ESSAYS ON DRUG DISTRIBUTION AND PRICING MODELS

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ABSTRACT OF THE DISSERTATION

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This dissertation investigates distribution and pricing models for the U.S. pharmaceutical industry. Motivated by recent events in this industry, we explore three areas of the pharmaceutical supply chain in an effort to streamline the drug distribution channel and to understand the underlying market forces and the pricing structure of pharmaceutical drugs.

First we present a mathematical model to compare the effectiveness of the resell distribution agreements (Buy-and-Hold and Fee-For-Service) and the direct distribution agreement (Direct-to-Pharmacy) for the U.S. pharmaceutical supply chain and its individual participants. The model features multi-period dynamic production-inventory planning with time varying parameters in a decentralized setting. While the resell agreements are asset-based, the direct agreement is not. We show that the Direct-to-Pharmacy agreement achieves the global optimum for the entire supply chain by eliminating investment buying and thus always outperforms the resell distribution agreements currently practiced in the industry. We also show that the Direct-to-Pharmacy agreement is flexible because it allows the manufacturer and the wholesaler to share the total supply chain profit in an arbitrary way. We further provide necessary conditions
for all supply chain participants to be better off in the Direct-to-pharmacy agreement.

Motivated by the public concern for the rising cost of prescription drugs, we next examine how four factors – the level of competition, the therapeutic purpose, the age of the drug, and the manufacturer who developed the drug play a role in the pricing of brand-name drugs. We develop measures for these factors based on information observable to all players in the pharmaceutical supply chain. Using data on the wholesale prices of prescription drugs from a major U.S. pharmacy chain, we estimate a model for drug prices based on our measures of competition, therapeutic purpose, age, and manufacturer. We observe that proliferation of dosing levels tends to reduce the price of a drug, therapeutic conditions which are both less common and more life threatening lead to higher prices, older drugs are less expensive than newer drugs, and some manufacturers set prices systematically different from others even after controlling for other factors.

Lastly, we investigate why brand-name drugs are priced higher than their generic equivalents in the U.S. market. We hypothesize that some consumers have a preference for brand names which outweighs the cost savings they could realize by switching to generics. Brand preferences are derived from two sources. First, brands may have a higher perceived quality due to advertising and marketing activities. Second, individuals are habitual in their consumption of prescription drugs, which leads to continued use of the brand in the face of generic competition. To explore these issues, we develop a structural demand model within one therapeutic class. We estimate the model using wholesale price and demand data from the years 2000 through 2004. Through this process, we estimate the brand preferences by customer utility equations. Conservatively, we see consumers willing to pay $400 more per month for a brand name drug than for its generic equivalent. In addition, consumers exhibit high switching costs for prescription drugs. Finally, we find that generic entry reduces sales only for the brand that it is replicating, but not for other brand drugs even if they treat the same condition.
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To my dissertation committee, I express great thanks: to Dr. Lei Lei whose leadership in our department has been inspiring. To Dr. James Sawhill for showing me how to tackle the most difficult problems. To Dr. Michael Katehakis for his vast knowledge and insightful comments. To Dr. Tan Miller whose encouragement and experience are much appreciated. To Dr. Rose Sebastianelli who inspired me to pursue a career in academia and whose commitment to teaching I can only hope to emulate.

I also want to express my appreciation for faculty at Rutgers Business School. My journey at Rutgers has been very rewarding thanks to the many professors that I have crossed paths with. I also want to extend a special thanks to Dr. Sharon Lydon, whose support and dedication to academic excellence has been an inspiration.
Dedication

I dedicate my dissertation to my husband and family:

To my husband, best friend, and biggest cheerleader, Chris, whose unwavering love and support has carried me through these many years of research.

I would like to extend a special thanks to my parents, Gregory and Kathleen Martino, who instilled the importance of hard work and encouraged me to pursue my degree.

To my brothers, Alex and Nick who have provided many nights of laughter when I needed a break from this “book report”.

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Chapter 1
Introduction

This dissertation studies two topics for the pharmaceutical supply chain: drug distribution and drug pricing. For drug distribution, we investigate contractual agreements for channel coordination analytically and numerically in order to improve the efficiency of the pharmaceutical supply chain. For drug pricing, we investigate the pricing decisions made by pharmaceutical manufacturers empirically to understand the market forces and consumer behavior. In this chapter, we provide motivation for our study and a summary of results. We also review the structure of the thesis.

1.1. Motivation and Summary of Results

The pharmaceutical industry has recently been under the spotlight of public interest. Public figures have voiced concerns over the rising cost of health care, of which prescription drugs account for 10% (Kaiser Family Foundation, 2009b). The U.S. health care spending has increased 2.4% faster than GDP since 1970 and is expected to exceed $4.3 trillion in 2018 (Kaiser Family Foundation, 2009b). In 2009, health care spending hits an unprecedented 17.6 percent of the GDP (Martin et al., 2011).

Inefficient distribution agreements within the supply chain and prescription drug costs have been two key contributors to the rise of health care expenditures. We shall discuss both in detail below and summarize the results of this dissertation.
1.1.1 Distribution Agreements

Beginning in 2005, the U.S. pharmaceutical supply chain went through a drastic transformation from Buy-and-Hold (BNH) agreements between manufacturers and wholesalers to the Inventory Management Agreements (IMA) and Fee-for-Service (FFS) agreements. Under the BNH agreement, the wholesaler buys drugs from the manufacturer and resells them to the pharmacies. The IMA and FFS agreements are identical to the BNH agreement except that the wholesaler demands a fee from the manufacturer for it to maintain a certain inventory-related performance measure.

Pharmaceutical manufacturers have mixed responses to these new agreements while the overall supply chain impact is still being debated by industry observers. Some manufacturers are experimenting with alternative models, such as a Direct-to-Pharmacy (DTP) agreement where drug wholesalers manage distribution for a fee and inventory ownership shifts upstream to the manufacturer.

Drug manufacturers face fundamental normative questions about the optimal go-to-market channel strategy: which contract (BNH, FFS or DTP) would be best for the pharmaceutical supply chain and its individual participants?

Unfortunately, the existing literature provides insufficient guidance to help managers make this important decision. In Chapter 2, we address this knowledge gap by developing a mathematical model to normatively compare three alternative channel models: BNH, FFS, and DTP. To capture key industry dynamics, our model features multiperiod decision making in a decentralized system with time varying price and demand. Under each distribution agreement, we formulate mathematical programming models to determine the profit maximizing production, inventory, and ordering decisions for the manufacturer and the wholesaler in a finite time horizon.

We show that the DTP agreement always outperforms the BNH and FFS agreements in terms of the supply chain total profit. Indeed, one cannot do better than the DTP agreement for the supply chain as a whole. The benefit comes from channel inventory
reduction. We also show that the DTP agreement is flexible because it allows the manufacturer and the wholesaler to split the supply chain total profit in an arbitrary way. Thus, for any FFS agreement, there always exists a DTP agreement that is at least as profitable as the former for both the wholesaler and the manufacturer. Lastly, we take each player’s perspective and develop insight on how each of them can benefit from the DTP agreement under an appropriate fee structure.

We demonstrate the real-world applicability of the model by comparing the BNH, FFS and DTP agreements based on data provided by a leading pharmaceutical manufacturer. We show that depending on the investment-buying inventory that the wholesaler is allowed to carry, the DTP agreement can improve the supply chain total profit by about $0.08 \sim 1\%$ (relative to FFS) and $5\%$ (relative to BNH). Finally, we go beyond the pharmaceutical industry and discuss general conditions under which a direct model (such as the DTP agreement) may or may not outperform a resell model (such as the BNH and FSS agreements) in a dynamic and decentralized supply chain.

1.1.2 Pricing Decisions

Prescription drug costs have been a key contributor to the rise of health care expenditures (CNN, 17 Nov 2009). Moreover, drug research and development (R&D) costs continue to rise, making it more difficult for manufacturers to maintain their high levels of profitability without increasing drug prices further. In response to public concerns, the vice president of PhRMA stated that “All companies make their own independent pricing decisions based on many factors, including patent expirations, the economy, ... and huge research and development costs...” (PhRMA, 2009). Whether these statements are true or not, it is in the public interest to identify factors that drive prescription drug prices because the rising price of prescription drugs affects all participants in the pharmaceutical supply chain, including manufacturers who set the price, wholesalers and pharmacies who distribute the drugs, private insurers, the government, and
ultimately the patients who pay for the drugs. Furthermore, the demand for these prescription drugs is substantial – 91 percent of seniors and 61 percent of non-seniors rely on prescription drugs on a daily basis (Kaiser Family Foundation, 2009a). As America’s population continues to age, it is reasonable to expect that spending on prescription drugs will continue to rise.

In Chapter 3, we analyze the prices of brand-name prescription drugs and develop a linear model to predict their list price (wholesale acquisition cost (WAC)) based on four classes of publicly observable factors: the level of competition, the nature of the condition that the drug treats (the therapeutic class), the number of years that the drug has had FDA approval, and the manufacturer who developed the product. While previous research has studied some of these factors, our analysis is unique in that it develops a unifying framework to explain prices by a broad range of factors that are observable to the public. We focus on observable factors so that all players in the supply chain may equip themselves with the knowledge necessary to determine fair and reasonable prices. Currently, all prices and rebates in this supply chain are based on the WAC price set by the manufacturer. In order to improve efficiency, prices should not be determined upstream, but rather actively negotiated between supply chain partners.

The results of our analysis reveal that many observable factors are significant in predicting drug prices. Specifically, we observe that proliferation of dosing levels tends to reduce the price of a drug, therapeutic conditions which are both less common and more life threatening lead to higher prices, older drugs are less expensive than newer drugs, and some manufacturers set prices systematically different from others even after controlling for other factors. These findings merit further study as it is apparent that observable factors can be used to explain drug prices.

Chapter 4 extends the research on pricing decisions to investigate why brand drugs are priced higher than their generic equivalents. There is no question that brand drugs are more expensive than generic drugs; in 2008 the average brand name prescription drug was $137.90 while the average price for a generic drug was $35.22 (Kaiser Family
Figure 1.1: Brand drug prices before and after patent expiration

Foundation, 2010). Furthermore, contrary to popular belief, brand drug prices usually do not fall when they go off patent and generic equivalents are introduced. Figure 1.1 shows the price of two brand drugs (drug A and drug B) before and after their generic equivalents were introduced. Note that in both cases, the price of the brand drug did not decrease after it went off patent. This pattern is confirmed by other studies in the literature, e.g., Frank and Salkever (1992, 1997), Grabowski and Vernon (1992), and Berndt (2002), and will be discussed further in Chapter 4.

We develop a structural demand model based on consumer utility for the U.S. prescription drug market within one therapeutic class. We proceed to estimate the model using wholesale price and demand data from the years 2000 through 2004. Through this process, we determine whether or not consumers exhibit brand loyalty and are willing to pay more for brand name drugs than their generic equivalents. Our analysis reveals that customers have a strong personal preference towards brand drugs. Conservatively,
we see consumers willing to pay $400 per month more for a brand name drug than for its generic equivalent. In addition, consumers exhibit high switching costs for prescription drugs. Finally, we find that generic entry reduces sales only for the brand that it is replicating, but not for other brand drugs even if they treat the same condition.

1.2. Thesis Structure

Given the cost and pricing issues faced by this industry, there is an apparent need for research that investigates and improves the efficiency of the pharmaceutical supply chain and its individual participants. The core of this dissertation (Chapters 2-4) provides tactical models for this purpose. In answering a call for greater efficiency in drug distribution, we compare new and existing distribution agreements in Chapter 2 and find an agreement that coordinates the distribution channel. In Chapter 3, we build an empirical model to explain prices of brand drugs by factors that can be observed by all supply chain players. In Chapter 4, we explore reasons why brand drugs do not lower their prices when generics are introduced and empirically model the consumer’s utility which simultaneously captures brand loyalty effects and reasonable substitution patterns. In summary, this dissertation is designed to address many of the key issues that supply chain and marketing managers face in the pharmaceutical industry.
Chapter 2

Resell versus Direct Models in Brand Drug Distribution

There are more than 130,000 pharmacy outlets in the U.S. demanding daily delivery of pharmaceutical drugs (BoozAllenHamilton, 2004). To simplify matters, pharmacies and hospitals order from 2 or 3 wholesalers as an one-stop shop rather than from over 500 manufacturers. In this way, they only receive a couple of mixed-load shipments from wholesalers. As a typical practice, pharmacies and hospitals tend to push inventory back to wholesalers and rely on them for full service. In 2009, the Big Three wholesalers: AmerisourceBergen, Cardinal Health and McKesson, generated about 85% of all revenue from drug wholesaling in the U.S.. Total U.S. revenue from the drug distribution divisions of these Big Three wholesalers was $257.1 Billion (Fein, 2010).

In general, wholesalers buy prescription drugs from manufacturers based on a wholesale acquisition cost (WAC). WAC is defined in the U.S. Code as “the manufacturer’s list price for the pharmaceutical or biological to wholesalers or direct purchasers in the United States, not including prompt pay or other discounts, rebates or reductions in price, for the most recent month for which the information is available, as reported in wholesale price guides or other publications of pharmaceutical or biological pricing data.” (United States, 2007).

According to data, the price (WAC) for brand drugs has always increased over time in the pharmaceutical industry since 1987 (BoozAllenHamilton, 2004). Figure
Figure 2.1: Drug Price Inflation (the % increase over the previous year) from 1992 to 2002. Source: The Kaiser Family Foundation and the Sonderegger Research Center, Prescription Drug Trends, A Chartbook Update.

2.1 shows the percentage price increase for brand prescription drugs from 1992 to 2002. Manufacturers typically increase the WAC at the same time each year, often in January. Thus, the timing and magnitude of the price increase are easily anticipated in the industry (BoozAllenHamilton, 2004).

**The Buy-and-Hold Agreement**

Prior to 2005, manufacturers and wholesalers in the U.S. pharmaceutical industry were engaged in the BNH agreement in which manufacturers compensated drug wholesalers by allowing them to purchase more products than required to meet customer needs. Consequently, wholesalers engaged in investment buying (i.e., forward buying) to maximize their profit, where they intentionally and actively sought to maintain higher inventory levels of prescription drugs than needed to meet short-term demand from their customers. A wholesaler could earn as much as 40% of their gross margin by investment buying (BoozAllenHamilton, 2004; Fein, 2005a).

Investment buying opened doors for many problems in drug distribution such as
enormous over-stock in the channel, secondary markets and counterfeit drugs, and false signals on demand. Under investment buying, wholesalers can carry up to four to six months of inventory (Harrington, 2005). The carrying cost of the highly valued inventory erodes supply chain profitability. Manufacturers found themselves unable to control the activities of their distribution channels. Wholesalers made money as speculators rather than as product distributors. Thousands of small wholesalers sprung up to buy and sell the excess channel inventory in a loosely and inconsistently regulated secondary market, creating opportunities for unscrupulous parties to introduce counterfeit or mishandled products into legitimate channels. In 2001, the FDA estimated that there were 6,500 secondary wholesalers purchasing from either primary wholesalers or other secondary wholesalers (Department of Health and Human Services U.S. Food and Drug Administration, June 2001).

The pharmaceutical drug distribution system during this period was not necessarily the most efficient or effective system for distributing pharmaceuticals to pharmacies. Neither manufacturers nor wholesalers had clear incentives to reduce inventory levels in the supply chain.

The Fee-for-Service Agreement

Channel relationships were transformed when manufacturers and wholesalers began signing inventory management agreements (IMAs) in 2004. Through an IMA, a wholesaler agrees to reduce or eliminate investment buying of a manufacturer’s products in return for a fee structure or payment from the manufacturer. This offsets some of the wholesaler’s economic loss from the discontinuation of investment buying.

FFS agreements add performance-based metrics to the IMA concept. Wholesalers get additional payments by meeting performance criteria established in negotiations with a manufacturer. FFS agreements are enabled by data-sharing between manufacturers and wholesalers via Electronic Data Interchange (EDI). The EDI data allow manufacturers to monitor a wholesaler’s performance under a fee-for-service agreement.
and compute payments due to the wholesaler.

IMA and FFS agreements led to sharp reductions in drug wholesalers’ inventory levels. Drug wholesalers avoided adding billions of dollars of inventory to their balance sheets in the past eight years even as overall revenues grew (Fein, 2005b; Zhao and Schwarz, 2010b). Although IMA and FFS agreements have reduced the inventory of the U.S. pharmaceutical wholesale industry from 40-60 days in March 2003 to about 28 days in March 2009 (Fein, 2010), they did not eliminate investment buying. Indeed, wholesalers are still making a portion of profit from investment buying (Fein, A.J., 2007) under IMA and FFS agreements. As an example, Figure 2.3 (in §2.3.1) shows that wholesalers are still investment buying but on a less visible scale.

The Direct-to-Pharmacy Agreement

In 2007, Pfizer implemented the DTP agreement in the U.K. with one of its former wholesalers as an alternative to IMA and FFS agreements. In the DTP agreement, the manufacturer maintains the ownership of the drug throughout the supply chain until it reaches retailers. The wholesaler manages drug distribution for the manufacturer for a fee and the manufacturer directly receives payment from retailers (Poulton, S., 2007). We call such a distribution model the direct model. In contrast, in the BNH and FFS agreements a manufacturer sells a drug to a wholesaler who then owns the inventory as an asset on its balance sheet and resells it to retailers (pharmacies and hospitals, etc.). We call such a distribution model the resell model. Thus the direct model differs from the resell model primarily in two areas: the ownership of the channel inventory and the flow of money among the manufacturer, the wholesaler, and retailers (see Figure 2.2). Under the DTP agreement, the wholesaler continues to provide the same services to the manufacturer as they did under the FFS agreement. Additionally, the pharmacy and hospitals receive the same services under both agreements. Thus, the material-handling and transportation costs are identical under all agreements. The flow of drugs remains the same, while the flow of money differs.
Figure 2.2: Money flows under BNH, FFS and DTP agreements. WAC stands for wholesale acquisition cost which is the manufacturer’s list price for the drug. WAC’ is the price at which wholesalers sell to pharmacies.

The direct model is similar in inventory ownership with the consignment contract (see, e.g., Wang et al. (2001)), but they differ in money flow and decision rights. Under a consignment contract, the supplier is compensated either by the buyer or by a share of the revenue, and the supplier determines the order quantity and delivery schedule. By contrast, under the direct model the supplier receives all the revenue and pays the wholesaler a fee for its service, and the latter makes distribution decisions. We refer the reader to Table 2.1 for a comparison among the DTP agreement, the consignment contract and the vendor-managed-inventory (VMI) arrangement.

In fact, the direct model resembles a non-asset based contract between a manufacturer and a 3rd party logistics (3PL) service provider where the wholesaler is hired by the manufacturer to manage the distribution. Thus, the wholesaler retains the decisions on ordering and inventory for the channel and bears the associated costs while the manufacturer only makes production-inventory decisions for itself and bears its own costs.
Industry Debate

The transition from Buy-and-Hold (BNH) agreements to Fee-for-Service (FFS) agreements has been watched closely by industry observers and the sustainability of the FFS agreement has been under heavy debate. The opinions of industry experts, although thought provoking, lack a solid analytic framework and often reflect self-interested perspectives on the pharmaceutical supply chain. For instance, one wholesaler executive suggested that the FFS agreement creates positive business opportunities for wholesalers to provide more services for manufacturers (Yost, 2005). A study funded by a trade association of wholesalers predictably concluded that bypassing wholesalers (e.g., direct shipping) would be much more costly (BoozAllenHamilton, 2004).

The opinions of manufacturers are more mixed. Some manufacturing executives believe that FFS agreements provide unnecessary compensation for wholesalers (Basta, 2004), causing some manufacturers to explore the option of using a 3PL to bypass wholesalers (Handfield and Dhinagaravel, 2005). However, the U.S. pharmaceutical supply chain is enormously complicated; it is a substantial challenge for drug manufacturers to manage distribution by themselves. Thus, it would be better to utilize the expertise of the drug wholesalers if a more adequate agreement (contract) exists that aligns the

<table>
<thead>
<tr>
<th></th>
<th>DTP</th>
<th>Consignment</th>
<th>VMI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inventory Ownership</strong></td>
<td>Supplier</td>
<td>Supplier</td>
<td>Either supplier or buyer. Depends on contract.</td>
</tr>
<tr>
<td><strong>Money Flow</strong></td>
<td>Supplier receives revenue. Supplier pays a fee to the logistics partner.</td>
<td>Buyer pays supplier or they share revenue.</td>
<td>Buyer pays supplier.</td>
</tr>
</tbody>
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Table 2.1: The DTP agreement, the consignment contract, and VMI.
wholesalers’ incentive with their task and also ensures mutual benefits. It is towards this goal that this chapter compares the effectiveness of the BNH, FSS, and Direct-to-Pharmacy (DTP) agreements and identifies general conditions under which the direct model may or may not outperform the resell model.

The remainder of this chapter is organized as follows. We review the related literature in 2.1. The model and analysis are presented in 2.2 and the potential benefits of using the DTP agreement are shown in an illustrative example in 2.3. Finally, we summarize the results in 2.4.

2.1. Literature Review

Research with potential relevance to resell and direct distribution models has developed independently in the academic literatures of production-inventory control, supply chain coordination and the bullwhip effect, and trade promotion and forward buying. We briefly consider key elements of these research streams with applicability to the issues being considered in this chapter.

Supply chain coordination and contracts have been studied extensively in decentralized systems. For example, Lariviere and Porteus (2001) examine the single wholesale price contracts between manufacturers and retailers in a single period model. Putting the contract in a multi-period setting, it is effectively a BNH agreement. Wang et al. (2001) studies the performance of consignment contracts with revenue sharing, and Corbett (2001) shows how consignment stock helps or worsens the inefficiencies caused by information asymmetry. We refer to Cachon (2003) for a thorough literature review. This literature focuses on single-period models or models with stationary demand and thus is unsuitable for the pharmaceutical industry because brand drugs have multiple years before patent expiration. Economies of scale in production and inflation in prices and demand require that the model must consider multi-period production planning and inventory control for each player.
Graves (1999) reviews optimization models for multi-period production planning and inventory control for centralized systems with predictable demand. The models include those with fixed costs and time varying demand/cost functions. For decentralized systems with multiple periods and predictable demand, there is a large body of literature in both marketing and operations management on quantity discounts and related issues, see, e.g., Jeuland and Shugan (1983), Dolan and Frey (1987), Chen et al. (2001), Corbett and deGroote (2000), Bernstein and Federgruen (2003), and Choi et al. (2004b). All these papers consider stationary demand (either constant or random) and constant price/cost parameters. In this literature, the order pattern (e.g., a few large orders) is driven by fixed costs. In contrast, the order pattern in pharmaceutical distribution is driven primarily by inventory appreciation. This chapter adds to this literature by ignoring the economies of scale in ordering and fulfillment and focuses on another dimension of complexity – time varying system parameters (e.g., price and demand).

The marketing literature of trade promotions explicitly considers manufacturer-supported price discounts and retailer’s forward buying behavior (Lal et al., 1996; Cui et al., 2008; Kumar et al., 2001). Some research compares off-invoice trade deals with scan-back deals in an attempt to find mutually beneficial trade promotions (Dreze and Bell, 2003; Arceus and Srinivasan, 2003). Recently, Desai et al. (2009) study cases where it may be beneficial for retailer(s) to forward buy even without trade-promotions from manufacturer(s).

However, these models provide limited insight for the pharmaceutical manufacturer. The pricing of brand drugs is a complex issue involving multiple parties such as the manufacturer, the government, pharmaceutical benefit managers and insurance companies. Therefore, the price is effectively exogenous to the decision about optimal channel contracting. In contrast to promotional discounting, the pharmaceutical industry operates with ongoing price inflation to the outside (retail) customers rather than high/low price promotion between trading partners. Furthermore, these models ignore production and
operational details, such as the fixed/variable production cost, capacity limit and minimum production quantities in multi-period settings. From the methodology standpoint, we study the supply chain coordination and contracting issues based on mathematical programming which differs from the literature mentioned above.

In the operations management literature, forward buying and price fluctuations have been identified as important contributors to the bullwhip effect (Lee et al., 1997a,b). Many models and strategies are proposed to mitigate the bullwhip effect, for example, information sharing (e.g., Gavirneni et al. (1999)), vendor managed inventory (VMI) (see, e.g., Aviv and Federgruen (1998); Fry and Kapuscinski (2001); Choi et al. (2004a)), and collaborative planning, forecasting and replenishment (CPFR) (see, e.g., Waller et al. (1999); Aviv (2001)).

Recently, Zhao and Schwarz (2010b) empirically study the impact of information sharing on wholesalers and manufacturers in the pharmaceutical industry. Our work differs from this literature in two ways: first, we study the effectiveness of a different strategy – the DTP agreement (the direct model), see Table 2.1 for a comparison among DTP, consignment, and VMI; second, our model has some distinct features – the time varying demand and price over a finite time horizon, significant economies of scale in production but insignificant economies of scale in shipping, ordering and fulfillment for wholesalers relative to the production/inventory costs. Zhao and Schwarz (2010a) mathematically examine the FFS agreement relative to the BNH agreement. Our work differs from this literature in that we expand the comparison to the DTP agreement and use deterministic demand to model the production and ordering decisions of the players in this supply chain.

Although there is a vast literature on 3PLs, there is little academic study on comparing 3PL and resell distribution models and their impact on individual players as well as the entire supply chain. We refer to Kopczak et al. (2000) for different models of 3PL in the information age, Bolumole (2001) for the role of 3PLs in supply chains, and Lee et al. (1997a) for some advantages of 3PL in mitigating the bullwhip effect.
2.2. Model Description and Analysis

We consider cases in which the aggregated demand from all retailers (pharmacies and hospitals) is relatively easy to forecast and thus a model of predictable demand is acceptable. As BoozAllenHamilton (2004) points out, consumer demand is often stable and predictable. This is especially true for drugs treating chronic diseases. As an example, we worked with a major pharmaceutical manufacturer in the U.S. on a sample of brand drugs and found its average forecast error for monthly shipments (i.e., monthly retail orders aggregated across the U.S.) to be roughly 6.5% (see §2.3.1 for more details). While the forecast is not completely accurate (this issue will be addressed in future research using a stochastic model), the model of predictable demand is an appropriate starting point as it captures the dynamics of investment-buying which is the key issue.

We also assume that the aggregated demand (from outside customers) is known by both the wholesaler and the manufacturer. In the FFS agreement wholesalers provide manufacturers with 852 and 867 data which show the point of sales and inventory levels at the wholesalers’ warehouses. Under the DTP agreement, manufacturers receive revenue directly from retailers and thus know the demand. Under the BNH agreement, manufacturers do not have complete information about the outside demand and thus this assumption over-estimates the profit for manufacturers and the supply chain under this agreement. We shall use this estimate as a lower bound for the performance gaps between the BNH and FFS agreements, and between the BNH and DTP agreements.

Let us consider a pharmaceutical supply chain with a single manufacturer, a single wholesaler, and a single brand drug. We assume that the manufacturer and the wholesaler produce and distribute the drug over a finite time horizon with periods ranging from $t = 1, 2, \ldots, N$. We define the following notation:

- $D(t)$: Aggregated demand in period $t$, nonnegative.
- $W(t)$: Wholesale’s price per unit in period $t$. It is the price at which wholesaler buys the drug. $W(t)$ is typically WAC less a negotiated volume discount.
- \( W'(t) \): Price per unit at which the wholesaler sells to pharmacies in period \( t \) (WAC').

As shown in figure 2.1, we assume that the wholesale price of the drug, \( W(t) \), is increasing in \( t \) and is predictable by the wholesaler. \( W'(t) \) is based on \( W(t) \) and is an increasing function of \( W(t) \).

We assume that both the manufacturer and the wholesaler are rational, i.e., making decisions to maximize their profit. Through discussions with industry experts, we also assume that the manufacturer knows the cost structure of the wholesaler and thus can predict its behavior. Given the predictable nature of the demand and high stock-out cost, we assume that the wholesaler and manufacturer must fill its demand immediately in full. Thus no backorders are allowed for the manufacturer and wholesaler. In practice, the manufacturer uses any means possible to avoid backorders as discussed in Zhao and Schwarz (2010b).

Because the demand is predictable, the manufacturer can always start production in advance and so we ignore the manufacturer’s production cycle time. In addition, all costs other than those associated with production and inventory (e.g., R&D, marketing, administration, shipping, order fulfillment and material handling costs) for the planning horizon remain the same under all contractual agreements for both players. Indeed, since the drug flow and company operations are not affected by the contract, these costs do not change as a result of a contract change. Moreover, because of the highly valued products and bulk shipments to wholesalers’ warehouses, the shipping cost and order fulfillment cost of the manufacturer is insignificant relative to its production and inventory costs. Wholesalers’ ordering costs are also negligible as the transaction is done by EDI. Thus, we can ignore these costs in the following discussion. Finally, we assume that the transportation lead time between the manufacturer and the wholesaler is negligible. This is reasonable because air-freight is common in pharmaceutical distribution and the lead time is one to two days, which is small compared to the wholesaler’s planning cycle, e.g., a month.
The manufacturer takes the lead by selecting a contractual agreement (BNH, FFS or DTP) and its terms (fee structure). The wholesaler responds by deciding its optimal ordering quantities, which are anticipated by the manufacturer who in turn makes its production decisions. To facilitate contract comparison, we consider each contractual agreement below with a predetermined fee structure with a scenario that the wholesaler accepts the contract and participates in the game.

2.2.1 Fee-for-Service Agreement

Under the FFS agreement, the wholesaler buys inventory and the manufacturer pays the wholesaler a fee for its services. Industry practice shows that the fee in FFS agreements is predetermined, per unit of product ordered. The wholesaler charges retailers a price of $W'(t)$. The money flow is depicted by Figure 2.2. By the contract set forth in the IMAs, wholesalers must maintain their inventory level below a certain limit.

Following the practice, the wholesaler first determines its optimal ordering policy and then the manufacturer follows by determining its optimal production schedule. For the wholesaler, we define the following variables:

- $F(t)$: Fee per unit in period $t$.
- $O(t)$: Ordering quantity that the wholesaler places in period $t$.
- $I_w(t)$: Inventory on-hand at the end of period $t$.
- $M_t$: Maximum allowable inventory level at the end of period $t$.
- $h_w(t)$: Holding cost per unit of inventory carried by the wholesaler from period $t$ to period $t + 1$.

$O(t) \geq 0$ is the decision variable at period $t$. Let initial inventory level $I_w(0) = 0$. The profit maximizing ordering quantities for the wholesaler are determined by the
following mathematical program:

$$\begin{align*}
\text{Max} & \quad \sum_{t=1}^{N} [F(t) \times O(t) + W'(t) \times D(t) - W(t) \times O(t) - h_w(t) \times I_w(t)] \\
\text{s.t.} & \quad I_w(t-1) + O(t) - D(t) = I_w(t), \quad t = 1, 2, \ldots, N \\
& \quad I_w(t) \leq M_t, \quad t = 1, 2, \ldots, N \\
& \quad \text{All decision variables are nonnegative.}
\end{align*}$$ (2.1)

We set $D(t) = 0$ for $t > N$. We denote the optimal order quantity by $O^*(t)$. Note that if we set $F(t) = 0$ for all $t$ and relax the constraint “$I_w(t) \leq M_t, t = 1, 2, \ldots, N$”, then the program solves for the optimal ordering quantities for the wholesaler under the BNH agreement.

For the manufacturer, we define the following variables:

- $P(t)$: The production quantity in period $t$.
- $I_m(t)$: Inventory on-hand at the end of period $t$.
- $h_m(t)$: Holding cost per unit of inventory carried by the manufacturer from period $t$ to period $t + 1$. Without loss of generality, we assume $h_m(t) \leq h_w(t)$ for all $t$.
- $c(t)$: Unit production cost
- $C(t)$: Production capacity limit in period $t$.
- $MPQ(t)$: Minimum production quantity in period $t$.

$P(t) \geq 0$ is the decision variable at period $t$. Let the initial inventory level $I_m(0) = 0$, given $O^*(t)$ for all $t$, the manufacturer determines the profit maximizing production
quantities by the following mathematical program:

\[
\begin{align*}
\text{Max } & \sum_{t=1}^{N} [(W(t) - F(t)) \times O^*(t) - c(t) \times P(t) - h_m(t) \times I_m(t)] \\
\text{s.t. } & I_m(t - 1) + P(t) - O^*(t) = I_m(t), \quad t = 1, 2, \ldots, N \\
& P(t) \leq C(t), \quad t = 1, 2, \ldots, N \\
& P(t) \geq MPQ(t), \quad t = 1, 2, \ldots, N \\
\end{align*}
\]

(2.2)

All variables are nonnegative.

If we set \( F(t) = 0 \) for all \( t \) in Problem (2.2), then we obtain the manufacturer’s problem under the BNH agreement.

Note that under the FFS agreement, the manufacturer satisfies the orders of the wholesaler, \( O^*(t) \), which are not necessarily equal to demand, \( D(t) \), because the wholesaler can still investment buy up to the maximum allowable inventory level.

### 2.2.2 Direct-to-Pharmacy Agreement

Under the DTP agreement, the manufacturer owns inventory in his facility and in the wholesaler’s facility. The manufacturer pays the wholesaler a fee for its service upon each unit sold to retailers. The fee is similar to that under the current FFS agreement in that it is per unit of inventory. While we still pay the wholesaler for their services through a set fee, we do not sell the drug to the them. When retailers (e.g., pharmacies) buy the drug at \( W'(t) \), the revenue goes directly back to the manufacturer (this can be done, for instance, through an invoice service provided by the wholesaler). Therefore the wholesaler is compensated only through the logistics services provided. The money flow for the supply chain under the DTP agreement is shown in Figure 2.2.

Similar to the FFS agreement, we assume that the wholesaler first determines its optimal ordering policy and then the manufacturer follows by determining its optimal production schedule.

The wholesaler has the same variables as defined in §2.2.1, i.e., \( F(t), O(t) \) and \( I_w(t) \)
for all periods. It is important to note that the fee, $F(t)$, in the DTP agreement can be different from the fee in the FFS agreement. Since the manufacturer now owns the inventory at the wholesaler’s facility, the wholesaler’s inventory holding cost under the DTP agreement $h_w'(t) \leq h_w(t)$ where $h_w(t)$ is the wholesaler’s inventory holding cost under the FFS/BNH agreements. For instance, $h_w'(t)$ may include utility, damage and facility costs but may not include capital costs.

Let $O(t) \geq 0$ be the decision variable at period $t$, and the initial inventory level $I_w(0) = 0$. The profit maximizing ordering quantities for the wholesaler are determined by the following mathematical program:

$$\begin{align*}
\text{Max} & \quad \sum_{t=1}^{N} [F(t) \times D(t) - h_w'(t) \times I_w(t)] \\
\text{s.t.} & \quad I_w(t-1) + O(t) - D(t) = I_w(t), \quad t = 1, 2, \ldots, N
\end{align*}$$

(2.3)

All decision variables are nonnegative.

Let $D(t) = 0$ for $t > N$. It is easy to see that the problem is equivalent to minimizing inventory cost, and the optimal order quantity for the wholesaler at period $t$ is $O^*(t) = D(t)$ and $I_w^*(t) = 0$. The maximum profit is $\sum_{t=1}^{N} [F(t) \times D(t)]$.

For the manufacturer, the decision at period $t$ is to produce $P(t) \geq 0$. Let the initial inventory level $I_m(0) = 0$, the mathematical program can be written as follows:

$$\begin{align*}
\text{Max} & \quad \sum_{t=1}^{N} [(W(t) - F(t)) \times D(t) - c(t) \times P(t) - h_m(t) \times I_m(t)] \\
\text{s.t.} & \quad I_m(t-1) + P(t) - D(t) = I_m(t), \quad t = 1, 2, \ldots, N \\
& \quad P(t) \leq C(t), \quad t = 1, 2, \ldots, N \\
& \quad P(t) \geq MPQ(t), \quad t = 1, 2, \ldots, N
\end{align*}$$

(2.4)

All variables are nonnegative.

Note that under the DTP agreement, the manufacturer is facing the wholesaler’s demand, $D(t)$, because the wholesaler just orders enough to satisfy the demand in each period.
2.2.3 Comparative Analysis

We now compare the effectiveness of the BNH, FFS and DTP agreements for the manufacturer, the wholesaler, and the supply chain as a whole.

Define the supply chain total profit to be the sum of the manufacturer’s profit and the wholesaler’s profit. We first show that the DTP agreement always outperforms the FFS agreement in total supply chain profit regardless of the fee structure.

**Theorem 1**  The DTP agreement always outperforms the FFS agreement in total supply chain profit.

**Proof.** Let the optimal solutions to Problems (2.1)-(2.2) be $O^*(t)$, $I^*_w(t)$, $I^*_m(t)$ and $P^*(t)$. These solutions satisfy the following equations:

\[
I^*_w(t - 1) + O^*(t) - D(t) = I^*_w(t), \quad t = 1, 2, \ldots, N
\]

\[
I^*_m(t - 1) + P^*(t) - O^*(t) = I^*_m(t), \quad t = 1, 2, \ldots, N
\]

\[
I^*_w(t) \leq M_t, \quad t = 1, 2, \ldots, N
\]

\[
P^*(t) \leq C(t), \quad t = 1, 2, \ldots, N
\]

\[
P^*(t) \geq MPQ(t), \quad t = 1, 2, \ldots, N
\]

Combining the first two equations yields,

\[
[I^*_m(t - 1) + I^*_w(t - 1)] + P^*(t) - D(t) = [I^*_m(t) + I^*_w(t)], \quad t = 1, 2, \ldots, N.
\]

It is easy to see that $(I^*_m(t) + I^*_w(t), P^*(t))$ is a feasible solution to Problem (2.4).

In addition, the supply chain total profit under the FFS agreement satisfies,

\[
\sum_{t=1}^{N} [W'(t) \times D(t) - h_w(t) \times I^*_w(t) - c(t) \times P^*(t) - h_m(t) \times I^*_m(t)]
\]

\[
\leq \sum_{t=1}^{N} [W'(t) \times D(t) - c(t) \times P^*(t) - h_m(t) \times (I^*_m(t) + I^*_w(t))].
\]
The inequality holds because $h_m(t) \leq h_w(t)$ for all $t$ (consistent with industry). Note the right-hand-side is the total supply chain profit under the DTP agreement with the solution $(I_m^*(t) + I_w^*(t), P^*(t))$. The proof is now complete. \qed

We next show a stronger result that no contractual agreement can do better than the DTP agreement in terms of the total supply chain profit.

**Theorem 2** The DTP agreement optimizes the total supply chain profit among all possible contractual agreements.

**Proof.** We just need to show that the total supply chain profit under the DTP agreement is equal to the total optimal supply chain profit under centralized control. The latter can be formulated as follows.

\[
\begin{align*}
\text{Max} \quad & \sum_{t=1}^{N} [W'(t) \times D(t) - c(t) \times P(t) - h_m(t) \times I_m(t) - h_w(t) \times I_w(t)] \\
\text{s.t.} \quad & I_m(t-1) + P(t) - O(t) = I_m(t), \quad t = 1, 2, \ldots, N \\
& I_w(t-1) + O(t) - D(t) = I_w(t), \quad t = 1, 2, \ldots, N \\
& I_w(t) \leq M_t, \quad t = 1, 2, \ldots, N \\
& P(t) \leq C(t), \quad t = 1, 2, \ldots, N \\
& P(t) \geq MPQ(t), \quad t = 1, 2, \ldots, N \\
\text{All variables are nonnegative.}
\end{align*}
\]

In the optimal solution of Problem (2.5), we must have $I_w^*(t) = 0$ and $O^*(t) = D(t)$ for all $t$. If this is not true, suppose $I_w^*(t) > 0$ for a certain $t$, then keeping the inventory $I_w^*(t)$ at the manufacturer rather than at the wholesaler will reduce inventory holding cost and increase profit. This is contradictory to the assumption of the optimal solution.
for the entire supply chain. Considering this fact, we can simplify Problem (2.5) into,

$$\text{Max } \sum_{t=1}^{N} \left[ W'(t) \times D(t) - c(t) \times P(t) - h_m(t) \times I_m(t) \right]$$

s.t. $I_m(t - 1) + P(t) - D(t) = I_m(t)$, $t = 1, 2, \ldots, N$

$P(t) \leq C(t)$, $t = 1, 2, \ldots, N$ \hfill (2.6)

$P(t) \geq MPQ(t)$, $t = 1, 2, \ldots, N$

All variables are nonnegative.

Clearly, Problem (2.6) has an identical solution as Problem (2.4), and therefore, the total supply chain profit under the DTP agreement is identical to that under the centralized control. The proof is now complete. □

By the proof of Theorem 2, we observe that the manufacturer’s optimal decision and the total supply chain profit under the DTP agreement are independent of the fee structure. Interestingly, the manufacturer’s optimal solution under the DTP agreement is also optimal for the entire supply chain, and the fee structure, $F(t)$, $t = 1, 2, \ldots, N$, provides the manufacturer and the wholesaler the flexibility to split the total supply chain profit in any way that they prefer.

To understand Theorems 1-2 intuitively, we point out that the total revenue of the supply chain remains the same under all contractual agreements because the demand and price (selling to pharmacies) are independent of the contractual terms between the manufacturer and the wholesaler. However, the total supply chain cost under the DTP agreement is lower than that under the BNH and FFS agreements because the wholesaler’s incentive to investment buy is completely eliminated and its inventory level is minimized. Indeed, under the DTP agreement, the wholesaler only carries enough inventory to satisfy demand in each period. In contrast, under the FFS agreement, the wholesaler has an incentive to investment buy within the allowable limit. Thus, the total supply chain profit increases as one moves from the FFS or BNH agreements to the DTP agreement.
We now consider individual supply chain members. The following result shows that starting from any FFS agreement, one can always find a DTP agreement that performs at least as well as the FFS agreement for both the manufacturer and the wholesaler.

**Theorem 3** Given a fee structure, $F'(t), t = 1, 2, \ldots, N$, for the FFS agreement, there must exist a fee structure, $F''(t), t = 1, 2, \ldots, N$, for the DTP agreement to be at least as profitable as the former for both the wholesaler and the manufacturer.

**Proof.** First, it is straightforward to show that under the DTP agreement, the wholesaler’s optimal profit is continuous and increasing in $F(t)$ for each $t$, and the manufacturer’s optimal profit is continuous and decreasing in $F(t)$ for each $t$. In addition, $F(t)$ affects neither the optimal solution for the manufacturer nor the total supply chain profit under the DTP agreement.

Given a fee structure, $F'(t), t = 1, 2, \ldots, N$, for the FFS agreement, it follows by Theorem 1 that there must exist a fee structure, $F''(t), t = 1, 2, \ldots, N$, for the DTP agreement, such that the wholesaler and manufacturer are at least as profitable as they were under the FFS agreement. \(\square\)

The next question, of course, is how to construct a fee structure under the DTP agreement such that both the wholesaler and manufacturer are better off relative to a FFS or BNH agreement? We provide the following necessary conditions.

**Theorem 4** Let $F'(t)$ and $F''(t)$ be the fee structure for the FFS and DTP agreement, respectively. If the wholesaler is better off under all demand sequences as one moves from the FFS to the DTP agreement, we must have $F''(t) \geq W'(t) - W(t) + F'(t), \forall t$. If the wholesaler is better off under all demand sequences as one moves from BNH to DTP, we must have $F''(t) \geq W'(t) - W(t), \forall t$.

**Proof.** We first note, in Problem (2.1), that is, the wholesaler’s problem under the FFS agreement, a feasible solution is $O(t) = D(t)$ for all $t$. Under this solution, the objective function is $\sum_{t=1}^{N} [(W'(t) - W(t) + F'(t))D(t)]$. For the wholesaler’s optimal
profit under the DTP agreement, \( \sum_{t=1}^{N} F''(t)D(t) \), to be greater than its counterpart under the FFS agreement for all demand sequences, one must at least have \( F''(t) \geq W(t)' - W(t) + F'(t), \forall t \). A similar logic applies to the BNH agreement.

Theorem 4 implies that as one moves from the FFS agreement to the DTP agreement, one has to increase the fee at least by the margin, \( W'(t) - W(t) \), in order to maintain the same profitability for the wholesaler.

We now uncover the intuition behind Theorems 3-4 and understand why each player can make more profit under the DTP agreement relative to the FFS agreement. By Theorem 4, the wholesaler’s net margin, \( F''(t) \), under the DTP agreement is higher than its net margin, \( W'(t) - W(t) + F'(t) \), under the FFS agreement. Thus under the DTP agreement, the wholesaler essentially relinquishes investment-buying in return for a higher net margin.

By Theorem 4, the manufacturer’s net margin, \( W'(t) - F''(t) \), under the DTP agreement is lower than its net margin, \( W(t) - F'(t) \), under the FFS agreement. To see why the manufacturer can still make more profit as it moves from the FFS to the DTP agreement, let’s consider a simple system with \( c(t) = c \) for all \( t \). We also relax the constraints of production capacity and minimum production quantity. Thus, the manufacturer’s optimal production plan is to carry no inventory under all agreements. Under the DTP agreement,

\[
\text{Manufacturer’s profit} = \sum_{t=1}^{N} [(W'(t) - F''(t))D(t) - cD(t)]
\]

\[
\text{Wholesaler’s profit} = \sum_{t=1}^{N} F''(t)D(t)
\]

\[
\text{The supply chain total profit} = \sum_{t=1}^{N} [W'(t)D(t) - cD(t)].
\]
Under the FFS agreement,

Manufacturer’s profit = \[\sum_{t=1}^{N} [(W(t) - F'(t))O^*(t) - cO^*(t)]\]

Wholesaler’s profit = \[\sum_{t=1}^{N} [W''(t)D(t) - (W(t) - F'(t))O^*(t) - h_{w}(t)I_{w}^*(t)]\]

The supply chain total profit = \[\sum_{t=1}^{N} [W'(t)D(t) - cD(t) - h_{w}(t)I_{w}^*(t)],\]

where \(O^*(t)\) is the wholesaler’s optimal order under the FFS agreement.

Clearly, \(\sum_{t=1}^{N} cD(t) = \sum_{t=1}^{N} cO^*(t)\). Thus, for the manufacturer’s profit, we only need to compare \(\sum_{t=1}^{N} [(W'(t) - F''(t))D(t)]\) (under DTP) and \(\sum_{t=1}^{N} [(W(t) - F'(t))O^*(t)]\) (under FFS). Although \(W''(t) - F''(t) \leq W'(t) - F'(t)\) for all \(t\) (by Theorem 4), the former can be greater than the latter because as \(W(t)\) and \(W'(t)\) are increasing, \(O^*(t)\) can be much greater than \(D(t)\) just prior to a price increase. Hence the manufacturer can lose a sizable amount of revenue under the FFS agreement relative to the DTP agreement since it sells the inventory \(O^*(t) - D(t)\) before price increases rather than after. This revenue is lost to the wholesaler who captures it by investment buying but at a much higher cost of inventory. By eliminating investment buying, the DTP agreement minimizes the channel inventory carried by the wholesaler and in this way, it achieves the global optimum for the supply chain as a whole.

### 2.3. Illustrative Example

In this section we first describe a few real-world examples, then we quantify the impact of the BNH, FFS and DTP agreements for the manufacturer, the wholesaler, and the supply chain as a whole.
2.3.1 Data

We collected data in cooperation with a major U.S. brand drug manufacturer and a large retail pharmacy chain. We refer the reader to Iacocca and Zhao (2009) for a detailed case study. Here, we summarize the main points. We consider a 24-month planning horizon and the pricing structure of three brand drugs that do not have generic substitutes. The fee that the wholesaler charges the manufacturer under the FFS agreement typically ranges between 3% and 7% in the industry. We also are told that the wholesaler gives discounts to pharmacies which range between 1% and 3% of WAC. The WAC prices are provided by the pharmacy chain and are predictable at the beginning of each year. The aggregated retailer demand and shipments to the wholesaler for the drugs are provided by the manufacturer. Figure 2.3 shows the manufacturer’s shipments (about 90.5% of shipments goes to the wholesaler), the manufacturer’s forecast, retailers’ orders (i.e., wholesaler’s shipments), and the wholesaler’s inventory for drug A. All data are marked up but their patterns remain unchanged. From the figure we can see that the manufacturer’s forecast is quite accurate and the wholesaler is still building inventory towards the end of each year.

Production costs vary from product to product. Production costs are set at 17.5% (in practice, it is between 15% and 20%) of the WAC price in the first year (i.e., 2006 in our data set) for all brand pharmaceutical products. The annual inventory holding cost for the manufacturer is 8% of their production costs, and the annual holding cost for the wholesaler is 8% of WAC. Neither the manufacturer nor the wholesaler have production and storage capacity limits at their facilities. The minimum production quantity for the manufacturer is two weeks of demand. The planning cycle is one month for the manufacturer and the wholesaler places orders on a monthly basis. Depending on volume, the maximum allowable inventory level, $M_t$, can be 1-2 weeks to 3-6 months of demand. In this study, we choose $M_t$ between two weeks and three months of demand. The WAC for the three brand drugs is shown in table 2.2.
Figure 2.3: Empirical data for drug A. 90.5% of manufacturer’s shipments goes to the wholesaler.

2.3.2 Numerical Results

For the real-world example, we solve the optimal ordering, production and inventory decisions for the wholesaler and manufacturer under the BNH, FFS and DTP agreements. Under the FFS agreement, we set $W = WAC$ and $W' = WAC'$, where $WAC'$ is typically $WAC$ less a discount. However, $WAC'$ must be greater than $WAC$ less the fee under FFS for the wholesaler to make a net profit. Consistent to practice, we tested

<table>
<thead>
<tr>
<th>Drug</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A</td>
<td>$484.03</td>
<td>$516.60</td>
<td>$557.00</td>
</tr>
<tr>
<td>Drug B</td>
<td>$362.54</td>
<td>$386.94</td>
<td>$417.20</td>
</tr>
<tr>
<td>Drug C</td>
<td>$717.96</td>
<td>$766.28</td>
<td>$826.20</td>
</tr>
</tbody>
</table>

Table 2.2: The Wholesale Acquisition Price (WAC) for each drug, 2006-2008. Note: Price increase takes place on the first business day each year.
a few fees ranging from 3% to 7% and a few discount values ranging from 1% to 3%. Under the DTP agreement, we set \( W' = \text{WAC}' \) as in the FFS agreement, and choose the fee in the same range as the FFS agreement. Finally, for the BNH agreement to be comparable to the FFS and DTP agreements, we set \( W' = \text{WAC}' \) as before and \( W = \text{WAC} \) less the fee of the FFS agreement.

In all examples, the first period begins in July and the wholesaler satisfies 24 periods (months) of demand. Recall that under the BNH agreement, the wholesaler does not have any buying restrictions. Thus, our numerical study shows that the optimal solution for the wholesaler is to buy enough inventory in the last period (December) before WAC increases to satisfy demand in full for the following eight periods (January through August). In September through November, the wholesaler only buys enough of the drug to satisfy demand during that period, and thus carries no investment-buying inventory during this time. Under the FFS agreement, the manufacturer limits how much inventory the wholesaler can carry. The optimal plan for the wholesaler under the FFS agreement is to order enough inventory in December up to the maximum allowable amount. Once that inventory is depleted, it returns to monthly ordering and carry zero investment-buying inventory. For example, under the FFS agreement with an inventory limit of three months, the optimal plan is to order sufficient quantity in December to satisfy demand in January through March next year. In April the wholesaler resumes ordering and only orders enough to satisfy demand in that period. Finally, under the DTP agreement the wholesaler’s incentive to investment buy is eliminated. Thus, it orders the demand in each period and carries zero investment-buying inventory.

Under all contractual agreements, the manufacturer produces enough in each period to satisfy the wholesaler’s order and carries no excess inventory. The solution is intuitive as the production cost remains constant over time.

Table 2.3 summarizes the total supply chain profit aggregated among the three drugs under the three agreements. For the FFS agreement, we compute the profit for each selected inventory limit. Our numerical results show that the total supply chain
Table 2.3: The supply chain total profits of the BNH, FFS and DTP agreements aggregated over three drugs. Note: All dollar amounts are shown in millions

<table>
<thead>
<tr>
<th>W</th>
<th>3% discount off WAC</th>
<th>1% discount off WAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTP</td>
<td>$5,442</td>
<td>$5,577</td>
</tr>
<tr>
<td>FFS (inventory limit $M_t = 2$ weeks)</td>
<td>$5,440</td>
<td>$5,575</td>
</tr>
<tr>
<td>FFS ($M_t = 1$ month)</td>
<td>$5,438</td>
<td>$5,573</td>
</tr>
<tr>
<td>FFS ($M_t = 2$ months)</td>
<td>$5,431</td>
<td>$5,566</td>
</tr>
<tr>
<td>FFS ($M_t = 3$ months)</td>
<td>$5,416</td>
<td>$5,551</td>
</tr>
<tr>
<td>BNH</td>
<td>$5,320</td>
<td>$5,455</td>
</tr>
</tbody>
</table>

profit under the BNH and FFS agreements does not depend on the fee of the FFS agreement. In terms of the total supply chain profit, Table 2.3 shows that the DTP agreement performs better than the FFS agreement, and the FFS agreement performs better than the BNH agreement, regardless of the discount, inventory limit, and fee structure. In the FFS agreement, the tighter the wholesaler’s inventory limit, the less it can investment buy, and thus the difference between the FFS and DTP agreements decreases as the inventory limit decreases.

Depending on the inventory limit, the DTP agreement can increase the supply chain total profit by about $0.04\% \sim 0.48\%$ (2.29%) compared to the FFS agreement (BNH agreement) when the pharmacy pays 97% of the WAC. The DTP agreement can increase the total supply chain profit by about $0.04\% \sim 0.47\%$ (2.22%) compared to the FFS agreement (BNH agreement) when the pharmacy pays 99% of the WAC. This percentage improvement only takes the production-inventory cost into account but ignores all other costs such as R&D costs, selling, marketing and administrative expenses, as well as transportation costs. By looking through companies’ annual reports, we found that wholesalers’ selling, distribution and administrative cost is about 3.46% of their sales, major brand-drug manufacturers typically spend 18% of sales on R&D, and 30% on selling and administration. After taking these expenses into consideration, on average, the DTP agreement can improve the supply chain total profit by about 0.08% to 1% relative to the FFS agreement and by about 5% relative to the BNH
agreement.

To illustrate the flexibility of the DTP agreement on increasing profits (relative to the FFS agreement) for both the manufacturer and wholesaler, we consider a special case of the FFS agreement with a 2-month inventory limit and assume that the manufacturer and wholesaler equally split the additional supply chain total profit generated by the DTP agreement (relative to FFS). In Tables 2.4-2.5, we show the profits of the wholesaler and the manufacturer under the DTP and FFS agreements. In Table 2.6 we show the corresponding fee structure of the DTP agreement.

<table>
<thead>
<tr>
<th>W’</th>
<th>3% discount off WAC</th>
<th>1% discount off WAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fee of FFS</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>FFS</td>
<td>$199.1</td>
<td>$332.4</td>
</tr>
<tr>
<td>DTP</td>
<td>$204.7</td>
<td>$338</td>
</tr>
<tr>
<td>% Improvement</td>
<td>2.84%</td>
<td>1.70%</td>
</tr>
</tbody>
</table>

Table 2.4: Wholesaler’s profit aggregated among three drugs. Note: All dollar amounts are shown in millions. The FFS agreement has a 2-month inventory limit.

<table>
<thead>
<tr>
<th>W’</th>
<th>3% discount off WAC</th>
<th>1% discount off WAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fee of FFS</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>FFS</td>
<td>$5,231.6</td>
<td>$5,098.3</td>
</tr>
<tr>
<td>DTP</td>
<td>$5,237.3</td>
<td>$5,104</td>
</tr>
<tr>
<td>% Improvement</td>
<td>0.11%</td>
<td>0.11%</td>
</tr>
</tbody>
</table>

Table 2.5: Manufacturer’s profit aggregated among three drugs. Note: All dollar amounts are shown in millions. The FFS agreement has a 2-month inventory limit.

<table>
<thead>
<tr>
<th>W’</th>
<th>3% discount off WAC</th>
<th>1% discount off WAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fee of FFS</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Fee of DTP</td>
<td>3.034%</td>
<td>5.011%</td>
</tr>
</tbody>
</table>

Table 2.6: The fee under the DTP agreement that equally splits the additional supply chain total profit between the manufacturer and wholesaler.

Table 2.6 is consistent to Theorem 4: In all cases, the wholesaler’s net margins under the DTP agreement (the fee of DTP) are greater than those under the FFS agreement.
(fee of FFS less pharmacy discount). In addition, as the wholesaler’s net margin under the FFS agreement increases, the percentage improvement of profit (from FFS to DTP) decreases for the wholesaler. The equal split in the additional supply chain total profit is chosen to illustrate the potential impact on profit for the manufacturer and wholesaler. In practice, the division of the additional supply chain total profit needs to be negotiated between the two players.

2.4. Generalization and Summary Remarks

In this chapter, we model and compare the resell distribution agreements (BNH, FFS) and the direct distribution agreement (DTP) for the U.S. pharmaceutical industry. We consider predictable demand and prices and show that by minimizing channel inventory, the DTP agreement achieves channel coordination and thus always outperforms the FFS and BNH agreements in terms of overall supply chain profit. The DTP agreement is also flexible because it allows the total supply chain profit to be split in an arbitrary way between the manufacturer and the wholesaler. We further provide necessary conditions for the fee under the DTP agreement to be “fair” – mutually beneficial to all supply chain participants relative to the BNH and FFS agreements.

This study allows us to settle the debate among industry observers regarding the impact of the distribution agreements – BNH, FFS and DTP on the pharmaceutical supply chain. It further shows that the DTP agreement allows the manufacturers to continue utilizing the wholesalers’ expertise to manage drug distribution while aligning their incentives and ensure mutual benefits.

These results and insights can be valid beyond the pharmaceutical industry. In what follows, we shall characterize the general assumptions under which they hold. As we define earlier, under the resell model wholesalers buy products from manufacturers (thus own the inventory) and resell them to outside customers; while under the direct model, wholesalers manage distribution for a fee (and they do not own the inventory),
and manufacturers receive revenue *directly* from outside customers. We restate here that the resell and direct models differ only by inventory ownership and payment flows. In both models, the wholesalers are responsible for logistics and distribution decisions and bear the associated costs.

Under the assumption of predictable price (to outside customers) and demand (from outside customers), it follows by our model and analysis (specifically Theorem 2 and its proof) that given all else being equal, the direct model should always outperform the resell model in total supply chain profit if the following assumptions hold:

1. The price and demand are exogenous to the contractual agreement between the manufacturer and wholesaler.

2. The manufacturer has lower inventory holding costs than the wholesaler under the resell model.

3. The wholesaler has negligible economies of scale in ordering, and the manufacturer has negligible economies of scale in demand fulfillment.

4. The service fee in the direct model is independent of the manufacturer’s production decision.

While these conditions cover a broad range of wholesale price schemes and service fees (e.g., volume dependent, time varying), and apply to industries with highly valued products and relatively insignificant shipping costs (such as the pharmaceutical industry of branded prescription drugs), they do not apply to industries with relatively low-value products and significant economies of scale in shipping and demand fulfillment, such as food, grocery, chemical and many consumer-packaged products. In these industries, the direct model does not coordinate the supply chain and may not outperform the resell model in total supply chain profit (Jeuland and Shugan, 1983). The direct model also may not outperform the resell model when the wholesaler has lower inventory holding costs than the manufacturer under the resell model.
For industries where these assumptions apply, the performance gap between the direct and the resell models depends on the pattern of the price (to outside customers). If the price is always increasing (as in pharmaceutical and biotech industries for brand drugs), the direct model outperforms the resell model in total supply chain profit. In industries where the price is always decreasing, such as computer and electronics, wholesalers have no incentive to investment buy. Thus given all else being equal, the direct model should have the same performance as the resell model. In industries where the price is oscillating but predictable, such as seasonal items, investment buying can occur in the resell model. Thus, the direct model outperforms the resell model.
Chapter 3

Explaining Brand-Drug Prices Through Observable Factors

In the previous chapter we compared different contract structures and showed that the Direct-to-Pharmacy agreement improves efficiency in drug distribution. However, all agreements discussed were based on the Wholesale Acquisition Cost (WAC), which is set by the manufacturers. This chapter is motivated by a lack of definitive answers as to what determines these WAC drug prices. One challenge of such research is data – some of the important factors, such as R&D costs, marketing efforts and supply chain costs of individual drugs, are not observable to the public. In absence of these data, we have to take a different approach by developing measures based on publicly observable information for four classes of factors: the level of competition, the nature of the condition that the drug treats, the number of years that the drug has had FDA approval, and the manufacturer who developed the product. The objective of this chapter is to test the significance of these measures in predicting prices for brand drugs.

To understand how prices are set in the industry, we note that most prescription drugs go through three owners before they reach the end-user. The manufacturer produces the drug and sells it to the wholesaler who then sells the drug to the pharmacy and hospital. The pharmacy or hospital then dispenses and sells the drug to the consumer. Manufacturers set the WAC price. Due to competition in the market, the final price that pharmacies pay is usually 1-3% less than WAC. Nonetheless, the initial setting of
the WAC is vital in the pharmaceutical supply chain because it serves as the basis for all other prices and reimbursements. Thus, the objective of this chapter is to study what - if any - factors influence the WAC price.

We develop a linear model to predict WAC using covariates that are easily accessible to all market participants. While previous research has studied some of these factors, our analysis is unique in two aspects: first, we develop measures for the aforementioned four classes of factors based on information observable to the public; second, we develop a unifying framework to explain prescription drug prices by this broad range of factors. With such a reference model at hand, wholesalers and insurers can be more informed and stand at a better position to predict and negotiate prices with the manufacturers.

The rest of this chapter is organized as follows: Section 3.1 provides a literature review. Section 3.2 presents the research methodology and several hypotheses regarding the drug prices in the pharmaceutical industry. We also discuss the data used in the study. In Section 3.3, we present our findings and discuss their implications in 3.4. Finally, we conclude the chapter and summarize the results in Section 3.5.

3.1. Literature Review

There are a number of recent studies which focus on the price-setting mechanism of prescription drugs. Dicken (2009) explain that the healthcare industry is different from other industries at price setting because the consumer is not always conscious of the price of a product. Indeed, if the patient has some form of insurance that pays for some or all of the drug’s cost, then the patient may not be aware of the drug price. Consequently, unlike other industries, the demand for prescription drugs may not be strongly influenced by prices. Kleinke (2001) discusses how the high cost of many drugs can lower healthcare expenses in the short-run or long-run. He defends the high price of prescription drugs, showing how an innovative drug can keep a patient out of the hospital altogether or delay the illness. He points out that while some drugs do not
reduce healthcare expenses, they do improve the quality of life. He argues that drug pricing should be based on the benefit provided to the patient. Lu and Comanor (1998) perform an empirical study and conclude that drug prices are determined by the level of therapeutic advancement and the prices follow a modified skimming/penetration pricing strategy introduced by Dean (1969).

Berndt (2002) examines the variables that influence manufacturers when they set the price of patent-protected brand drugs. He concludes that the price is determined by the marginal value that the drug brings to the end users rather than marginal production cost. He notes that prices are relatively constant across dosage levels and concludes that prices are not affected by active ingredient levels. In addition, he discusses a number of other economic factors which contribute to drug prices, but argues that for short-run pricing, R&D costs are sunk and therefore irrelevant to the manufacturer’s pricing decision. The authors refer the reader to Scherer (1993) for a summary of the trade off between maintaining low prices to stimulate demand versus high prices to provide incentives for new product development.

Building on this line of work are a number of papers that discuss the retail price of brand drugs when generic substitutes are introduced. Berndt (2002) finds that brand drugs do not engage in price competition with generic substitutes. Instead, brand drug prices actually increase and sales are concentrated in the smaller market of brand-loyal customers. Other studies have found that after the introduction of generics, brand prices actually rose (Frank and Salkever, 1992; Grabowski and Vernon, 1992). Some others found that brand prices may fall but only by a small percentage. For instance, Caves et al. (1991) performed a regression study on thirty drugs that went off patent between 1976 and 1987 and concluded that brand-drug prices have a small response when generics are introduced. A more recent econometric analysis was done by Frank and Salkever (1997) to study the pricing behavior when generics were introduced. They found that increased competition among generic drug producers did account for reduced generic prices. However, this increased competition of generic drugs did not affect
brand-drug prices.

Our work in this chapter is closely related to the empirical studies of Berndt (2002), Frank and Salkever (1997), Lu and Comanor (1998), and Caves et al. (1991). Our analysis is unique because it develops a unifying framework to explain brand-name drug prices by a broad range of factors that are observable by the public. These factors include the level of competition, therapeutic objective, age of the drug, and the manufacturer.

3.2. Research Methodology

Public statements, such as those made by PhRMA (see Chapter 1), have suggested that manufacturers consider R&D and raw material costs when determining the WAC price. Regardless of the validity of these statements, drug-specific R&D and raw material costs are not observable to most supply chain participants. We propose that the variation in WAC prices can be explained by other factors such as the level of competition, the therapeutic purpose, the age of the drug, and the manufacturer. We consider these factors because they are observable to all parties in the pharmaceutical supply chain. In this section, we first discuss a set of hypotheses that connect these observable factors and WAC prices, then we proceed to test them empirically.

3.2.1 Hypotheses

HYPOTHESIS 1: Increased competition in the market decreases the WAC price of a drug.

H1a: The more drugs (both brand and generic) in a therapeutic class, the lower the price for drugs in that therapeutic class.

H1b: The number of generic drugs in a therapeutic class depresses the price of a brand drug in that therapeutic class.

H1c: The number of dosing levels of a brand drug decreases its average WAC price.
This set of hypotheses is based on the standard economic theory that more competition results in lower overall prices. In \( H1a \), we posit the most general theory that more competitors drive down prices. \( H1b \) represents a refinement of \( H1a \) reflecting the fact that generic competitors are more aggressive in competing on price than brand competitors. This is true because brand manufacturers compete on both price and non-price factors (e.g., advertising) while generic manufacturers typically compete only on price. Finally, \( H1c \) incorporates much of the thinking underlying the other two hypotheses with respect to competition. As a therapeutic class becomes more competitive, manufacturers may feel the need to differentiate themselves by offering more dosing levels.

**HYPOTHESIS 2: There are differences in drug prices which are driven by the conditions treated**

\( H2a \): The WAC price of a drug tends to be high if the conditions treated are uncommon.

\( H2b \): The WAC price of a drug tends to be high if the conditions treated are life-threatening.

\( H2c \): The WAC price of a drug tends to be high if the conditions treated are both uncommon and life-threatening.

We posit in \( H2a \) that drugs treating uncommon conditions are likely to be more expensive than their counterparts that treat common conditions. Uncommon conditions by definition have fewer patients with fewer prescriptions. Therefore fixed costs (i.e., R&D, etc.) will need to be spread over a smaller volume, resulting in higher prices per unit for drugs treating uncommon conditions. \( H2b \) suggests that drugs treating life-threatening conditions have higher prices than drugs treating conditions that are not life-threatening. It seems plausible that life-saving drugs are more expensive than life-improving drugs, as supported by Berndt (2002) who suggested that manufacturers price branded drugs based on the marginal value to the consumer. Consider two patients:
one suffering from heart disease and is prescribed a medication that reduces the risk of a stroke; and the other suffering from allergies and is prescribed a medication to relieve her stuffy nose and watery eyes. It is plausible that the former patient is willing to pay more for the potentially life-saving medication than the latter patient for the quality-of-life enhancing medication.

We also propose a new theory in \( H2c \) to explain why drugs may be priced differently. We hypothesize that uncommon conditions that are not life-threatening may have limited demand unless prices are set relatively low. In addition, life-threatening conditions that are common will experience increased competition and thus also maintain lower prices. However, if the condition is uncommon and life-threatening, then there are no constraints from either the demand or the supply side to place downward pressure on prices. Therefore, we expect a drug to be more expensive if the following two conditions hold simultaneously: 1a) the condition treated is uncommon, and 1b) the condition treated is life-threatening. By the logic above, \( H2c \) may be true even if \( H2a \) and \( H2b \) are false. The combination of the uncommon and life-threatening variables may be significant while each alone may not be significant to explain WAC prices.

We define common and uncommon therapeutic classes by ranking the total prescriptions dispensed in 2007 over all drugs in each therapeutic class. We use data from Verispan VONA, select the median class as the base, and mark all therapeutic classes above it as common and the rest as uncommon. A detailed list of common and uncommon therapeutic classes is presented in Section 3.2.3.

The definition of life-threatening and non-life threatening therapeutic classes comes from statistics of the causes of deaths in 2007 from the U.S. Department of Health and Human Services. In the report, the Centers for Disease Control and Prevention lists the fifteen leading causes of death in 2007. Those therapeutic classes corresponding to a cause listed in the report are marked as life-threatening while all others are marked non-life threatening. A detailed list of therapeutic classes that treat life threatening or non-life threatening conditions is shown in Section 3.2.3.
**HYPOTHESIS 3: Older drugs are less expensive than newer drugs.**

Hypothesis 3 conjectures that as new drugs enter the market, they will be priced higher than their close substitutes in the same therapeutic class that are older. In the U.S. pharmaceutical industry, drug prices are generally increasing over time. Despite this fact, we posit that older drugs do not raise their prices to the extent that they are priced higher than their close substitutes that are newer. For example, in the antidepressant therapeutic class, Prozac was the first Selective Serotonic Reuptake Inhibitor (SSRI) and came on the market in 1988. Prozac was followed by a number of branded SSRIs including Zoloft in 1992, Paxil in 1993, Luvox in 1994 and Celexa in 1998. Thus, we would expect Prozac’s price to be lower than Celexa’s price. If this hypothesis holds true, then a further study is required to find out why older drugs are priced lower than their newer counterparts. The price differential may come from competition, newer technology, or greater drug efficacy. In this study we simply test to see if older drugs are priced lower than newer drugs in the same therapeutic class.

**HYPOTHESIS 4: There are differences in prices among manufacturers that cannot be explained by the observable factors mentioned above.**

Hypothesis 4 examines whether manufacturers systematically set their drug prices differently. If this hypothesis is true, then a further study is required to find out why manufacturers differ in their price setting after controlling for factors such as competition and therapeutic purpose. For example, differences across manufacturers could come from differences in drug efficacy, side effects and advertising costs. There may also be differences in the production and supply chain processes which lead to differences in cost of goods sold which are in turn reflected in prices. In this study we test whether manufacturers differ on drug prices controlling for other factors. We shall leave it to future research to uncover the source of the difference in prices attributable to manufacturer.
3.2.2 Model

We use a simple linear model to evaluate the contribution that the observable variables have on WAC prices. Consider a market of $J$ brand drugs, $j = 1, \ldots, J$, whose price can be represented by the following function:

$$
\ln(\text{Price}_j) = \beta_0 + \beta_1 x_j + \beta_2 g_j + \beta_3 p_j + \beta_4 d_j \\
+ \beta_5 r_j + \beta_6 t_j + \beta_7 r_j t_j + m_j \lambda' + e_j.
$$

(3.1)

In this equation, $x_j$ represents the number of years that the drug has had FDA approval, $g_j$ is the number of generics in the therapeutic class, $p_j$ is the number of total competitors (brand and generic) in the therapeutic class, and $d_j$ is the number of dosing levels available for drug $j$. $r_j$ and $t_j$ are dummy variables, where $r_j = 1$ if drug $j$ is a member of a therapeutic class that treats an uncommon condition, $r_j = 0$ otherwise; $t_j = 1$ if drug $j$ is a member of a therapeutic class that treats a life-threatening condition, $t_j = 0$ otherwise. There are $K$ manufacturers, $k = 1, \ldots, K$. $m_j$ is a $K$ vector of dummy variables. $m_{jk} = 1$ if drug $j$ is produced by manufacturer $k$, 0 otherwise.

The parameters $\beta_2, \beta_3, \beta_4$ are designed to test Hypothesis 1 regarding the effect of competition on prices. Under our hypothesis, we expect each of these parameters to be negative – more competition leads to lower prices. The parameters $\beta_5$, $\beta_6$, and $\beta_7$ are designed to test Hypothesis 2. We expect $\beta_5$ and $\beta_6$ to be positive as uncommon or life-threatening conditions lead to higher prices. $\beta_7$ is also expected to be positive as the combination of uncommon and life-threatening conditions is expected to produce the smallest downward price pressure. Parameter $\beta_1$ is designed to test Hypothesis 3. We expect this parameter to be negative because the longer the drug has been on the market, the less expensive we expect it to be. Finally, $\lambda = (\lambda_1, \lambda_2, \ldots, \lambda_K)$ is a $K$ dimensional parameter vector for the manufacturers. We expect some elements of $\lambda$ to be different from zero, reflecting our Hypothesis 4 that some drug manufacturers set
prices differently than others even after controlling for all other observable factors.

In addition to Eq. (3.1), we estimate another equation to gain additional insight into drug prices:

$$\ln(Price_j) = \beta_0 + \beta_1 x_j + \beta_2 g_j + \beta_3 p_j + \beta_4 d_j + \mathbf{tc}_j \gamma' + \mathbf{m}_j \lambda' + e_j.$$  \hspace{1cm} (3.2)

Here we replace the covariates on life-threatening and common conditions with a vector of dummy variables to represent the different therapeutic class. This enables us to see differences in pricing across therapeutic classes. There are \(N\) therapeutic classes, \(n = 1, ..., N\), thus \(\mathbf{tc}_j\) has \(N\) elements: \(tc_{jn} = 1\) if drug \(j\) is a member of therapeutic class \(n\) and \(tc_{jn} = 0\) otherwise. \(\gamma = (\gamma_1, \gamma_2, ..., \gamma_N)\) is an \(N\) dimensional parameter vector for the therapeutic classes. Estimating this vector allows us to further explore Hypothesis 2 by testing for differences in pricing between therapeutic classes. We expect those elements of \(\gamma\) that correspond to therapeutic classes that are life-threatening and/or uncommon to be positive, while elements of \(\gamma\) that correspond to therapeutic classes that are non-life threatening and common to be negative.

All of these parameters are estimated using ordinary least squares (OLS) using robust standard errors (White, 1980). In addition to being computationally convenient, OLS is well suited to this application. By using the natural logarithm of price as the dependent variable, we model price as a non-linear function of the covariates. We can interpret the parameters as the % change in price which will result from increasing a specific right-hand-side variable. By using robust standard errors, we allow for the possibility that the variance of \(e_j\) is not constant across drugs. With the exception of the number of drugs (competitors), all of the right-hand-side variables are completely exogenous. It is possible that the number of competitors is endogenous. For example, it could be argued that a class with high prices will attract a large number of competitors. Modeling the number of competitors as endogenous would require a dynamic entry model which is beyond the capability of our data as we observe only a single period.
snapshot. We are effectively assuming that firms decide to enter a therapeutic class prior to making pricing decisions. Given the long lead time for R&D and FDA approval, this assumption seems appropriate. There is no reason to expect that any of the right-hand-side variables is linearly dependent on any combination of the others, hence the matrix of covariates has full-column rank in expectation. As a check, we run a correlation matrix for the covariates and find all the sample correlations to be less than 0.29 in absolute value. Finally, given the relatively large number of drugs in this analysis (J=252), we can use the large sample properties of the OLS estimator and do not make any assumptions regarding the underlying distribution of the disturbances.

### 3.2.3 Data

The data on prescription drug characteristics came primarily from a large North American retail pharmacy. Data is available on the WAC price for the 2,000 most commonly prescribed drugs in 2007 (of which 598 are brand) as well as dosing levels for each drug. The prices for every drug were for a 1-month of supply. Additional information is available on whether the drug was brand or generic.

Additional data collection was done to find the manufacturer and therapeutic class of each drug, the date of FDA approval, as well as the number of dosing levels available and the number of prescriptions dispensed for each therapeutic class. The therapeutic classes were determined by the Blue Cross Blue Shield Therapeutic Class Workbook. There are two levels of therapeutic classes that were collected – micro and macro levels. A preliminary analysis revealed that the micro-level of therapeutic classes would yield a large number of variables with a small number of observations in each class. Therefore the macro-level was used to create a sufficiently large number of drugs in each therapeutic class. Finally, the process for assigning drugs to “common” or “life-threatening” conditions is described above in §3.2.

598 prescription brand drugs were used in this analysis. Many drugs have multiple dosing levels that would lead to biased results as the same drug may be added into the
Table 3.1: Descriptive statistics across the entire data set.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Variable</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real Price</td>
<td>234.07</td>
<td>251.79</td>
<td>Log Price</td>
<td>5.12</td>
<td>0.78</td>
</tr>
<tr>
<td>Years Since FDA Approval</td>
<td>11.67</td>
<td>9.39</td>
<td>Number of Dosing Levels</td>
<td>2.24</td>
<td>1.73</td>
</tr>
</tbody>
</table>

model more than once. To resolve this issue, drugs with multiple dosing levels were consolidated into one drug, with the price being the average of the WAC prices over all dosing levels. This reduced the number of observations in our analysis to 252 drugs.

Table 3.2: Statistics on the number of generics and manufacturers in a therapeutic class.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Variable</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic Drugs</td>
<td>2.94</td>
<td>2.93</td>
<td>Manufacturers</td>
<td>9.56</td>
<td>4.76</td>
</tr>
</tbody>
</table>

Table 3.1 shows the descriptive statistics for the dependent variable, price, and two additional variables. The mean and standard deviation are taken over all drugs in the data set. Table 3.2 shows descriptive statistics on the number of generics and number of manufacturers in a therapeutic class. Tables 3.3 and 3.4 show the descriptive statistics on the price for each therapeutic class and each manufacturer, respectively. Table 3.3 also presents the classification of each therapeutic class.

The gastrointestinal therapeutic class (not life-threatening but common) was used as a reference when coding the therapeutic classes for common and uncommon classes. It is selected because on the ranking of total prescriptions filled in 2007 over all drugs in a therapeutic class, the gastrointestinal class stands as the median. Using this class as a base we marked the eight therapeutic classes above it as common and the eight therapeutic classes below it as uncommon.
<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Mean (n=252)</th>
<th>Standard Deviation</th>
<th>Uncommon Condition</th>
<th>Life Threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Infective</td>
<td>313.73</td>
<td>218.99</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Blood Modifying</td>
<td>434.52</td>
<td>278.71</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cancer</td>
<td>286.13</td>
<td>52.52</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>239.57</td>
<td>22.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye</td>
<td>90.87</td>
<td>12.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>231.10</td>
<td>32.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>148.98</td>
<td>24.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart and Circulatory</td>
<td>176.32</td>
<td>19.63</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Hormones</td>
<td>160.47</td>
<td>20.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>105.54</td>
<td>19.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>410.49</td>
<td>210.25</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>201.48</td>
<td>22.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Relief</td>
<td>156.60</td>
<td>14.83</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Respiratory</td>
<td>168.32</td>
<td>52.75</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Skin Conditions</td>
<td>173.14</td>
<td>26.33</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Topical</td>
<td>119.81</td>
<td>30.09</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Viral Infections</td>
<td>637.69</td>
<td>70.46</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Table 3.3: Classification and Statistics of real price for each therapeutic class.

3.3. Empirical Analysis

We estimate Eqs. (3.1) and (3.2) by OLS. To test our hypotheses above, we include the full set of explanatory variables for competition, therapeutic class, age, and manufacturer. In Eq. (3.1), there are a total of 37 explanatory variables, including 30 manufacturers, the number of years since FDA approval, the number of generics in the therapeutic class, the number of dosing levels available, the number of competitors in the therapeutic class, and three dummy variables for rare and life threatening therapeutic classes. In Eq. (3.2), there are a total of 51 explanatory variables as we replace the three dummy variables for rare and life threatening therapeutic classes by the 17 therapeutic classes.

The $R^2$ value for this model using Eq. (3.1) is 0.413. By Table 3.5, we can observe the result of this initial estimation: Six (or four) parameters are significantly different from zero at $\alpha = 0.10$ (or 0.05, respectively). This includes three manufacturers, drugs
<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Mean (n=252)</th>
<th>Standard Deviation</th>
<th>Variable</th>
<th>Mean (n=252)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>217.61</td>
<td>167.53</td>
<td>M2</td>
<td>213.49</td>
<td>34.22</td>
</tr>
<tr>
<td>M3</td>
<td>165.00</td>
<td>58.56</td>
<td>M4</td>
<td>227.63</td>
<td>15.47</td>
</tr>
<tr>
<td>M5</td>
<td>236.70</td>
<td>16.29</td>
<td>M6</td>
<td>235.18</td>
<td>16.03</td>
</tr>
<tr>
<td>M7</td>
<td>248.18</td>
<td>61.02</td>
<td>M8</td>
<td>145.97</td>
<td>38.69</td>
</tr>
<tr>
<td>M9</td>
<td>154.86</td>
<td>15.38</td>
<td>M10</td>
<td>678.74</td>
<td>84.90</td>
</tr>
<tr>
<td>M11</td>
<td>227.89</td>
<td>40.00</td>
<td>M12</td>
<td>460.46</td>
<td>180.88</td>
</tr>
<tr>
<td>M13</td>
<td>157.94</td>
<td>41.38</td>
<td>M14</td>
<td>236.38</td>
<td>58.40</td>
</tr>
<tr>
<td>M15</td>
<td>154.39</td>
<td>28.08</td>
<td>M16</td>
<td>156.10</td>
<td>26.64</td>
</tr>
<tr>
<td>M17</td>
<td>120.05</td>
<td>11.90</td>
<td>M18</td>
<td>166.16</td>
<td>15.93</td>
</tr>
<tr>
<td>M19</td>
<td>1000.88</td>
<td>833.05</td>
<td>M20</td>
<td>199.26</td>
<td>104.91</td>
</tr>
<tr>
<td>M21</td>
<td>198.97</td>
<td>36.01</td>
<td>M22</td>
<td>214.07</td>
<td>101.46</td>
</tr>
<tr>
<td>M23</td>
<td>205.61</td>
<td>128.69</td>
<td>M24</td>
<td>268.14</td>
<td>103.25</td>
</tr>
<tr>
<td>M25</td>
<td>189.45</td>
<td>16.94</td>
<td>M26</td>
<td>269.93</td>
<td>100.18</td>
</tr>
<tr>
<td>M27</td>
<td>203.12</td>
<td>45.37</td>
<td>M28</td>
<td>292.46</td>
<td>64.01</td>
</tr>
<tr>
<td>M29</td>
<td>301.60</td>
<td>108.21</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.4: Statistics on real price for each manufacturer.

that treat both uncommon and life threatening conditions, the number of dosing levels, and the number of years since FDA approval (the age of the drug).

The $R^2$ value using Eq. (3.2) is 0.490. By Table 3.6, we observe that nine (or eight) parameters are significantly different from zero at $\alpha = 0.10$ (or 0.05, respectively). This includes three therapeutic classes, four manufacturers, the number of dosing levels, and the number of years since FDA approval. Note the increase in $R^2$ from adding 14 explanatory variables in Eq. (3.2) is relatively modest.

By Tables 3.5 and 3.6, the price can be predicted as follows:

$$\hat{\ln(Price)}_j = 5.176 - 0.015x_j - 0.038d_j$$
$$+ 0.827r_jt_j + 0.74M_{12} + 1.418M_{19} + 0.5M_{28}, \quad (3.3)$$

and

$$\hat{\ln(Price)}_j = 5.145 - 0.012x_j - 0.024d_j + 0.911TC_1 - 0.257TC_2$$
$$+ 1.262TC_3 + 0.864M_{12} + 1.263M_{19} + 0.774M_{28} + 0.6283M_{29}. \quad (3.4)$$
<table>
<thead>
<tr>
<th>Variable</th>
<th>Est. Coefficient</th>
<th>Variable</th>
<th>Est. Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>5.176***</td>
<td>M12</td>
<td>0.740**</td>
</tr>
<tr>
<td>Years</td>
<td>−0.015***</td>
<td>M13</td>
<td>0.013</td>
</tr>
<tr>
<td># of Comp</td>
<td>0.007</td>
<td>M14</td>
<td>0.208</td>
</tr>
<tr>
<td># of Generics</td>
<td>0.008</td>
<td>M15</td>
<td>−0.002</td>
</tr>
<tr>
<td># of Dosing Levels</td>
<td>−0.038*</td>
<td>M16</td>
<td>−0.016</td>
</tr>
<tr>
<td>Rare</td>
<td>−0.133</td>
<td>M17</td>
<td>−0.033</td>
</tr>
<tr>
<td>Life Threatening</td>
<td>−0.164</td>
<td>M18</td>
<td>−0.024</td>
</tr>
<tr>
<td>Rare &amp; Life Threatening</td>
<td>0.827***</td>
<td>M19</td>
<td>1.418***</td>
</tr>
<tr>
<td>M1</td>
<td>−0.467</td>
<td>M20</td>
<td>−0.194</td>
</tr>
<tr>
<td>M2</td>
<td>0.167</td>
<td>M21</td>
<td>0.227</td>
</tr>
<tr>
<td>M3</td>
<td>−0.097</td>
<td>M22</td>
<td>−0.175</td>
</tr>
<tr>
<td>M4</td>
<td>0.378</td>
<td>M23</td>
<td>−0.071</td>
</tr>
<tr>
<td>M5</td>
<td>−0.308</td>
<td>M24</td>
<td>0.397</td>
</tr>
<tr>
<td>M6</td>
<td>−0.033</td>
<td>M25</td>
<td>0.236</td>
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<tr>
<td>M7</td>
<td>0.341</td>
<td>M26</td>
<td>0.343</td>
</tr>
<tr>
<td>M8</td>
<td>−0.423</td>
<td>M27</td>
<td>0.119</td>
</tr>
<tr>
<td>M9</td>
<td>0.082</td>
<td>M28</td>
<td>0.500*</td>
</tr>
<tr>
<td>M10</td>
<td>0.549</td>
<td>M29</td>
<td>0.516</td>
</tr>
<tr>
<td>M11</td>
<td>−0.099</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.5: Model Estimated Coefficients (Eq. 3.1). ***= significant at α = 0.01, **= significant at α = 0.05, *= significant at α = 0.1.

### 3.4. Discussion

#### 3.4.1 Competition

By Table 3.5, we see that our hypothesis $H1c$ holds, but $H1a$ and $H1b$ do not. When all other variables are held constant, the WAC price decreases by 3.8% for every additional dosing level introduced. It may be true that some drugs are found to have higher efficacy at lower doses. Since lower dosing levels are typically priced lower, we would expect more dosing levels to be associated with lower prices. An increase in dosing levels has been shown by Berndt (2002) to intensify marketing efforts. If the marketing efforts are in the form of promotions and advertising, we would expect the price to increase. However, we would expect the price to decrease if the marketing efforts were in the area of price competition. Our results differ from Berndt (2002) because we predict...
Table 3.6: Model Estimated Coefficients with Therapeutic Classes (Eq. 3.2). ***= significant at $\alpha = 0.01$, **= significant at $\alpha = 0.05$, *= significant at $\alpha = 0.1$.  

<table>
<thead>
<tr>
<th>Variable</th>
<th>Est. Coefficient</th>
<th>Variable</th>
<th>Est. Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>5.411***</td>
<td>M5</td>
<td>-0.389</td>
</tr>
<tr>
<td>Years</td>
<td>-0.014***</td>
<td>M6</td>
<td>-0.111</td>
</tr>
<tr>
<td># of Comp</td>
<td>0.000</td>
<td>M7</td>
<td>0.340</td>
</tr>
<tr>
<td># of Generics</td>
<td>-0.004</td>
<td>M8</td>
<td>-0.483</td>
</tr>
<tr>
<td># of Dosing Levels</td>
<td>-0.051**</td>
<td>M9</td>
<td>0.229</td>
</tr>
<tr>
<td>Anti Infective</td>
<td>0.099</td>
<td>M10</td>
<td>0.138</td>
</tr>
<tr>
<td>Blood Mod</td>
<td>0.052</td>
<td>M11</td>
<td>-0.127</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.711**</td>
<td>M12</td>
<td>0.648**</td>
</tr>
<tr>
<td>Central Nervous</td>
<td>0.152</td>
<td>M13</td>
<td>0.039</td>
</tr>
<tr>
<td>Insulin</td>
<td>-0.720</td>
<td>M14</td>
<td>0.468</td>
</tr>
<tr>
<td>Eye</td>
<td>-0.556</td>
<td>M15</td>
<td>0.049</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>-0.276</td>
<td>M16</td>
<td>-0.213</td>
</tr>
<tr>
<td>Heart/Circulatory</td>
<td>-0.147</td>
<td>M17</td>
<td>-0.057</td>
</tr>
<tr>
<td>Hormones</td>
<td>-0.430**</td>
<td>M18</td>
<td>-0.062</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>-0.014</td>
<td>M19</td>
<td>1.207***</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>0.256</td>
<td>M20</td>
<td>-0.367</td>
</tr>
<tr>
<td>Pain Relief</td>
<td>-0.148</td>
<td>M21</td>
<td>0.310</td>
</tr>
<tr>
<td>Respiratory</td>
<td>-0.411</td>
<td>M22</td>
<td>-0.032</td>
</tr>
<tr>
<td>Skin Conditions</td>
<td>-0.410</td>
<td>M23</td>
<td>-0.066</td>
</tr>
<tr>
<td>Topical</td>
<td>-0.352</td>
<td>M24</td>
<td>0.203</td>
</tr>
<tr>
<td>Viral Infections</td>
<td>1.086***</td>
<td>M25</td>
<td>0.215</td>
</tr>
<tr>
<td>M1</td>
<td>-0.206</td>
<td>M26</td>
<td>0.491</td>
</tr>
<tr>
<td>M2</td>
<td>0.177</td>
<td>M27</td>
<td>0.181</td>
</tr>
<tr>
<td>M3</td>
<td>0.039</td>
<td>M28</td>
<td>0.721**</td>
</tr>
<tr>
<td>M4</td>
<td>0.094</td>
<td>M29</td>
<td>0.568*</td>
</tr>
</tbody>
</table>
prices to drop with additional dosing levels. However, if the reduction in price is due to the increased price competition, then our results are consistent with Berndt (2002)’s “marketing intensity” theory.

3.4.2 Therapeutic Classes

By Table 3.5, we find that neither the uncommon variable nor the life-threatening variable alone is significant, but the combination of the two is significant. A drug is not significantly more expensive if it treats a condition that is just uncommon (but not life-threatening) or just life-threatening (but common). But we find that drugs that treat conditions that are both uncommon and life-threatening are 82.7% more expensive than other drugs. Our results imply that $H_2c$ holds while $H_2a$ and $H_2b$ do not. We now use Eq. (3.2) to look deeper into this hypothesis.

By Table 3.6, we see that “Hormones” is the only therapeutic class that is statistically less expensive than the gastrointestinal therapeutic class, our reference group. Specifically, we find that if a brand drug is in the therapeutic class “Hormones” ($-0.257$), then its WAC price will be lower than drugs in gastrointestinal therapeutic class after controlling for other factors. Similarly, the results show that two classes, “Cancer” and “Viral Infections” ($0.911$ and $1.262$) are statistically more expensive than the gastrointestinal therapeutic class.

A majority of drugs in the “hormone” class, such as birth control and thyroid regulation medications, treat common non-life threatening ailments. Many drugs in the “Viral infections” class are used to treat HIV. Both “Viral infections” and “Cancer classes meet conditions 1a and 1b because they treat life-threatening conditions that are not commonly occurring. The remaining therapeutic classes are not statistically different than the gastrointestinal class.
3.4.3 The Age of a Drug

By Table 3.5, we see that our hypothesis $H3$ holds. When all other variables in the model are held constant, our statistical observation shows that newer drugs are priced higher than older drugs in the same therapeutic class (1.5% increase in price for each year newer). Reasons for this observation may be competition, greater efficacy, or advances in technology. We leave it to a future research to determine why newer drugs are priced higher than their older substitutes.

3.4.4 Manufacturers

From the coefficients in the model we see that five manufacturers have higher prices than our reference manufacturer, M30, and none have prices that are statistically lower even after controlling for all other factors. Our data reveals that manufacturers typically produce in more than one therapeutic class, but none of them produce in all classes. This is not surprising as they would want to keep their R&D close to their core competencies and not stretch themselves too thin. They also would not want to produce exclusively in one therapeutic class, as they would want to diversify and not to compete against themselves for market share. Regardless of a manufacturer’s therapeutic class portfolio, it is interesting to find that their average prices are all statistically similar at a 95% level, with the exception of five manufacturers.

For example, from Table 3.5 a drug manufactured by M12 (for confidentiality purposes, we mark the name of the manufacturer) is 74% more expensive than our reference manufacturer when all other factors are held constant. While these results confirm hypothesis $H4$, further analysis needs to be done to explain why these five manufacturers price their drugs differently than the other 25 manufacturers in the analysis. A possible explanation is that their drugs have higher efficacy or their costs are higher (e.g., less efficient supply chains) than their competitors.
Table 3.7: Summary of results.

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Accept</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1a</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>H1b</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>H1c</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>H2a</td>
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<td>H2c</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>H3</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>H4</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

3.5. Conclusion

This chapter continues a long-standing debate as to what factors contribute to the WAC price for brand prescription drugs. It initiates an empirical analysis that incorporates publicly observable factors into a linear model to explain drug manufacturers’ WAC prices. The WAC prices serve as a base for all other prices, discounts and reimbursements downstream in the pharmaceutical supply chain. Such a model can be utilized by downstream players (such as insurance companies) who most likely only have the publicly observable factors available. The empirical study is based on 598 most commonly prescribed brand drugs at a major pharmacy chain store in the U.S.

We show that prices are affected by factors previously not explored such as the interaction between uncommon and life-threatening variables. We also show that the WAC price of a drug decreases as the number of dosing levels increases and newer drugs (measured by the years after FDA approval) have higher prices. Finally, we find that three manufacturers statistically set higher prices than the other 27 manufacturers when all other factors are held constant.

Table 3.7 summarizes the results of this chapter. We find that neither the number of competitors ($H1a$) nor the number of generic drugs ($H1b$) in a therapeutic class explains the price of a brand drug. We do however find that the number of dosing levels ($H1c$) and the number of years since FDA approval ($H3$) contribute to the price of a brand drug. We also find that drugs that treat uncommon and life threatening conditions are
priced significantly higher than others, while uncommon or life threatening conditions alone do not lead to a higher or lower price. Therefore we find evidence supporting $H2c$ but not $H2b$ or $H2a$. Finally, we conclude that there are differences in manufacturers’ price-setting decisions that cannot be explained by the factors that we consider in this chapter.
Chapter 4

The Effect of Generic Entry on Pharmaceutical Demand

The purpose of this chapter is to determine why brand-drug prices do not fall to compete with generics when the brand is no longer patent protected, or more generally, when a generic substitution is available. To this end, we examine drugs within one therapeutic class (to protect proprietary information, we shall not mention its name). While some brand drugs in this therapeutic class have chemically equivalent generics, others do not. Nevertheless, these drugs serve as substitutes for one-another because they all treat the same condition. Characteristics of the drugs that differentiate them from one another (such as efficacy, side effects, and consumer preference) will be accounted for in our model.

One possible explanation for the price differential between a brand drug and its generic equivalents are that consumers exhibit brand loyalty and are willing to pay more for brand name drugs. A brand name drug may be priced higher than its generic equivalents because consumers and health care providers have a strong preference for the brand drug due to perceived quality advantages. In addition, since brand drugs enjoy exclusive selling rights before patent expiration, many patients begin taking the brand before the generic version is available. If the brand drug is working effectively, many patients do not wish to switch even to a generic equivalent. Berndt (2002) suggests that upon patent expiration, brands may focus their marketing efforts on those patients
and providers who are willing to pay a higher premium as a result of brand loyalty. Consequently, brand prices generally do not decrease in the face of generic competition when they go off patent. The persistence of high prices for brand drugs is well illustrated in Figure 1.1 which shows the price of brand drugs before and after a generic equivalent enters the market.

This chapter considers the problem of estimating demand in a therapeutic class (TC) with product differentiation. We develop a model to determine the utility of a consumer for each drug during a given time period. The utility of the patient depends on drug characteristics and personal preferences. The drug characteristics include the price of the drug, the perceived quality of a brand drug, whether or not the drug is new to the market, and the utility which is observed by market participants but not by the researcher. We expect newer drugs and drugs with higher perceived quality to increase utility while higher prices to decrease utility. Our model captures the presence of drug characteristics that are unobservable to the researcher but are observable to the patient as these characteristics are obvious determinants of demand. Personal preferences are captured in our model through an inertia parameter, as well as through the error term. We expect inertia to have a positive effect on the utility of a drug, as utility should be higher if the patient consumed that drug in previous periods. Reasonable substitution patterns are assumed in the way that a patient will switch to a generic version of a brand drug before they switch to another brand drug. We derive product level market shares based on the patient’s drug choice and invert these shares to obtain the utility levels of drugs within our TC.

Our model provides insight on factors that affect an individual consumer’s utility and is extended to examine the market shares of each drug in the TC. By using this model, pharmaceutical drug manufacturers can understand how the factors mentioned above can influence (either positively or negatively) their market share. For example, manufacturers may be interested in knowing how changes in their drug price (or their competitor’s price) impact consumer utility and ultimately their market share. Outside
the pharmaceutical industry, it is our hope that this work will provide insight to the public as to why brand drugs are priced higher than their generic equivalents.

The rest of this chapter will be outlined as follows: §4.1 provides a literature review. §4.2 presents the model and research methodology, as well as the data used in this study. In §4.3, we present our findings and discuss their implications. Finally, we conclude the chapter and summarize the results in §4.4.

4.1. Literature Review

There are two main streams of literature on the impact of generic drug entry. Both study the industry response as generics enter the market; however, the first stream focuses on competitive pricing strategies and dynamics, while the second stream looks at how brand drug market shares are affected. We will review both of these streams, and close this section with a brief discussion of the brand choice models in equilibrium.

4.1.1 Pharmaceutical Industry Pricing Dynamics

Lu and Comanor (1998) find that new drug prices are influenced by the therapeutic gain of the product and competition in the market. Drugs that are similar to existing ones are priced competitively. On the other hand, drugs that introduce new therapeutic gains are more expensive than currently existing brand drugs. Berndt (2002) examines the variables that influence manufacturers when they are setting the price of patent-protected brand drugs. Supporting Lu and Comanor (1998), he concludes that the price is determined by the marginal value that the drug brings to the end user rather than marginal production cost. He observes that brand-name producers do not increase prices as dosing levels increase. Due to this “flat pricing” phenomenon, he argues that prices are not affected by active ingredient levels. He also argues that for short-run pricing, R&D costs are sunk and therefore irrelevant. We refer to Bhattacharya and Vogt (2003) and Berndt (2002) for further information on pricing strategies in the pharmaceutical
industry and an extensive discussion on the economic factors that contribute to drug prices.

Chen and Rizzo (2010) examine pricing dynamics in the pharmaceutical industry by taking into consideration the perceived quality of the drug. They conclude that product differentiation plays a role when the manufacturer determines whether a market penetration or price skimming strategy is optimal. They look at antidepressants and find that higher quality antidepressants engage in a market penetration strategy. Market penetration strategies are consistent in markets where there is an uncertainty in a new drug’s therapeutic improvement or product differentiation is low and consumers develop a preference for a particular drug.

From the marketing literature, Reiffen and Ward (2005) empirically study how the pharmaceutical industry moves from monopoly pricing toward competitive pricing as generic drugs enter the market. They find that as the number of competitors increase, the price of a generic drug decreases. They also find that the expected market size influences the generic manufacturers’ decisions. Reiffen and Ward (2007) examine the consequences of brand-drug manufacturers introducing generic versions of their drug prior to patent expiration (known as branded generic entry). They find that those generic prices are higher and brand manufacturers experience higher profits when branded generic entry occurs.

Bergman and Rudholm (2003) study the pricing behavior of brand drugs in Sweden and determine that both potential (generic entry forthcoming) and actual competition lowers the price of brand name drugs. This is contrasted by work done by Ellison and Ellison (2000) who found that brand drug prices actually increased during the last three years of patent protection. One explanation for these results is that the Swedish market is more homogeneous than the U.S. market.

4.1.2 Market Share

Aronsson et al. (2001) analyze how market shares for brand name drugs are affected
by generic competition. They examine European drug prices at a micro-level. Their results reveal that the brand drugs that had a higher price than the generic substitutes experienced a significant decrease in market share. Grabowski and Vernon (1992) find that the price differential between brand and generic drugs explains the increase in the market share for generic drugs directly after patent expiration. However, there is a level of brand loyalty due to efficacy of drugs that influence market share. Crawford and Shum (2005) find that patients are risk-averse and do not typically switch from a given drug once prescribed and doctors prescribe a drug that minimizes the dis-utility of an illness. Finally, they find that due to uncertainty and risk aversion, there are high switching costs, even when alternative drugs are close substitutes. Our model captures the findings of Crawford and Shum (2005) by considering past shares when determining future market share of a brand drug.

Finally, there has been work done on brand and generic pricing strategies in other industries. Specifically, Cotterill and Putsis (2000) examine the brand-generic pricing and market share relationship in a supermarket setting. They simultaneously estimate market share and price equations to determine the consumer’s response to pricing decisions and the interdependence of brand and generic pricing behavior. They find that as the market share of brands increases, both brand and generic prices increase. While promotions increase market share, their effects for brand and generics are asymmetric, with brand promotions being more effective than generic promotions. Finally, they find that generic prices have very little impact on brand sales but brand prices have a significant impact on generic sales. This is consistent with other findings by Blattberg and Wisniewski (1989) and Allenby and Rossi (1991). In this chapter, we intend to expand these findings into the pharmaceutical industry and expect to yield similar results. Furthermore, we will expand this area of research by using disaggregated data to examine competitive interactions within therapeutic classes.
4.1.3 Brand Choice Models in Equilibrium

The methodology applied in this chapter is closest to that discussed in Berry (1994) and Berry et al. (1995). We assume that prices and quantities are equilibrium outcomes of the interaction between supply and demand. Under this framework, estimating the price sensitivity of demand can be problematic. The problem stems from the fact that while some product attributes are observed by the researcher, others (e.g., side effects) are not. These attributes observed by the market but not by the researcher likely affect price. Thus, estimates of the price sensitivity of demand can be biased unless these unobserved factors are accounted for. In a similar fashion, Trajtenberg (1989), Berry et al. (1995), and Villas-Boas and Winer (1999) also discuss the importance of accounting for unobserved product characteristics. Compounding the problem is that demand is typically not a linear function of product attributes - both price and non-price.

However, following Berry and others (see also Nevo, A. (1998)), we assume that market shares are a function of the utilities of all products in the market, and that the utility function is linear in the demand parameters. It can be shown that under mild regularity assumptions the market share function is one-to-one with mean utility (Berry (1994)). Thus, by inverting the market share function, we can recover the unique vector of mean utilities which underly the market shares observed. Once the mean utilities are obtained we can estimate the utility function using standard instrumental variables techniques, thus removing the potential for bias in the estimate for price sensitivity.

4.2. Model and Analysis

Consider the market for a number of prescription drugs grouped in a specific therapeutic class (TC) where all these drugs treat the same condition. The TC has $J$ drugs indexed by $j = 1, \ldots, J$, out of which, there are $K$ brand drugs, $k = 1, \ldots, K$. The consumer makes a choice between $J + 1$ alternatives, including the outside option of not taking a
drug in this TC. The alternatives are grouped or nested into $G \leq J + 1$ groups indexed by $g = 1, \ldots, G$. Drugs in the same group will have a similar chemical compound (i.e., a brand drug and its generic equivalent). There are $I$ consumers, $i = 1, \ldots, I$, whose utility for drug $j \in g$ at time $t$, $t = 1, \ldots, T$ is given by:

$$U_{ijt} = \alpha + D_j \beta' + \lambda P_{jt} + \psi t + \kappa F_{jt} + \omega L_{ij(t-1)} + \xi_{jt} + \zeta_{igt} + (1 - \sigma)e_{ijt}, j \in g. \quad (4.1)$$

In Eq. (4.1), $\alpha$ is the utility associated with all drugs in the TC. $\beta$ is a $K$-dimensional vector indicating the relative brand strength, e.g., $\beta_k$ is the brand strength of the $k$th brand. If a drug is brand $k$ then the $D_j$ has a 1 in the $k$th column. If the drug is a generic, $D_j$ is a $K$ vector of zeros normalizing the brand strength to zero. $P_{jt}$ is the price of the drug $j$ at time $t$ and $\psi$ is a parameter indicating the market growth over time. $F_{jt}$ is a dummy variable indicating whether drug $j$ entered the market at time $t$. If drug $j$ is not a new drug at time $t$, then $F_{jt}$ is zero; otherwise, it is 1. $\kappa$ measures a consumer’s preference towards new drugs. $L_{ij(t-1)}$ is an indicator variable which equals 1 if consumer $i$ took drug $j$ in period $(t-1)$, and zero otherwise. $\omega$ is then the inertia factor associated with consuming the drug in the previous period. $\omega$ differs from $\beta$ because $\omega$ represents an individual consumer’s resistance to change drugs due to personal preference while $\beta$ is the perceived brand quality common to all consumers that is generated by aggregated advertising and other marketing activities. $\xi_{jt}$ is the utility which is observed by market participants but not by the researcher. Consumer $i$’s idiosyncratic utility is represented by $\zeta_{igt} + (1 - \sigma)e_{ijt}$.

To further explain the modeling of idiosyncratic utility, note that $\zeta_{igt}$ is i.i.d. across groups but is the same for all drugs $j \in g$. The last term, $(1 - \sigma)e_{ijt}$, represents the random utility specific to drug $j$. We assume that the $e_{ijt}$s are i.i.d. random variables and follow the Type I extreme value distribution. $\zeta_{igt}$ is assumed to follow a distribution such that if $e_{ijt}$ is an extreme value random variable then the random variable $\zeta_{igt} + (1 - \sigma)e_{ijt}$ is also an extreme value random variable. Cardell (1997) shows
that such a distribution exists for all $\sigma \in (0, 1)$ and terms this distribution $C(\sigma)$. $\sigma$ is an indicator (although not a measure) of the correlation in random utility within a group. As $\sigma$ goes to 1, the in-group correlation approaches 1, and when $\sigma$ goes to 0, the in-group correlation goes to 0. The between group correlation will always be 0. Thus, this model avoids unreasonable substitution patterns. For example, a large estimate of $\sigma$ would suggest that consumers are much more likely to substitute a generic for a brand than switch to another brand in a different group.

The demand parameters $\Theta = (\alpha, \beta, \lambda, \psi, \kappa, \omega, \sigma)$ are known to both the consumers and firms and will be estimated by the researchers. We rewrite $\Theta = (\Theta_1, \Theta_2)$ where $\Theta_1 = (\alpha, \beta, \lambda, \psi, \kappa)$ and $\Theta_2 = (\omega, \sigma)$. The common utility is linear in $\Theta_1$ but not in $\Theta_2$.

Inertia will cause consumers to have different product preferences. That is, a consumer who took drug $j$ in the last period is more likely to take drug $j$ in this period than one who did not. This conjecture is consistent to the observation of Crawford and Shum (2005) on how difficult it is to change prescriptions due to the high switching costs. The increased utility that comes from inertia is captured by $\omega$ in our model. We can then rewrite consumer $i$’s utility for product $j$ as:

$$U_{ijt} = \delta_{jt} + \nu_{ijt}, j \in g, \quad (4.2)$$

where $\delta_{jt}$ is the utility level of product $j$ at time $t$ common to all consumers:

$$\delta_{jt} = \alpha + D_j \beta + \lambda(P_{jt}) + \psi t + \kappa F_{jt} + \xi_{jt}. \quad (4.3)$$

Note that $\delta_{jt}$ depends on $j$ but not on $i$ and is linear in the parameters $\Theta_1$. $\nu_{ijt}$ captures the consumer-specific utility:

$$\nu_{ijt} = \omega L_{ij(t-1)} + \zeta_{igt} + (1 - \sigma)e_{ijt}, j \in g. \quad (4.4)$$
We assume that a consumer takes at most one drug within the TC. Consumers also have the option of taking no medications from the TC and pursue alternative treatment options. We denote this outside option by \( j = 0 \) and normalize its common utility across all consumers, \( \delta_0 \), to zero. This option is nested into group 0 and is the only member of the group.

The consumer chooses the option which yields the highest utility. That is, consumer \( i \) chooses drug \( j \) at time \( t \) if and only if for all \( k \geq 0 \) and \( k \neq j \), \( U_{ijt} > U_{ikt} \). We define the \((J + 1) \times 1\) vector \( \nu_{it} \) to be the consumer specific utilities across all options at time \( t \), i.e., \( \nu_{it} = \{\nu_{i0t}, \nu_{i1t}, ..., \nu_{ijt}\} \). For each option \( j = 0, ..., J \), there is a region \( A_{jt} = \{\nu_{it} | \delta_{jt} + \nu_{ijt} > \delta_{kt} + \nu_{ikt} \ \forall \ k \neq j \} \) where consumer \( i \) prefers drug \( j \) over all other options.

The market share of drug \( j \) at time \( t \) is then the probability that \( \nu_{it} \in A_{jt} \). This is given by \( \int_{A_{jt}} dF(\nu_{it}) \) where \( F(\cdot) \) is the cumulative distribution function of \( \nu_{it} \). We now have a model for market share as a function of the observed product characteristics (e.g., prices), the distribution of \( \nu_{it} \), and the parameters in the consumer’s utility. In the following section we discuss the distributional assumptions and how we calculate this integral.

### 4.2.1 Mixed-Nested Logit

We first describe how to calculate market shares in the absence of an inertia parameter (that is, \( \omega = 0 \)). Let \( \delta_t \) be a short-hand notation for the vector \( \delta_{jt} \) at time \( t \). For notation clarity, we define \( X_{it} \) to be a random variable representing the drug that customer \( i \) decides to take at time \( t \). \( X_{it} \in \{0, 1, ..., J\} \) where \( \{0, 1, ..., J\} \) is the sample space. Under the distributional assumptions of \( \zeta_{igt} \) and \( \epsilon_{ijt} \) described above, the probability of choosing product \( j \) at time \( t \) given that group \( g \) has been chosen is:

\[
P\{X_{it} = j | X_{it} \in g\} = \hat{S}_{jt|g}(\delta_t, \sigma) = \frac{e^{\delta_{jt}/(1-\sigma)}}{\sum_{j \in g} e^{\delta_{jt}/(1-\sigma)}}.
\]  

\[(4.5)\]
As discussed above, $\sigma$ is an indicator of the correlation among the $e_{ijt}$s in a group and Eq. (4.5) is exactly the share of drug $j$ at time $t$ conditioning on choosing group $g$.

Now let us incorporate the inertia in the model (i.e., $\omega \neq 0$). The probability of choosing product $j$ at time $t$ conditioning that it must be in group $g$ and the consumer took drug $x$ at time $t-1$ is a modification of Eq. (4.5):

$$P\{X_{it} = j | X_{it} \in g, X_{i(t-1)} = x\} = \hat{S}_{jt|g,x(t-1)}(\delta_t, \Theta_2) \tag{4.6}$$

$$= \begin{cases} 
\sum_{k \in g} e^{\delta_{kt}/(1-\sigma)} + e^{(\delta_{xt}/(1-\sigma) - e^{\delta_{xt}/(1-\sigma)} & \text{if } x = j \\
\sum_{k \in g} e^{\delta_{kt}/(1-\sigma)} + e^{(\delta_{xt}/(1-\sigma) - e^{\delta_{xt}/(1-\sigma)} & \text{if } x \in g, x \neq j \\
\sum_{k \in g} e^{\delta_{k}/(1-\sigma)} & \text{if } x \notin g 
\end{cases}$$

Note that there are three possible scenarios for the share of drug $j$ conditioning on it being in group $g$. First, the patient may have previously taken drug $j$. In that case, the inertia factor ($\omega$) is added into the numerator in Eq. (4.6). Second, the patient may have previously taken drug $x$ that is different than drug $j$, but in the same group as drug $j$. For example, they may have previously taken the brand drug but are switching to the generic version. Here, the inertia factor is only added to the denominator of Eq. (4.6). It is reasonable to assume that patients who do switch prescriptions are more likely to switch within groups that they have already taken a drug from than to an outside group. Finally, the patient may have previously taken drug $x$ that is not in group $g$, or may have previously selected the outside option. In this case, inertia is not added into the equation.

For simplicity, let us define $V_g$ to be the denominator of Eq. (4.6),

$$V_g \equiv \begin{cases} 
\sum_{k \in g} e^{\delta_{kt}/(1-\sigma)} + e^{(\delta_{xt}/(1-\sigma) - e^{\delta_{xt}/(1-\sigma)} & \text{if } x \in g \\
\sum_{k \in g} e^{\delta_{kt}/(1-\sigma)} & \text{if } x \notin g 
\end{cases} \tag{4.7}$$
It follows by Eq. (4.7), the probability of choosing group $g$ is (McFadden, 1974):

$$P\{X_{it} \in g\} = \hat{S}_g(\delta_t, \Theta_2) = \frac{V_g^{(1-\sigma)}}{\sum_h V_h^{(1-\sigma)}}, \quad (4.8)$$

The probability of consumer $i$ choosing drug $j$ conditioning on s/he taking drug $x$ at time $t-1$:

$$P\{X_{it} = j | X_{i(t-1)} = x\} = \hat{S}_{jt|\delta_t(x_{t-1})}(\delta_t, \Theta_2) = \begin{cases} 
\frac{e^{(\delta_{jt} + \omega)/(1-\sigma)}}{V_g \sum_h V_h^{(1-\sigma)}} & \text{if } x = j \\
\frac{e^{\delta_{jt}/(1-\sigma)}}{V_g \sum_h V_h^{(1-\sigma)}} & \text{if } x \neq j 
\end{cases} \quad (4.9)$$

Define $S_{jt}$ to be the observed market share of drug $j$ at time $t$. The probability that a consumer chooses drug $j$ at time $t$ is then:

$$P\{X_{it} = j\} = \hat{S}_{jt}(\delta_t, \Theta_2) = \sum_{x=0}^{J} (\hat{S}_{jt|\delta_t(x_{t-1})} \hat{S}_{x(t-1)}). \quad (4.10)$$

Note that probability distribution for the drug taken at time $t-1$ is determined empirically from the observed market shares in the data.

Given the demand parameters, $\Theta$, we can now calculate market shares. Loosely speaking, our goal is to estimate $\hat{\Theta}$ so as to explain the variance in market share by our model as much as possible. We will go into a discussion of the estimation procedure in the following section.
4.2.2 Estimation

Given the demand parameters $\Theta$ and $\xi_j$, we can calculate market shares by the model detailed in the previous section (i.e., Eq. 4.10) as follows,

$$S_{jt} = \hat{S}_{jt}(\delta_t, \Theta_2),$$  \hspace{1cm} (4.11)

where $\hat{S}_{jt}$ is the market share for drug $j$ at time $t$ calculated by the model and $S_{jt}$ is the observed market share of drug $j$ at time $t$.

Let $S_t$ and $\hat{S}_t$ be a shorthand notation for the $J \times 1$ vector of observed and model market shares, $S_{jt}$ and $\hat{S}_{jt}$, at time $t$ respectively. It can be shown that under general regularity conditions, every vector of market shares, $S_t$, can be explained by one and only one vector of common utilities, $\delta_t$, (Berry, 1994). That is, given a $\Theta_2$, there is only one $\delta_t$ such that $S_t = \hat{S}_t(\delta_t, \Theta_2)$. Thus, Eq. (4.11) can be inverted to derive a unique common utility, $\delta_t$, for a given $\Theta_2$ and $S_t$ by,

$$\delta_t(S_t, \Theta_2) = \hat{S}_t^{-1}(S_t, \Theta_2).$$ \hspace{1cm} (4.12)

Performing the inversion above for each time period in the data yields the vector $\delta_t$ ($t = 1, \ldots, T$) across time periods. Given $\delta_t$, we can estimate $\Theta_1$ by Eq. (4.12) using least squares. As we discussed in §4.1.3, the price is likely to be positively correlated with a number of factors including competition, efficacy, and quality. These factors are not observed by the researcher but do affect the consumer utility (and thus the market share) which is captured by $\xi_{jt}$ in Eq. (4.12). The correlation between price and $\xi_{jt}$ means that ordinary least squares (OLS) will result in inconsistent estimates for $\Theta_1$. To address this issue, we use the 2-stage least squares method with the number of quarters the drug has been on the market as an instrument for price. Length of time on the market has been shown in Chapter 3 to be a determinant of price. For example, individual side effects are unlikely to be correlated with time on the market.
and therefore this is a valid instrument. By using this estimate of price which is not correlated with unobserved utility, we will be able to develop consistent estimates of the demand parameters. We refer the reader to Greene (2003) for more information on 2-stage least squares.

Our goal is to explain as much of the variance in market shares by our model and minimize the variance in market shares that can be explained by $\xi_{jt}$. We can achieve this by minimizing the sum of squared errors (SSE) for the 2-stage least squares aforementioned. This can be done in the following recursive process described in Figure 4.1: we begin with an initial guess for $\omega$ and $\sigma$ (i.e., $\Theta_2$). For each guess of $\Theta_2$, for each time period we compute the unique $\delta_t$ that allows us to achieve the observed market shares, $S_t$. To do so, we solve Eq. (4.13) below recursively,

$$T(\delta_t) = \delta_t + \ln(S_t) - \ln(\hat{S}_j(\delta_t, \Theta_2)),$$

until $T(\delta_t) = \delta_t$ or alternatively, $S_t = \hat{S}_t$. We shall point out that in Eq. (4.13), $\hat{S}_t$ is computed by Eq. (4.11) using the current $\delta_t$; and the current $\delta_t$ will be updated by $T(\delta_t)$ in the next recursion. The recursion always converges because $T(\cdot)$ is a contraction mapping from real space $R^J \to R^J$.

Once we have an estimate of $\delta_t$ for each time period, we form $\delta$ and use Eq. (4.12) and the 2-stage least squares procedure to estimate $\Theta_1$ and calculate the SSE. We proceed by modifying $\Theta_2$ and continue until we minimize the SSE. We use the Nelder-Mead simplex algorithm to search for the $\Theta_2$ that minimizes the SSE. Developed in 1965, this algorithm is widely used for unconstrained minimization. We refer the reader to Lagarias et al. (1999) for a review. Once the SSE is minimized, we have our parameters $\Theta$ estimated.
Choose initial candidate values for $\omega$ and $\sigma$. Calculate $\delta$ recursively through contraction mapping using Eq. (4.13).

Estimate $\theta_1$ through 2-stage least squares by regressing the given $\delta_j$ on the right hand side variables in Eq. (4.12).

Is SSE Minimized? 

Finalize $\theta = (\theta_1, \theta_2)$

End

YES

NO

Revise values for $\omega$ and $\sigma$

Figure 4.1: Steps used in the model to find utility.

4.2.3 The Data

The data on prescription drug characteristics came from a leading health care market research firm. Data are available on the price and number of scripts written for all prescription drugs from 2000 through 2004. The data is presented quarterly, thus giving us up to 20 quarters of data for each drug. Some drugs entered the market after 2000, thus providing less than 20 periods of data in the dataset. Each drug is characterized as brand or generic and includes information on what therapeutic class it belongs to and who manufactures the drug. Additional data collection was done to find what brand drugs had generic equivalents. From the dataset, we find that at most 24,000 units (across all drugs) were sold in each quarter so we estimate the total potential market size each quarter for this TC to be 30,000. This is the sum of those consumers that took a drug in the TC and those consumers who chose the outside option.

Our analysis included 356 data points from a specific therapeutic class that had
sales of $11 billion in 2008. The study period began with 13 (11 brand and 2 generic) drugs in the therapeutic class and ended with 24 (17 brand and 7 generic) drugs. Five drugs came off patent during the study period and a corresponding number of generics came on the market. One brand drug exited the market over the five year of analysis. Figure 4.2 shows that the average price for brand drugs is much higher than the average price for generic drugs in this therapeutic class. Furthermore, the price of the brand drug does not decrease when a generic equivalent is introduced (see more discussion in Chapter 1).

4.3. Results and Discussion

4.3.1 Results

Table 4.1 summarizes the result of our estimation. Seven (or six) parameters are significantly different from zero at $\alpha = 0.05$ (or 0.01, respectively). This includes five brand drugs, the time period, and whether or not the drug entered the market this period. Our model for predicting market shares has an excellent fit with 80% of the variance
<table>
<thead>
<tr>
<th>Variable</th>
<th>Est. Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>(-4.566^{***})</td>
</tr>
<tr>
<td>D1</td>
<td>0.3621</td>
</tr>
<tr>
<td>D2</td>
<td>(-0.7006^{***})</td>
</tr>
<tr>
<td>D3</td>
<td>0.4474***</td>
</tr>
<tr>
<td>D4</td>
<td>0.4372***</td>
</tr>
<tr>
<td>D5</td>
<td>0.106</td>
</tr>
<tr>
<td>D6</td>
<td>0.3901**</td>
</tr>
<tr>
<td>D7</td>
<td>(-0.5666^{***})</td>
</tr>
<tr>
<td>(\ln(P_{jt}))</td>
<td>-0.0525</td>
</tr>
<tr>
<td>Time</td>
<td>0.0188***</td>
</tr>
<tr>
<td>New</td>
<td>0.6392***</td>
</tr>
<tr>
<td>Omega</td>
<td>1.1894***</td>
</tr>
<tr>
<td>Sigma</td>
<td>0.7419**</td>
</tr>
</tbody>
</table>

Table 4.1: Model Estimated Coefficients. \(*=\) significant at \(\alpha = 0.01\), \(**=\) significant at \(\alpha = 0.05\).

explained by our model and both \(\omega\) and \(\sigma\) are significant. With these two parameters known, our two-stage least squares regression has a \(R^2\) value of 0.6157.

\[
\hat{U}_{ijt} = -4.566 + 0.3621(D_1) - 0.7006(D_2) + 0.4474(D_3) + 0.4372(D_4) + 0.106(D_5) + 0.3901(D_6) - 0.5666(D_7) - 0.0525(\hat{P}_{jt}) + 0.0188(t) + 0.6392(F_{jt}) + 1.1894(L_{ij(t-1)}). \quad (4.14)
\]

From the estimated utility function, Eq. (4.14), we can see that inertia is prevalent in this industry and is in fact the strongest determinant of patient preference. If a patient previously consumed a drug, there is a high level of resistance to switch to other drugs due to inertia. The market, which is composed of doctors, patients, and insurance companies, behaves as if it has a preference towards brand drugs D1, D3, D4, D5, and D6 (for confidentiality purposes, we cannot reveal the name of the drugs). The preference toward a particular drug may come from a number of factors. For instance, direct-to-consumer marketing efforts may increase a patient’s desire for a specific drug. Fewer side effects, better efficacy, and samples may increase the doctor’s preference toward prescribing a drug. Finally, pricing promotions and rebates increase
the insurance company’s drug preference. The combination of factors and players in this industry contributes to the unique results of the above utility equation.

The $\sigma$ value of 0.7419 leads to the conclusion that preferences within a group are highly correlated. These results support the belief that patients who do switch drugs are more likely to switch within groups of similar drugs than between groups. We also see from the model that the market for this therapeutic class is growing over time and that there is a higher preference for new drugs, regardless of whether they are brand or generic. New brand drugs have a higher preference due to the surge of marketing intensity when a drug is launched. When a drug goes off patent and a generic is available, there is a higher preference for the newly introduced generic because they indirectly benefit from the brand drug’s preference. Finally, our results show that the demand for prescription drugs in this TC is relatively inelastic. That is, for every dollar the price increases, we only lose 0.004 preference points. This finding is consistent with previous research (see Rosehthal et al. (2003) for a summary).

4.3.2 Managerial Implications

In the following section, we highlight ways in which pharmaceutical managers can implement our model. Specifically, we look at how market shares are affected by three events: when a company changes the price of their drug; when a company changes their marketing strategy; and when competitors reduce their drug prices.

Price Changes

With many drugs competing for market share, a firm may lower their drug’s price in order to take market share away from their competitors and thus increase the consumption of their drug. So then, the question becomes: How much would a firm lower its price in order to gain a 1% increase in market share? To answer this question, we take the derivative of Eq. (4.10) with respect to price and divide 0.01 by this derivative. We find that it is not reasonable to lower your price to gain market share because lowering
the brand drug price does not result in sufficient share, and therefore is not practiced in the industry. This finding directly answers the question raised by our chapter, that is, why brand drugs are priced higher than generics?

For example, our analysis reveals that D4 would have to lower their price by $1393.00 in order to gain 1% of the market share in the last period of data. Even if a brand drug decreased their price by 50%, they would gain less than 1% of the market share. It is evident that this increase in market share does not justify the price decrease. For a brand drug, it is more advantageous to charge a higher price and accept a lower market share than lowering their price for only a minimal gain.

Since it is evident that a decrease in price does not result in a significant increase in market share, a firm may then consider what initial price to set for the brand drug in order to optimize market shares. Given the low price sensitivity, it would appear that firms are pricing drugs on an inelastic demand curve. However, when we consider the strong inertia parameter, we find that a change in price today will affect current and future periods. Thus, a forward looking firm will price their drug lower than a non-forward looking firm. We leave further investigation of price optimization in the pharmaceutical industry to future research.

Changes in Marketing Strategy

Instead of lowering their price in an effort to gain market share, firms may decide to increase marketing efforts. Marketing efforts may include direct-to-consumer advertising, providing samples to physicians, or increased rebates to insurance companies. Similar to above, if we take the derivative of market share (Eq. (4.10)) with respect to brand strength ($\beta$) and multiply it by the change in marketing effort, we can determine the change in market share. We find that increasing brand loyalty through marketing efforts is a more effective way to increase a drug’s market share than lowering prices. This also supports our observation that brands do not lower their prices to compete with market share, but do continue marketing activities through the drug’s patent life.
For example, our analysis reveals that if drug D4 increased their brand loyalty (through marketing activities) by 55%, they would gain 1% of the market share. While this amount may not seem substantial, it is obviously easier to gain market share through increasing a brand drug’s loyalty than by reducing its prices.

**Changes in Competition**

While it is evident that internal activities, such as pricing and marketing activities, may have an impact on a drug’s market share, it may be beneficial to know how external activities by competitors affect the market share of a firm. It turns out that firms are not very sensitive to activities of their competitors. In fact, a firm (firm A) would gain less than 1% of the market share if a competitor (firm B), doubled their drug’s price. These results hold, regardless of whether or not firm B’s drug is in the same group as firm A’s drug. These results are not surprising, as we saw above that if a firm changes their price, their market share is unlikely to change. Obviously, if firm A does not lose market share from increasing their price (as we saw above), then we do not expect firm B to benefit from firm A’s pricing decision either.

We find similar results when looking at the marketing efforts of a firm’s competitors. We find that firm A is slightly affected by the increase in loyalty in firm B’s drug, although the effect is not as great as when firm A increases the loyalty of their own drug. For example, if drug B’s (produced by firm B) brand loyalty doubles, then drug A (produced by firm A) loses 0.5% market share. These results are consistent with the findings above as we would not expect there to be a 1 : 1 relationship between changes in market share of two drugs. We expect firm B’s increased market share to come partially from multiple competitors and partially from the outside option.

### 4.4. Summary

This chapter continues the stream of research on prescription drug prices. We explain why brand drugs are priced higher than their generic equivalents by modeling customer
preferences and inertia in their utility functions for a therapeutic class. We find that prices are correlated with unobserved characteristics such as quality that are captured in the error term. We use instrumental variable techniques to estimate customer preferences and ultimately the mean utility of each drug for individual consumers.

Our results reveal that consumers have a strong brand loyalty for brand drugs. The utility function shows that the market behaves as if it has a preference toward brand drugs over their generic equivalents. We also find that the consumers are not price sensitive, showing that doubling the price of a drug will have a minimal effect on demand.

The results show that brand drugs are more expensive than their generic equivalents as a result of both marketing efforts and personal preferences acquired after consuming the drug previously. Marketing efforts play a role in higher prices as we observe that patients have a strong personal preference toward specific brand drugs. The inertia factor, a reflection of personal preference, is the strongest determinant of customers’ choices of brand drugs. We also find that consumers have a higher preference for new drugs and that the market is growing over time.
Chapter 5

Concluding Remarks

In the introductory chapter of this dissertation, we motivated the need for more effective distribution and better understanding of pricing decisions for the pharmaceutical supply chain. Through recent industry transition in distribution contracts and public awareness of increasing health care expenses, we see opportunities to create value for this supply chain. That opportunity, as is shown in Chapters 2-4, can be seized by tailoring contract theory and pricing models to the unique aspects of the pharmaceutical industry. In Chapter 2, we examine contractual agreements in drug distribution and study their impact on the performance of the supply chain and its individual participants. Chapter 3 looks at observable factors that can be used to explain the price of prescription drugs. Chapter 4 examines the effect of generic entry on the price of brand drugs by modeling consumer’s brand loyalty and the cost of switching through utility functions.

Going forward beyond the scope of the dissertation, research on the pharmaceutical supply chain in general, on drug distribution and pricing in particular, promises to be both fruitful to practitioners due to the need for customized models, and to academicians due to the unique aspects of the industry. The potential in optimizing and coordinating this supply chain has recently been recognized both in academia and in industry. We conclude this dissertation by discussing limitations and future research directions:

1. *Stochastic Demand and Price*: We consider predictable demand and price in Chapter 2. Although it is not hard to identify cases where the price and demand are
quite predictable, it would be more interesting and useful to incorporate uncertainties in price and demand. With these uncertainties, we expect that the mathematical model and analysis in Chapter 2 would be much more complex, but the Direct-To-Pharmacy agreement may still be more beneficial than the BNH and FFS agreements as directly responding to outside demand reduces the manufacturers’ safety-stock requirement.

2. *Pharmacy Distribution Agreements*: In Chapter 2, we assume that the pharmacies are exogenous. Because it is a common practice for self-warehoused pharmacy chains to do investment buying, one important question not yet answered is: how to coordinate the distribution agreements in the pharmaceutical supply chain beyond the wholesaler level to the pharmacy level?

3. *Integration of Decisions*: In Chapter 2, we ignore the potential benefit of integrating production, inventory, and shipping decisions – one benefit of VMI because of the relative insignificance of shipping costs in the pharmaceutical supply chain. In future research, we plan to explore ways to integrate the direct model and VMI.

4. *Multi-Period Pricing Model*: The data used in Chapter 3 has WAC prices at a single point in time. Although these data were appropriate for the study in Chapter 3, it would be more interesting to extend the model to include WAC prices over time. With this extension of data, a more in-depth analysis could be performed to see if the results found in this study changes over multiple time periods.

5. *Incorporate Active Ingredient Levels*: Further analysis can be done to look at the role that the active ingredient plays in the WAC price. Although it is not disputed that the amount of active ingredient plays a role in the price, it has been observed frequently that levels of active ingredients do not change the price of a drug. It would be interesting to find if there exists a critical level exceeding which the price increases. If doctors and patients knew this level, they could prescribe a dosage
amount that minimizes the cost (i.e. prescribe a lower dose more frequently, or a higher dose less frequently).

6. **Examining Other Therapeutic Classes:** Chapter 4 looks into a therapeutic class where prescription drugs treat a condition that cannot be cured. It would be interesting to expand this analysis into the therapeutic class where drugs can cure a condition, such as an infection. If patients take a drug for only a period of time until they are cured rather than repeatedly treating a chronic condition, it would be interesting to see if our results on brand preferences and price sensitivity hold.

7. **Varying Level of Price Sensitivity:** Chapter 4 assumes that all consumers have the same level of price sensitivity. However, it may be possible that people have different levels of price sensitivity due to different levels of prescription drug coverage. It would be interesting to see if our results in Chapter 4 hold if we relax this assumption.

8. **Price Optimization:** It would be interesting to expand the model in Chapter 4 to determine the optimal price of drugs when they enter the market. While it is evident that prices in this industry are inelastic, it would be interesting to determine the price that not only optimizes the market share, but also optimizes the profit.
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