

As Howard et al. (2015) note, drug manufacturers may set launch prices high so they can avoid having to raise post-launch prices to offset the impact of the 340B program. This is likely a

[7] A 2017 paper by Alpert et al. looking at the impact of 340B expansion under the ACA found that ACA-expansion 340B entities—i.e., entities that got 340B status due to the ACA expansion—explains very little of the recent consolidation in the oncology space. This finding, however, fails to negate the earlier finding from the Community Oncology Alliance and Berkeley Research Group because DSH 340B entities (i.e., entities that have 340B status because they serve a significant number of low-income patients) were not significantly impacted by the ACA expansion, and these are the 340B entities that are most likely to provide cancer care and, therefore, the most likely to purchase private oncology practices.
[8] Howard et al. 2015 used the ASP Drug Pricing Files to identify launch prices.

strategic decision meant to avoid negative publicity. After all, large price increases post-launch are often seen as attempts to price-gouge patients and tend to be received negatively in the press. As an example, one need only consider the publicity Martin Shrkeli and Turing Pharmaceuticals received after their massive price hike (over 5,000%) on Daraprim, a drug used to treat AIDs-related and AIDs-unrelated toxoplasmosis. But not all post-launch price increases are large enough to trigger a negative publicity campaign. Indeed, the price increases manufacturers institute to recoup revenue lost through the 340B program may be quite small. Over time, however, these small increases add up and can have a significant impact on consumers.

To my knowledge, no research to date has looked at how the 340B program affects post-launch drug prices. Thus, there is a gap in the knowledge necessary to understand how the 340B program impacts consumers and the health care system. This project aims to fill that gap by analyzing how growth in a subset of 340B entities—namely, DSH-340B sites—affects the post-launch price of physician-administered drugs.

CHAPTER 4

DATA DESCRIPTION

In this chapter, I discuss the data sources I use to construct the panel data set to test my hypothesis that growth in the number of DSH-340B sites causes the price of physician-administered drugs to rise. The panel consists of 9.5 years of pricing data on 35 drugs. Drug price serves as the dependent variable, the number of DSH-340B sites as the independent variable of interest, and a slew of other variables as controls.

Physician-Administered Drugs

The sample consists of 35 physician-administered drugs (see table 2). The sample consists entirely of this type of drug because there is available price data (CMS's ASP Drug Pricing Files, discussed below) that has been used in previous drug price research. This data exists because CMS requires all drug manufacturers that wish to be listed on the Medicaid formulary to submit quarterly average sales prices (ASP) for their physician-administered drugs. Medicare uses this data to set the rate that they will reimburse providers, and they make the data publicly available to provide transparency to beneficiaries, providers, and the public.

The sample does not include any self-administered drugs because data on pricing for this class of drugs is simply too challenging to locate or too costly to acquire. Since Medicare doesn't directly reimburse pharmacies for self-administered outpatient drugs (the pharmacy benefit manager administering the part D plan does that), they don't require drug manufacturers to submit data on the average sales prices of these drugs. And, the pharmacies that purchase drugs and then

Table 2. Physician-Administered Drugs in Entire Sample and Price Changes

Drug Name	Brand Name	Primary Disease	Overall Price Change[9]	Periods	Annual Price Change	Patent Protection
Adalimumab	Humira	Arthritis	171%	19	18%	Expired pd 18
Afilbercept (optical)	Eylea	Ocular	0%	6	0%	Yes
ziv-Afilbercept	Zaltrap	Cancer	-14%	7	-4%	Yes
Basiliximab	Simulect	Transplant	133%	19	14%	Yes
Bevacizumab	Avastin	Cancer	19%	19	2%	Yes
Bortezomib	Velcade	Cancer	38%	19	4%	Expired pd 19
Cabazitaxel	Jevtana	Cancer	11%	11	2%	Expired pd 17
Capecitabine oral	Xeloda	Cancer	-45%	15	6%	Expired pd 12
Carboplatin	Paraplatin	Cancer	-57%	19	-6%	No
Certolizumab pegol	Cimzia	Crohns	105%	15	14%	Yes
Cetuximab	Erbitux	Cancer	19%	19	2%	Expired pd 17
Cisplatin	Platinol	Cancer	-19%	19	-2%	No
Docetaxel	Taxotere	Cancer	-76%	19	-8%	Expired pd 5
Eculizumab	Soliris	Bd	34%	17	4%	Yes
Everolimus oral	Afinitor	Cancer	33%	11	6%	Yes
Filgrastim G-CSF	Neupogen	Cancer	48%	16	6%	Expired pd 12
Filgrastim tbo	Granix	Cancer	-12%	6	-4%	Yes
Golimumab	Simponi	Arthritis	0%	6	0%	Yes
Infliximab	Remicade	Arthritis	57%	19	6%	Yes
Ipilumimab	Yervoy	Cancer	11%	11	2%	Yes
Methotrexate	Trexall	Arthritis	0%	19	0%	No
Necitumumab	Portrazza	Cancer	.	1	.	Yes
Nivolumab	Opvido	Cancer	3%	3	2%	Yes
Paclitaxel inj	Taxol	Cancer	-57%	19	-6%	No
Panitumumab	Vectibix	Cancer	38%	19	4%	Yes
Pefgfilgrastim	Neulasta	Cancer	75%	19 (missing time pd 4)	7.9%	Expired pd 16
Pembrolizumab	Keytruda	Cancer	3%	3	2%	Yes
Pemetrexed	Alimta	Cancer	38%	19	4%	Yes
Pentostatin	Nipent	Cancer	0%	19 (missing time pd 4 & 6)	0%	No
Ramucirumab	Cyramza	Cancer	3%	3	2%	Yes
Ranibizumab	Lucentis	Ocular	0%	19	0%	Yes
Rituximab	Rituxan	Cancer	57%	19	6%	Expired pd 18
Sipuleucel-T	Provenge	Cancer	11%	11	2%	Yes
Trastuzumab	Herceptin	Cancer	57%	19	6%	Yes
Topotecan (oral)	Hycamtin	Cancer	14%	7	4%	No (not available until pd 8 when it went off patent)

[9] The overall and annual price changes noted here are not adjusted to account for inflation.

are reimbursed by pharmacy benefit managers on behalf of Medicare and commercial insurers rarely share their acquisition costs as this is considered a confidential part of their pricing contracts. Thus, there is no publicly available data on the pricing of self-administered drugs like there is for physician-administered drugs.

It is worth noting that many of the drugs in the sample are very costly—well over $1,000 per treatment. The fact that the sample is largely comprised of high-cost drugs could bias the project's findings. For instance, it could be that the findings only apply to high-cost physician-administered drugs. I discuss this point in the conclusion when I review limitations of the project.

ASP Drug Pricing Files

The physician-administered drug prices (i.e., drug prices) are from the CMS ASP (average sales price) Drug Pricing Files. These files, which are updated every three months, provide the ASP of all physician-administered drugs for which Medicare reimburses providers.[10] As already noted, because the acquisition cost of these drugs varies by purchaser and is kept confidential, the Medicare ASP is the best indicator of the drugs' prices.

DSH-340B Sites

The explanatory variable of interest is the subset of 340B covered entity sites that have that status because they are disproportionate share hospitals or outpatient departments of a disproportionate share hospital (i.e., DSH-340B sites).[11] To identify the number of DSH-340B sites for each year, I analyzed the registry of 340B covered entities maintained by Health Resources and Services Administration (HRSA). The registry's annual count is used as the site count for the first

[10] The ASP for each drug is a per-unit price, and different drugs are priced at different units. For example, a unit of Avastin is 10mg and it is dosed at 10mg/kg, while a unit of Humira is 20mg and it is dosed at 40mg for adults. Thus, in 2017, a dose of Humira for an adult would cost $1,068.52 and a dose of Avastin would cost $5,449.93.

[11] A single 340B covered entity can have multiple covered entity sites. For instance, Hospital X is a covered entity because it has 340B status and the five hospital outpatient departments located at different addresses that are part of the Hospital X system are covered entity sites, meaning that the drugs they prescribe are eligible for 340B pricing.

half of the year (January-June). To determine the number of sites for the second half of the year (July-December), I subtracted the current year's count from the following year's count, divided this by 2 and then added this to the current year's count.[12] Figure 3 illustrates the number of DSH-340B sites for the period January 1, 2008- January 1, 2017.

Figure 3. 10-Year Growth in DSH-340B Sites (January 1, 2008 to January 1, 2017)

The analysis focuses on DSH-340B sites because growth among this group is the most likely to impact the price of physician-administered drugs. This is because DSH-340B sites are the type of 340B entity that provides significant amounts of physician-administered drug services—e.g., infusions, transfusions, injections.

It is worth pointing out that the current analysis does not include freestanding cancer hospitals with 340B status. This may seem odd given that freestanding cancer hospitals provide a substantial number of physician-administered drugs to patients. However, given that there is only

[12] Formula: [{number of DSH-340B sites (year t+1) - number of DSH-340B sites (year t)}/2] + number of DSH-340B sites (time period t)= number of DSH-340B sites (July-December time period).

one freestanding cancer hospital—City of Hope—with 340B status, the actual number of physician-administered drugs provided by 340B freestanding cancer hospitals is likely minimal. Leaving them out is unlikely to bias the project's findings.

Time Periods

The data set covers 19 time periods. Each time period covers six months from January 1, 2008 to January 1, 2017. The six-month periods run from January to June (e.g., period 1) and July to December (e.g., period 2). The six-month blocks coincide with the Medicare pricing report for the first quarter (prices for January through March) and the third quarter of the year (prices for July through September). Some drugs do not have 19 periods of data as they were either brought to market or taken off market between January 1, 2008 and January 1, 2017.

CHAPTER 5

RESULTS

The following chapter reviews the results of several analyses. The first section provides descriptive analysis of DSH-340B sites and the physician-administered drugs in the sample. The second section reports results from the statistical analysis of the data.

Descriptive Analysis

DSH-340B Sites

A review of the data reveals that the number of DSH-340B sites grew by 744% over the 9.5 year period (see figure 3). Table 3 offers year over year growth. While the years 2011 and 2012 experienced the greatest percentage growth, the number of DSH-340B sites increased by at least 2,000 annually between 2011 and 2017. Growth is primarily due to hospitals acquiring private practices throughout the period, and not to a larger number of hospitals receiving DSH-340B status (Vandervelde , 2014).

It's important to note that the period 2011-2015 was a time of increased consolidation across health care. Hospitals with 340B status and those without sought to acquire private practices or other hospitals to gain economics of scale, increase negotiating power with commercial payers, and secure referrals (Ginsburg, 2016; Alpert et al., 2017). This increase in consolidation was partially a response to commercial payers' attempts to gain greater negotiating power through mergers and acquisitions and rein in costs by decreasing network size (i.e., the number of health care providers in the insurer's network). As noted earlier, there is some evidence that hospitals

with 340B status were more likely to acquire private practices than those without 340B status during this period (Avalere Health LLC, 2016).

Table 3. Percent Change in number of DSH-340B Sites (January 1, 2008 to January 1, 2017)

2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
15%	14%	9%	66%	49%	38%	28%	23%	11%

Drug Prices

A review of the period price for each drug from January 2008 to January 2017 reveals extensive variation. Table 3 reports the percent price change for each drug in the sample. Not all drugs were available for the entire 19 time periods as some came to market during this time while others went off market. Commonly-used, patent-protected drugs like Adalimumab (mean price $1,068.52) and Bevacizumab (mean price $5,449.93) increased substantially over the 9.5 year period.[13] As figures 4 and 5 illustrate, prices shot up around 2012, the tenth time period. This coincides with a period of increased growth in the number of DSH-340B sites (see figure 3 above). In general, the price of drugs that were on-patent as of 2008 increased or stayed steady.

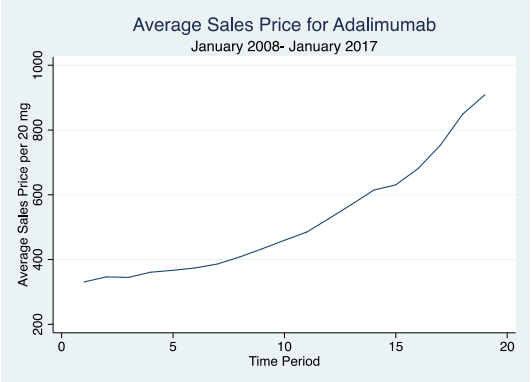

Figure 4. Average Sales Price for Adalimumab (January 1, 2008-January 1, 2017)

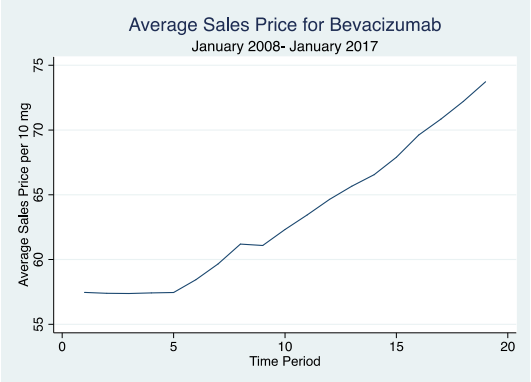

Figure 5. Average Sales Price for Bevacizumab (January 1, 2008-January 1, 2017)

[13] Mean price formula: (drug_price pd1 + drug_price_pd2 +… drug_price_pdk)/K adjusted to dosage required for an 80kg adult.

Relatively new drugs, such as Nivolumab (mean price $6,291.72) and Pembrolizumab (mean price $9,383.50), showed very little price fluctuation (see table 3). It is possible that the launch prices of these drugs were set with the impact of 340B in mind and, therefore, there has been less need to increase the post-launch prices of these drugs. This explanation is consistent with the Howard et al. (2015) hypothesis regarding the impact of 340B on drug launch prices. It is also possible that these drugs are so new that the manufacturers have yet to increase the prices.

Carboplatin and Methotrexate, two older drugs whose patents expired prior to 2008, experienced substantial price decreases over the 9.5 year period. Figure 6 illustrates price changes for Carboplatin (mean price $74.30), which was off-patent for the entire 9.5 year period. Interestingly, the greatest price change for this drug occurred prior to the explosion of growth in DSH-340B sites. The initial drop followed by relative stability could be due to entry of generic drugs. Methotrexate (mean price $4.76), a drug that has been available since the 1940s experienced a sharp decline during the first ten time periods and then rebounded, only to drop again (figure 7).

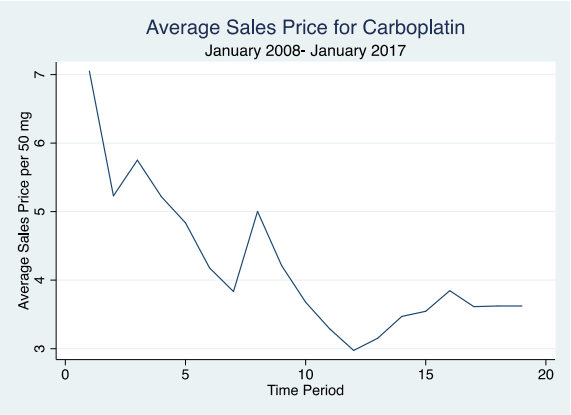

Figure 6: Average Sales Price for Carboplatin (January 1, 2008-January 1, 2017)

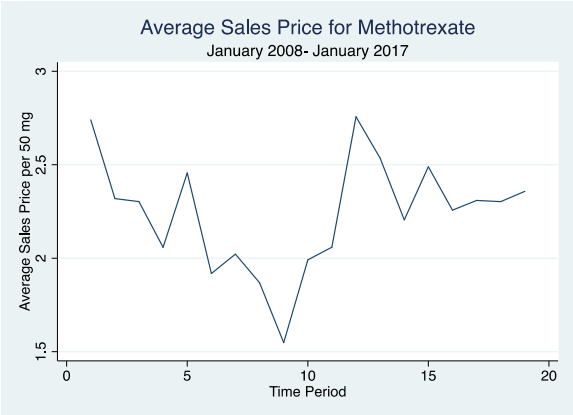

Figure 7: Average Sales Price for Methotrexate (January 1, 2008-January 1, 2017)

Figure 8 illustrates how patent-expiration can affect a drug's price. Capecitabine oral (mean price $127.80) went off patent around the 12th time period. Its price rose steadily until the 14th

period, and then it entered a steady decline. Finally, the price of Filgrastim (mean price $352) rose until the 13th time period where it plateaued (figure 9).[14] The plateau coincides with the drug's patent expiration (12th time period).

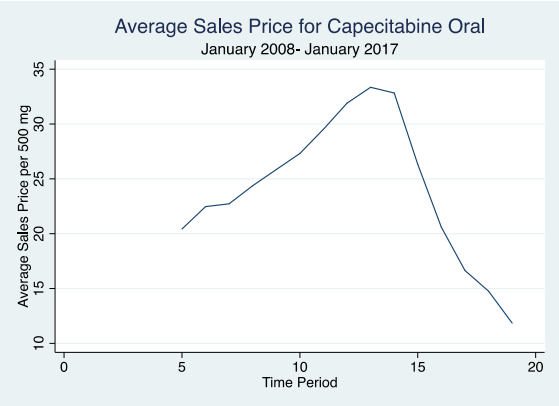

Figure 8: Average Sales Price for Capecitabine (January 1, 2008-January 1, 2017)

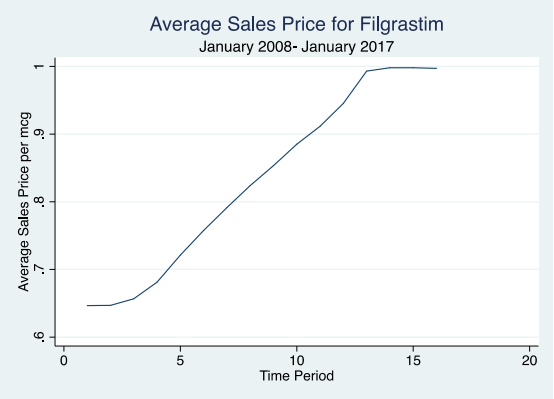

Figure 9: Average Sales Price for Filgrastim (January 1, 2008-January 1, 2017)

Statistical Analysis

Certain subsets of drugs are more likely to be impacted by growth in the 340B program, so the analysis was run on five different groups (see table 4). The first group (group A) included all drugs in the sample, and addresses the question of whether DSH-340B expansion impacts all drugs, regardless of whether they are patent-protected or not.

Drugs that are off-patent and have generic substitutes may respond differently to growth in the number of DSH-340B sites, so the analysis was run on two other groups (group B and group C) that excluded off-patent drugs. Group B only excluded drugs that were off-patent for the entire 9.5 year period.

The third group (group C) excluded drugs that were off-patent for more than four time periods (24 months). Regression analysis looking at a large number of lags on patent-expiration

[14] ASP data for Filgrastim was not available for time periods 17, 18, and 19.

indicated that the prices for drugs that went-off patent during the 9.5 year period did not usually start to decrease until the fifth time period after patent expiration. The delay in price reduction associated with patent expiration is probably due to the time lag between patent expiration and generic entry (i.e., it often takes several months to years for generics to get approval and enter the market) and the time lag needed to obtain pricing data that reflects generic entry (CMS sets ASP on the previous quarter's sales data, so the impact of generics on ASP will not be reflected immediately). The drugs in group C provide insight into how growth in the number of DSH-340B sites impacts drugs that do not have generic substitutes or whose prices have not yet been impacted by generics in the market.

The fourth group (group D) includes drugs that were top 20 bestsellers in 2016. All of these drugs were patent-protected in 2008 if they were on the market. Several of the drugs in this sample did not come to market until after 2008. This group is important because these drugs contribute such a large amount to their manufacturers' revenue streams. Given their contribution, manufacturers may be more inclined to raise the prices of these drugs than the prices of drugs that make a smaller revenue contribution to recover money lost through the 340B program. Accordingly, growth in the number of DSH-340B sites should have a more significant impact on this group—both practically and statistically—than it does on groups A, B, or C.

The fifth and final group consists of all drugs that were off-patent for more than four periods. This group is used to provide insight into how growth in the number of DSH-340B sites impacts the price of drugs that aren't patent-protected and have generic substitutes in the market.[15]

[15] The group only includes drugs off-patent for more than four periods to ensure generics have been on the market long enough to impact price.

Table 4. Drugs Included in Each Group

Group A Entire Sample	**Group B Entire Sample Excluding Drugs Off Patent Before 2008**	**Group C Entire Sample Excluding Drugs Off Patent More Than 4 Periods**	**Group D Blockbuster Drugs**	**Group E Drugs Off Patent More Than 4 Periods**
Adalimumab	Adalimumab	Adalimumab	Adalimumab	
Afilbercept (optical)	Afilbercept (optical)	Afilbercept (optical)	Afilbercept (optical)	
ziv-Afilbercept	ziv-Afilbercept	ziv-Afilbercept		
Basiliximab	Basiliximab	Basiliximab		
Bevacizumab	Bevacizumab	Bevacizumab	Bevacizumab	
Bortezomib	Bortezomib	Bortezomib		
Cabazitaxel	Cabazitaxel	Cabazitaxel		
Capecitabine oral	Capecitabine oral			Capecitabine oral
Carboplatin				Carboplatin
Certolizumab pegol	Certolizumab pegol	Certolizumab pegol		
Cetuximab	Cetuximab	Cetuximab		
Cisplatin				Cisplatin
Docetaxel	Docetaxel			Docetaxel
Eculizumab	Eculizumab	Eculizumab		
Everolimus oral	Everolimus oral	Everolimus oral		
Filgrastim G-CSF	Filgrastim G-CSF		Filgrastim G-CSF	Filgrastim G-CSF
Filgrastim tbo	Filgrastim tbo		Filgrastim tbo	Filgrastim tbo
Golimumab	Golimumab	Golimumab		
Infliximab	Infliximab	Infliximab	Infliximab	
Ipilumimab	Ipilumimab	Ipilumimab		
Methotrexate				Methotrexate
Necitumumab	Necitumumab	Necitumumab		
Nivolumab	Nivolumab	Nivolumab		
Paclitaxel inj				Paclitaxel inj
Panitumumab	Panitumumab	Panitumumab		
Pefgfilgrastim	Pefgfilgrastim	Pefgfilgrastim	Pefgfilgrastim	
Pembrolizumab	Pembrolizumab	Pembrolizumab		
Pemetrexed	Pemetrexed	Pemetrexed		
Pentostatin				Pentostatin
Ramucirumab	Ramucirumab	Ramucirumab		
Ranibizumab	Ranibizumab	Ranibizumab		
Rituximab	Rituximab	Rituximab	Rituximab	
Sipuleucel-T	Sipuleucel-T	Sipuleucel-T		
Trastuzumab	Trastuzumab	Trastuzumab	Trastuzumab	
Topotecan (oral)				Topotecan (oral)

The analysis of the panel data set was conducted using a random-effects generalized least squares model (see model specification below). The model uses log transformations of both real drug prices,[16] the dependent variable, and number of DSH-340B sites, the independent variable of interest. The model includes controls for:

1. Patent expiration and two lags of patent expiration because off-patent drugs may respond differently to changes in the number of DSH-340B sites than patent-protected drugs
2. Two lags of a dummy variable for the time period that the Patient Protection and Affordable Care Act (PPACA) was passed because this program expanded the scope of the 340B program and may have induced manufacturers to raise prices more aggressively
3. A dummy variable for periods when Democrats controlled both the house and the presidency because manufacturers may preemptively raise drug prices to counteract cost-shifting and drug cost-containment policies they assume Democrats will pursue when they have control
4. The unemployment rate for each period because changes in unemployment translate to changes in the size of the population of low-income individuals and this can impact the number of hospitals eligible for DSH-340B status

GLS Random Effects Model

$$\Upsilon_{log\_of\_real\_drug\_price} = \beta_{log\_of\_DSH\_340B\_entities} + \beta_{patent\_expiration\_period} + \beta_{lag\_1\_of\_patent\_expiration\_period} + \beta_{lag\_2\_of\_patent\_expiration\_period} + \beta_{lag\_1\_of\_PPACA} + \beta_{lag\_2\_of\_PPACA} + \beta_{unemployment} + \beta_{democratic\_control} + \varepsilon$$

The random effects model was chosen after running the hausman test and finding that the null hypothesis—that individual level effects are appropriately captured by the random effects model—could not be rejected (prob >chi^2 = 0.2882).

[16] The real price of drugs was obtained using CPI. All prices were indexed to January 2008.

Table 5 reports the results from the GLS random effects model.[17] The most relevant finding is that the number of DSH-340B sites is significant for groups C and D. For group C, a 1% change in the number of DSH-340B sites is associated with a 0.11% change in drug price. While this seems modest, it actually translates into a fairly substantial price increase given that growth in sites ranged between 66% and 11% annually over the 9.5 year period. For example, the 33% growth that occurred in the first half of 2011 translates into a 3.6% increase in drug price for this period. See table 6 for the actual dollar amount of the increase for select drugs.

For group D, a 1% change in the number of DSH-340B sites is associated with a 0.16% change in drug price (5.3% price increase given a 33% increase in the number of DSH-340B sites). This suggests that the impact of DSH-340B growth is slightly greater on group D drugs (blockbuster drugs) than group C drugs. This finding seems reasonable given that these drugs contribute so much revenue and manufacturers are probably looking to protect these drug prices more aggresively.

Growth in 340B entities is negatively associated with the price of drugs in group E (i.e., drugs off-patent for more than four periods). A 1% increase in the number of DSH-340B sites is associated with a 0.36% decrease in drug price (11.9% price decrease given a 33% increase in the number of DSH-340B sites). Despite this finding, it is unlikely that growth in the number of DSH-340B sites is actually causing the price drop for group E drugs. The more likely explanation is that expanded health insurance coverage and the aging of the population which is leading to increased disease incidence[18] is increasing demand for these drugs. And, because there are relatively few

[17] The analysis was run using several variants of this model to test the significance of other potential control variables. The first model (appendix A) replaced the log of DSH-340B sites with the first lag of this variable because it is possible that growth in the number of DSH-340B sites has a delayed affect on drug prices. The model was run to explore whether the lag of the independent variable of interest (number of DSH-340B sites) has a greater impact on drug prices than the present period independent variable. The second model included dummies for time period 3 through time period 19 (Appendix B). The third model added a time trend variable to the base model (Appendix C). The fourth model added a lag of the dependent variable to construct a time series model (Appendix D). The results from these models are included as appendices.

[18] Expanded health insurance coverage is largely due to passage and implementation of the Patient Protection and Affordable Care Act (PPACA). Increasing cancer incidence is likely the primary driver here given that most drugs in the sample are anti-cancer drugs.

barriers to market entry for generics since these drugs are off-patent, the increase in demand is causing the price of group E drugs to drop. Unfortunately, the model doesn't control for increasing disease incidence or changes in health insurance coverage so it is difficult to properly assess this hypothesis.[19]

Growth in the number of DSH-340B sites was insignificant for groups A and B. Given what we know about the negative association between off-patent drug prices and number of DSH-340B sites (group E findings) and the positive association between on-patent drug prices and number of DSH-340B sites (group C and group D findings), this is not terribly surprising. After all, group A and group B include both off-patent drugs and on-patent drugs. Because the model didn't control for increasing demand[20], the DSH-340B variable may have picked up the effect of this—i.e., the decrease in off-patent drug prices. If this is what happened, then the impact of DSH-340B sites may have been counterbalanced by the impact of demand and the resulting estimate for the DSH-340B variable may have been subject to ommitted variable bias. Thus, we need to interpret the findings regarding group A and group B drugs cautiously.

The Patient Protection and Affordable Care Act (PPACA) is associated with a very small, delayed increase in the price of drugs in group C and D. Manufacturers may have increased prices for the drugs in these two group in anticipation of declining revenue resulting from the PPACA's expansion of the 340B program. The PPACA increased the size of the 340B program by making it possible for critical access hospitals and freestanding cancer hospitals[21] that meet DSH requirements to get 340B status.[22] The PPACA's expansion of 340B may not have affected the other

[19] Importantly, growth in disease incidence is unlikely to impact the price of drugs in group C and group D because there are barriers to entry since these drugs are either patent-protected or just off patent.
[20] Increasing demand due to increasing disease incidence and expanded health insurance coverage.
[21] Freestanding Cancer hospitals are specialty hospitals that only treat cancer patients. At present, there are only eleven freestanding cancer hospitals in the United States, and only one of them meets the DSH requirements and has 340B status.
[22] The estimated lagged impact of the PPACA is probably so small because expansion of the 340B program under the PPACA was unlikely to significantly impact drug manufacturers' revenue since most critical access hospitals do not provide a large number of physician-administered drugs and there is only one freestanding cancer hospital that meets the DSH requirements.

Table 5. Regression Results for GLS Random Effects Model

Log of Real Drug Price	**Group A**	**Group B**	**Group C**	**Group D**	**Group E**
Log of number of DSH-340B entities	-0.0614 (0.074)	0.0245 (0.0832)	**0.1161*** (0.0294)**	**0.1585*** (0.0334)**	**-0.3556*** (0.1313)**
Patent Expiration period	**0.3024** (0.1218)**	**0.2804* (0.1507)**	0.0525 (0.0693)	**0.1163* (0.0645)**	
Lag 1 of patent expiration period	**0.3676*** (0.1218)**	**0.3458** (0.1615)**	0.1071 (0.0846)	**0.1472** (0.0688)**	
Lag 2 of patent expiration period	**0.3611** (0.1665)**	**0.3299* (0.1841)**	0.0224 (0.067)	**0.0776* (0.0457)**	
Lag 1 of Patient Protection and Affordable Care Act	-0.1203 (0.1207)	0.0025 (0.023)	0.0071 (0.0128)	**0.0174* (0.0097)**	-0.3464 (0.3386)
Lag 2 of Patient Protection and Affordable Care Act	0.0059 (0.0421)	-0.0103 (0.0422)	**0.0421*** (0.0085)**	**0.0591*** (0.0111)**	-0.0212 (0.1080)
Unemployment rate	-0.023 (0.0198)	0.0129 (0.0092)	-0.0028 (0.0053)	-0.0031 (0.0046)	-0.0658 (0.0537)
Democratic control of presidency and house	0.1399 (0.1377)	-0.0278 (0.0353)	0.0306 (0.014)	**0.0283* (0.0158)**	0.374 (0.3996)
Constant	4.6105 (0.6264)	3.9464 (0.7551)	3.7 (0.4659)	3.074 (1.0204)	5.4697 (1.409)
<u>Key</u> P<10% * P<5% ** P<1% ***	Observations: 488 Groups: 35 R-sq (within): 0.0526 Prob>chi2= 0.000	Observations: 388 Groups: 29 R-sq (within): 0.1160 Prob>chi2= 0.000	Observations: 332 Groups: 25 R-sq (within): 0.4892 Prob>chi2= 0.000	Observations: 141 Groups: 9 R-sq (within): 0.7612 Prob>chi2= 0.000	Observations: 156 Groups: 10 R-sq (within): 0.1735 Prob>chi2= 0.0444

Table 6. Impact of 33% Growth in DSH-340B Sites on Mean Drug Price

	Drug Group	Mean price per unit	Price for 80KG patient	Group C 3.6% price increase	Group D 5.3% price increase	Group E 11.9% price decrease
Adalimumab	C, D	534.26 /20mg	$1,068.52	$38.47	$56.63	-$127.15
Cabazitaxel	C	148.82 /1mg	$7,441	$267.88	$394.37	-$885.48
Carboplatin	E	5.16 /50mg	$74.30	$2.67	$3.94	-$8.84
Filgrastim	D, E	0.88 /1mcg	$352	$12.67	$18.66	-$41.89
Infliximab	C, D	70.47 /10mg	$1,128	$40.61	$59.78	-$134.23
Pegfilgrastim	C, D	3131.39 /6mg	$3,131.39	$112.73	$165.96	-$372.64
Pentostatin	E	1527.48 /10mg	$1,221.98	$43.99	$64.76	-$145.42
Trastuzumab	C, D	79.28 /10mg	$3,805.44	$137	$201.69	-$452.85

drug groups because they include off-patent drugs that may have experienced a price decrease due to greater demand created by increasing disease incidence and expansion of insurance coverage.

The analysis also reveals that patent expiration is associated with a price increase for group A, group B, and group D drugs. The period a drug goes off patent is associated with a 30% price increase for group A, a 28% price increase for group B, and a 12% price increase for group D. In addition to its association with increased price in the current time period, patent expiration continues to be asssociated with a price increase for at least two more periods in these groups. As noted earlier, for most drugs that went off-patent during the 9.5 year period, prices continued to rise for three or four periods after patent expiration and only started decreasing thereafter (e.g., see Figure 8: Capecitabine oral). The post-patent expiration price increase is likely due to two things: 1) delayed market entry because generic manufacturers need to obtain approvals, licenses, and set up production, and 2) the name-brand manufacturer attempting to extract as much revenue as possible from the drug before generics enter the market. The price decline occuring several periods after patent expiration reflects the actual entry of generics into the market. The conclusion discusses the issue of manufacturer game-playing around patent-expiration in a bit more detail.

Having a Democratic controlled house and presidency was only significant for group D drugs. Democratic control of these branches of government is associated with a small price increase—about 0.02%. One explanation for this finding is that Democrats are more likely to pass laws that attempt to cross-subsidize health care, such as expanding the scope of the 340B program, and if these laws attempt to shift costs to drug manufacturers, they may simply shift them on to consumers in the form of higher drug prices. While statistically significant, the coefficient on this variable is practically insignificant.

The unemployment rate was insignificant across all drug groups. This variable was included because greater unemployment would presumably lead to more individuals falling in the low-income bracket, and growth in this population would mean that more hospitals would likely serve a

large enough number of low-income patients to become eligible for DSH-340B status. One result of growth in the number of DSH-340B sites due to unemployment, at least according to my hypothesis, is that drug prices would go up. The analysis found no evidence that unemployment had an impact on drug prices.

CHAPTER 6

CONCLUSION

The previous analyses show that my original hypothesis—that growth in the number of DSH-340B sites is causing physician-administered drug prices to rise—is only partially supported because growth in the number of DSH-340B sites was only found to be associated with a price increase for certain types of physician-administered drugs—namely, on-patent drugs and drugs that have not been off-patent for more than four periods.

My findings suggest that the 340B program may not actually be accomplishing the cross-subsidization it aims for. In theory, the program has pharmaceutical manufacturers subsidize care for low-income patients by requiring them to sell drugs to 340B eligible sites at a discount. What appears to happen, however, is that drug manufacturers simply shift the cost of the discount to other payers by increasing the price they charge for drugs. So, individuals end up subsidizing low-income patients' care because their insurance premiums and the taxes they pay to support Medicare increase in order to cover the higher drug prices. Policy makers need to keep this finding in mind as they evaluate the impact of the 340B program and whether it is meetings its proposed aim.

In addition, policymakers need to determine whether it matters if the 340B program is meeting its intended goal of having drug manufacturers subsidize care for low-income patients. After all, if the more immediate concern is to use the program to cross-subsidize care for low-income individuals, regardless of who ends up shouldering the final cost, then the 340B program is functioning perfectly well as it is. If, however, the program's success is tied to having drug

manufacturers shoulder these costs, then it appears to be failing, and policymakers should consider pursuing other means to achieve this end.

Moving forward, there are several possibilities policymakers should consider.[23] First, cross-subsidies are not uncommon in health care (e.g., commercial payers reimburse providers at a rate substantially higher than Medicaid and Medicare to help subsidize the cost of care for Medicaid and Medicare patients), and it could be argued that it is justified to shift some of the cost of physician-administered drugs to individuals. This would be tantamount to letting the 340B program continue as it is. Second, the 340B program could be revamped to ensure that 340B hospitals only receive 340B pricing for drugs administered to patients that are low-income. At present, DSH-340B hospitals receive the reduced price on drugs for all of their patients, even if the patient is not low-income. This sort of change would decrease the impact of the 340B program on drug manufacturers' revenue and would reduce their need to shift costs by increasing post-launch prices. HRSA's[24] *340B Program Omnibus Guidance* sought to implement this sort of change, but it was officially withdrawn by the Trump administration in early 2017. Third, the 340B program could be redesigned to ensure that drug manufacturers actually shoulder the cost of the 340B program. It is unclear how this could be achieved, but it would probably require more governmental intervention than the current administration is likely to allow.

Another interesting finding from this project centers on the way that drug prices change around the patent expiration period. As noted before, the analysis reveals that a drug's price increases at a higher rate for about three to four periods after the patent expires. One would assume that the price would drop after patent-expiration since generics can enter the market. However, several factors, including delay between patent-expiration and generic entry and the lag between generic market entry and impact on name-brand price, can take some time. During this period, manufacturers are likely trying to extract as much revenue as possible. It is also possible

[23] All of these potential moves are widely discussed in policy and academic circles.
[24] The Department of Health and Human Services Health Resources and Services Administration.

that manufacturers understand that certain consumers will be brand loyal and willing to pay a premium for the name-brand drug. So, they may be attempting to increase the price as much as possible with the understanding that the remaining market (i.e., those that are brand-loyal) will be less price-sensitive.[25] Policymakers need to keep these findings around patent-expiration in mind as they continue to explore how patent policy affects drug prices and the role of generics in the drug market.

Before concluding, it is worth noting that the findings from this analysis may not generalize to self-administered drugs. The way these drugs are paid for is slightly different and, as a result, they may respond differently to growth in the number of DSH-340B sites. It is also possible that the findings do not apply to low-cost physician-administered drugs. Because the sample was largely comprised of drugs that cost over $1,000 per dose, it is unclear whether the findings will generalize to drugs at all cost-levels.

To address these limitations, next steps in the project would likely include obtaining a larger data set with more off-patent drugs and lower-cost physician-administered drugs. If possible, it would also help to run a similar analysis on self-administered drugs. And finally, further analysis should attempt to identify proxies to control for increasing disease incidence and changes in health insurance coverage.

[25] The topics of brand-loyalty and price sensitivity for drugs and the market conditions necessary for generics to reduce brand-name prices have been discussed in some detail in the literature (see e.g., Conti & Berndt, 2014). Space constraints do not allow for further discussion of these topics in this paper.

Appendix A
Regression Results for Model Using Lag of DSH-340B

$\gamma_{log\_of\_real\_drug\_ASP} = \beta_{lag\_of\_log\_of\_DSH\_340B\_entities} + \beta_{patent\_expiration\_period} + \beta_{lag\_1\_of\_patent\_expiration\_period} + \beta_{lag\_2\_of\_patent\_expiration\_period} + \beta_{lag\_1\_of\_PPACA} + \beta_{lag\_2\_of\_PPACA} + \beta_{unemployment} + \beta_{democratic\_control} + \varepsilon$

Log of Real Drug Price	**Group A**	**Group B**	**Group C**	**Group D**	**Group E**
Lag of log of number of DSH-340B entities	-0.0913 (0.0967)	0.0255 (0.0897)	**0.1215*** (0.0294)**	**0.1669*** (0.0341)**	**-0.4332** (0.1891)**
Patent expiration period	**0.3039** (0.1296)**	0.284* (0.1549)	0.0507 (0.067)	**0.1110* (0.0627)**	
Lag 1 of patent expiration period	**0.3793** (0.1496)**	0.35** (0.1667)	0.1034 (0.0823)	**0.1423** (0.067)**	
Lag 2 of patent expiration period	**0.3676** (0.1762)**	0.3381* (0.1917)	0.0207 (0.0639)	**0.0726* (0.0439)**	
Lag 1 of Patient Protection and Affordable Care Act	-0.1115 (0.1119)	0.0011 (0.0199)	0.0017 (0.0123)	0.0097 (0.0094)	-0.3133 (0.3147)
Lag 2 of Patient Protection and Affordable Care Act	0.0128 (0.0334)	-0.016 (0.029)	**0.0189*** (0.008)**	**0.0277*** (0.0068)**	-0.0403 (0.0948)
Unemployment rate	-0.0359 (0.0319)	0.0147 (0.0089)	0.004 (0.0059)	0.0063 (0.0047)	-0.1095 (0.086)
Democratic control of presidency and house	0.1400 (0.1289)	-0.0323 (0.0285)	0.0113 (0.0164)	0.0025 (0.0141)	0.4112 (0.3665)
Constant	4.9564 (0.9206)	3.928 (0.8311)	3.6225 (0.4726)	2.96 (1.0398)	6.407 (2.2008)
Key P<10% * P<5% ** P<1% ***	Observations: 469 Groups: 35 R-sq (within): 0.0534 Prob>chi2= 0.0083	Observations: 374 Groups: 29 R-sq (within): 0.1219 Prob>chi2= 0.0001	Observations: 320 Groups: 25 R-sq (within): 0.4888 Prob>chi2= 0.000	Observations: 134 Groups: 9 R-sq (within): 0.7555 Prob>chi2= 0.000	Observations: 149 Groups: 10 R-sq (within): 0.1698 Prob>chi2= 0.0233

This model used the lag of log of DSH-340B sites as the independent variable of interest. The findings are analagous to those for the model using the log of DSH-340B sites as the independent variable (the model discussed in the results section). The key difference is that the magnitude of the coefficients on the independent variable of interest—number of DSH-340B sites—is slightly greater for both groups C and D and lower for group E (off-patent drugs) in this model.

Appendix B
Regression Results for Model with Time Dummies

$\gamma_{log\_of\_real\_drug\_ASP} = \beta_{log\_of\_DSH\_340B\_entities} + \beta_{patent\_expiration\_period} + \beta_{lag\_1\_of\_patent\_expiration\_period} + \beta_{lag\_2\_of\_patent\_expiration\_period} + \beta_{time\_pd\_3 - time\_pd\_19} + \varepsilon$

Log of Real Drug Price	**Group A**	**Group B**	**Group C**	**Group D**	**Group E**
Log of number of DSH-340B entities	-0.6797 (0.3716)	-0.2738 (0.1532)	**-0.2941*** (0.1118)**	**-0.3392*** (0.0948)**	**-1.9014** (0.9557)**
Patent expiration period	**0.3353** (0.1382)**	**0.2985* (0.1616)**	0.0475 (0.0741)	**0.1251* (0.0658)**	
Lag 1 of patent expiration period	**0.3925*** (0.1272)**	**0.3642** (0.1703)**	0.0967 (0.0918)	**0.1488* (0.0765)**	
Lag 2 of patent expiration period	**0.3825** (0.1686)**	**0.347* (0.189)**	0.0097 (0.0769)	0.0757 (0.0541)	
Time period dummies	Time period 10 and later are significant at the 15% level	A number of time periods are significant at the 10% level	All time periods significant at the 1% level or better	All time periods significant at the 1% level or better	Many time periods significant at the 15% level
Constant	9.1982 (2.778)	6.3038 (1.1258)	6.833 (0.8467)	3.338 (4.572)	16.8843 (7.4655)
Key P<10% * P<5% ** P<1% ***	Observations: 488 Groups: 35 R-sq (within): 0.0762 Prob>chi2= 0.000	Observations: 388 Groups: 29 R-sq (within): 0.1243 Prob>chi2= 0.000	Observations: 332 Groups: 25 R-sq (within): 0.4951 Prob>chi2= 0.000	Observations: 141 Groups: 9 R-sq (within): 0.7694 Prob>chi2= .	Observations: 156 Groups: 10 R-sq (within): 0.2365 Prob>chi2= 0.0346

This model includes dummies for time period 3 through time period 19. Time periods 1 and 2, the 2 lags on PPACA, the dummy variable for Democratic control, and the unemployment variable were excluded because there was collinearity when they were included. Inclusion of these variables did not seem necessary as the aim here was to identify significant time periods.

Log of DSH-340B is still significant for groups C , D, and E, but the direction of the association is opposite what was found in the paper. Furthermore, for most drug groups, time periods were statistically significant. It is important to note that there is a positive trend in both the number of DSH-340B sites and most drug prices over the 9.5 year period. Thus, it is possible that the time dummies were picking up the effects of each period, which included growth in DSH-340B sites. Accordingly, each time period may be significant because the number of DSH-340B sites increased each period. This possibility helps to explain why the estimates in this model are so different from the estimates reported in the results section.

Appendix C
Regression Results for Model with Time Trend Variable

$\gamma_{log\_of\_real\_drug\_ASP} = \beta_{log\_of\_DSH\_340B\_entities} + \beta_{patent\_expiration\_period} + \beta_{lag\_1\_of\_patent\_expiration\_period} + \beta_{lag\_2\_of\_patent\_expiration\_period} + \beta_{lag\_1\_of\_PPACA} + \beta_{lag\_2\_of\_PPACA} + \beta_{unemployment} + \beta_{democratic\_control} + \beta_{time\_trend} + \varepsilon$

Log of Real Drug Price	**Group A**	**Group B**	**Group C**	**Group D**	**Group E**
Log of number of DSH-340B entities	0.1190 (0.1473)	0.1436 (0.1151)	0.0482 (0.0504)	0.0909 (0.0933)	0.259 (0.549)
Patent expiration period	**0.3077** (0.1216)**	**0.2841** (0.1513)**	0.0471 (0.0714)	**0.114** (0.0638)**	
Lag 1 of patent expiration period	**0.3751*** (0.1213)**	**0.3521** (0.1619)**	0.0981 (0.0881)	**0.1412** (0.0686)**	
Lag 2 of patent expiration period	**0.3706** (0.1633)**	**0.3364** (0.1832)**	0.0104 (0.0734)	**0.0757** (0.0439)**	
Lag 1 of Patient Protection and Affordable Care Act	-0.0952 (0.1068)	0.019 (0.0257)	-0.0025 (0.012)	0.0077 (0.013)	-0.26 (0.3025)
Lag 2 of Patient Protection and Affordable Care Act	0.0606 (0.0685)	0.0258 (0.0365)	**0.0216* (0.0111)**	**0.0393* (0.0239)**	0.163 (0.2014)
Unemployment rate	-0.0192 (0.0188)	0.0154 (0.0107)	-0.0043 (0.0055)	-0.0049 (0.0059)	-0.0514 (0.0526)
Democratic control of presidency and house	0.1529 (0.1448)	-0.0192 (0.0310)	**0.0261* (0.0141)**	0.0245 (0.016)	0.4148 (0.4181)
Time trend	-0.0233 (0.0186)	-0.0154 (0.0138)	0.0088 (0.0064)	0.0088 (0.0129)	-0.0792 (0.0657)
Constant	3.287 (1.122)	3.074 (1.0017)	4.197 (0.579)	3.572 (1.327)	0.945 (4.184)
Key P<10% * P<5% ** P<1% ***	Observations: 488 Groups: 35 R-sq (within): 0.0538 Prob>chi2= 0.000	Observations: 388 Groups: 29 R-sq (within): 0.1176 Prob>chi2= 0.000	Observations: 332 Groups: 25 R-sq (within): 0.4911 Prob>chi2= 0.000	Observations: 141 Groups: 9 R-sq (within): 0.7624 Prob>chi2= 0.000	Observations: 156 Groups: 10 R-sq (within): 0.1784 Prob>chi2= 0.0346

This model included a time trend variable to control for unknown factors that may impact drug prices. The time trend variable includes all time periods (time_trend=1 if time_pd==1, time_trend=2 if time_pd==2, . . . time_trend==19 if time_pd==19). Inclusion of the time trend washed out the significance of DSH-340B sites. This is probably because there is an upward trend in the number of DSH-340B sites and the time trend variable picked this up.

Appendix D
Regression Results Using Lag of Drug Price

$\gamma_{log\_of\_real\_drug\_ASP} = \beta_{log\_of\_DSH\_340B\_entities} + \beta_{lag\_1\_log\_of\_real\_drug\_ASP} + \varepsilon$

Log of Real Drug Price	**Group A**	**Group B**	**Group C**	**Group D**	**Group E**
Log of number of DSH-340B entities	0.007 (0.0078)	-0.0056 (0.0064)	**0.0042*** **(0.0024)**	0.0052 (0.0045)	0.0183 (0.0289)
Lag of log of real drug price	**0.9909***** **(0.0155)**	**1.0048***** **(0.003)**	**1.0012***** **(0.0022)**	**1.0037***** **(0.003)**	**0.9462***** **(0.0662)**
Constant	-0.0269 (0.0889)	0.0331 (0.0493)	-0.0317 (0.0233)	-0.047 (0.0451)	-0.1022 (0.2809)
Key P<10% * P<5% ** P<1% ***	Observations: 466 Groups: 34 R-sq (within): 0.0848 Prob>chi2= 0.000	Observations: 370 Groups: 28 R-sq (within): 0.9410 Prob>chi2= 0.000	Observations: 316 Groups: 24 R-sq (within): 0.9278 Prob>chi2= 0.000	Observations: 138 Groups: 9 R-sq (within): 0.9742 Prob>chi2= 0.000	Observations: 150 Groups: 10 R-sq (within): 0.0608 Prob>chi2= 0.0000

A lag of the log of the real drug price was added to the base model to construct a time series model. The lag dependent variable was strongly predictive of the log of drug prices for every group indicating trends in drug prices. DSH-340B is statistically significant for group C, though the impact is miniscule (0.004% increase in real price per 1% growth in DSH-340B sites).

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