PRESCRIPTION DRUG CHOICE: EXAMINING PHYSICIAN PRESCRIBING BEHAVIOR AND THE DEMAND FOR PRESCRIPTION DRUGS[1]

BY

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[1] This paper are sections of the author's dissertation entitled "Influencing Physician Prescribing Behavior: Direct-to-Consumer Advertising and the Demand for Me-Too Drugs" which is available at http://iris.lib.neu.edu/law_pub_pol_diss/13/

ABSTRACT

This study examines the variables that may influence physicians' choices of medication for their patients and the effect of the entry of me-too drugs on the market of breakthrough and generic drugs. Using the 2006 National Ambulatory Medical Care Survey (NAMCS), drugs belonging to the drug classes statin, cardioselective beta blockers, proton pump inhibitors and selective serotonin reuptake inhibitors were classified as generic, breakthrough and me-too drugs and analyzed separately. This study uses the discrete choice model of demand in analyzing the relationship between physician prescribing behavior and patient, physician and drug characteristics. This study found age, sex, race, ethnicity and number of current medication influence physicians' prescribing behavior. Some physicians tend to prescribe one type of drug over the other. The study also found an indication of moral hazard. Price, direct-to–consumer advertising and certain characteristics of drugs that may indicate quality affect the likelihood of a drug to be prescribed.

The findings on the effect of direct-to-consumer advertising expenditure of me-too drugs on the market share of generic drugs and breakthrough drugs give empirical support to the proposed policy of approving new drugs on the basis of their efficacy against existing drugs in the market. With direct-to-consumer advertising, the findings of this study suggest that me-too drugs may reduce the market share of breakthrough drugs and generic drugs. It implies an increase on prescription drug spending but with little associated quality gain. The study validates previous findings that me-too drugs compete with breakthrough drugs and reduce incentives to invest in research.

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GENERAL INTRODUCTION

Me-too drugs are new drugs that are not generic drugs, but nevertheless "duplicate the actions of existing drugs and offer little or no therapeutic gain" (Rogawski, 2006:23). Data from the U.S. Food and Drug Administration (FDA) show that from 1990 to 2006, 77% of the 1,135 unique drugs approved by the FDA "appears to have therapeutic qualities similar to those of one or more already marketed drugs" (CDER, 2004, 2007). Pharmaceutical companies invest more resources in producing and selling these drugs than in developing drugs with significant medical advancement (Angell, 2004; Goozner, 2004).

Given the increase of me-too drugs in the pharmaceutical market, this study examines the factors that may influence physician prescribing behavior in prescribing a generic, breakthrough or me-too drug to a patient. Previous studies (Hellerstein, 1994, 1998) used the 1989 NAMCS data to examine the importance of physicians in prescription decision and the factors that influenced them to prescribe branded or generic drugs. This research adds to existing studies by expanding the physicians' choice of prescribing breakthrough, me-too, generic me-too and generic drugs to their patients. In addition, the influence of patients' increased awareness of drugs through direct-to-

consumer advertising on physician's prescribing behavior is examined. The increased role of patients in selecting their medication is examined through the relationship between direct-to-consumer (DTC) advertising and physicians' prescribing behavior.

This study uses the 2006 National Ambulatory Medical Care Survey (NAMCS), a cross-sectional consumer-level data. Drugs belonging to the drug classes statin, cardioselective beta blockers, proton pump inhibitors and selective serotonin reuptake inhibitors were analyzed separately. The 2006 National Ambulatory Medical Care Survey (NAMCS) is an annual national level survey of office-based physicians who are primarily engaged in direct patient care. Information about patient visits and physician prescribed medication are available. The 2006 expenditures on direct-to-consumer advertising are incorporated in the model to examine the relationship between DTC advertising and the demand for prescription drugs. Since direct-to-consumer advertising is the patients' primary source of information about particular drugs, it may serve as a proxy to estimate the role of patients in physician prescribing behavior. The DTC data were from TNS Media Intelligence, a leading provider of direct-to-consumer advertising expenditure and occurrence data. Price data are from Consumer Reports Best Buy Drugs publication of Consumers Union (Consumers Union, 2006a, 2006b, 2007a, 2007b).

Additionally, this study examines the effect of me-too drugs on the market share of breakthrough drugs and generic drugs. Me-too drugs compete with breakthrough drugs when introduced during patent exclusivity (J. A. DiMasi, 2000; Lee, 2004; Lu & Comanor, 1998). The period of marketing exclusivity for breakthrough drugs have fallen overtime from a median of 10.2 in the 1970s to 1.2 years in the late 1990s (Joseph A. DiMasi & Paquette, 2004). This will have

negative implications on research and development of new drugs as the monopoly profit which serves as incentives for research and development is reduced.

When me-too drugs enter the market after patent expiration, it may increase industry profit of branded prescription drugs but may compete with generic drugs. This implies an increase on prescription drug spending but with little associated quality gain. The entry of new drugs in the market in the 1990s is a major driver of drug-spending growth (Danzon & Pauly, 2002). The Center for Medicare and Medicaid Services estimated that spending for prescription drugs grew at an average annual rate of 14.5 percent from 1997 to 2002 reaching a total spending of $162 billion in 2002. Drug spending grew faster than spending for any other kind of medical goods and services. Prescription drug spending was the third-largest category of personal health care expenditures, after hospital and physician services in 1999 (Baker, 2004).

This research answers the following questions:

1. What factors influence the physician's choice to prescribe breakthrough, me-too, generic or generic me-too drug?

    - What characteristics of an individual will increase the likelihood that he or she will be prescribed a breakthrough, me-too, generic or generic me-too drug?

    - What physician characteristics will increase the likelihood of prescribing a patient with breakthrough, me-too, generic or generic me-too drug?

- What drug characteristics will increase the likelihood of prescribing a patient with breakthrough, me-too, generic or generic me-too drug?

2. What is the relationship between direct-to-consumer advertising and prescribing physician's choice of drugs?

3. What is the effect of direct-to-consumer advertising and price of me-too drugs on the market share of generic drugs and breakthrough drugs?

This study includes patient characteristics (patient's age, gender, ethnicity and number of medication) and physician characteristics (specialization, region of practice and primary source of income) without any predicted effect on the physician decision to prescribe a specific type of prescription drug. This study tests the hypothesis that an increase in price will decrease the likelihood that a drug is prescribed. This study also hypothesizes that the increase in the length of time the drug has been in the market increases the likelihood that a drug is prescribed. Theory on physician prescribing behavior suggests that physicians tend to prescribe established drugs thus creating a positive relationship between length of time in the market and likelihood of prescribing older drugs. The hypothesis that direct-to-consumer advertising increases the likelihood of a drug from being prescribed is also tested. This research also tests whether a patient's generous insurance coverage increases the likelihood of being prescribed a more expensive drug like me-too drug than a generic drug. Furthermore, this study also tests whether the price, length of time in the market and direct-to-consumer advertising of me-too drugs have negative effects on the market share of generic and breakthrough drugs.

EXAMINING PHYSICIAN PRESCRIBING BEHAVIOR

1.1 CHAPTER INTRODUCTION

The decision on what drugs to consume is not entirely determined by the consumers' tastes but primarily by the preference of the prescribing physicians and pharmacists who dispensed the drugs. The process of choosing a drug for a patient is a two-stage process—the prescription stage where the physicians choose the medication and method of treatment and the dispensing stage where the pharmacists' influence the consumers' decision on what specific prescription drug to purchase particularly in the case of multisource drugs[2] (Caves, Whinston, Hurwitz, Pakes, & Temin, 1991; S. F. Ellison, Cockburn, Griliches, & Hausman, 1997; Poutiainen, 2007).

This chapter examines the relationship between the physician's choice of medication and the variables that may influence the physician's prescribing behavior like drug characteristics, patient characteristics and physician characteristics. The analysis was done using the 2006 National Ambulatory Medical Care Survey (NAMCS), a cross-sectional consumer-level data. Drugs belonging to the drug classes statins, cardioselective beta blockers, proton pump inhibitors (PPI), selective serotonin reuptake inhibitor (SSRI) were analyzed separately. The specific drugs were classified into four types: breakthrough drugs, generic drugs, me-too drugs and generic me-too drugs.

This section specifically answers the following questions:

[2] Multisource drug or multiple source drug refer to "drug for which there is at least one other drug product which is rated as therapeutically equivalent, is pharmaceutically equivalent and bioequivalent, as determined by the FDA…" (Centers for Medicare & Medicaid Services, 2008).

1. What factors influence the physician's choice to prescribe breakthrough, me-too or generic or generic me-too drugs?

    - What patient characteristics will increase the likelihood of a physician prescribing a breakthrough, me-too or generic or generic me-too drug?

    - What physician characteristics will increase the likelihood of prescribing a patient with a breakthrough, me-too or generic or generic me-too drug?

    - What drug characteristics will increase the likelihood of prescribing a patient with a breakthrough, me-too or generic or generic me-too drug?

2. What is the relationship between direct-to-consumer advertising and prescribing physician's choice of drugs?

Patient characteristics include the patient's age, gender, ethnicity and number of medication the patient is taking. Physician characteristics include specialization, location of the physician's practice and the physician's primary source of income. These variables were included in the regression model without any predicted effect on the physician's decision to prescribe a specific type of prescription drug. A patient's generous insurance coverage is predicted to increase the likelihood of being prescribed a more expensive drug like me-too drug than a generic drug.

Drug characteristics include price, and quality indicators like extended or delayed release feature which may differentiate the quality of the drug from the others and the length of time the drug has been in the market. This study tests the hypothesis that an increase in price will decrease

the likelihood that a drug is prescribed. This study also hypothesizes that the increase in the length of time the drug has been in the market increases the likelihood that a drug is prescribed. Theory on physician prescribing behavior suggests that physicians tend to prescribe established drugs thus creating a positive relationship between length of time in the market and likelihood of prescribing older drugs. The study also examines the patient's influence to the prescribing physician. Patients' role in choosing their medication has been increasing. Their primary source of information about drugs is direct-to-consumer advertising. In this study, patient's role in choosing their prescription is indirectly reflected by the direct-to-consumer advertising expenditure of the drug. The hypothesis is that direct-to-consumer advertising increases the likelihood of a drug from being prescribed.

The subsequent section presents the review of existing literature on physician prescribing behavior and the factors that may influence the doctor and patient's choice of prescription drug. The quantitative model and the results are presented thereafter.

1.2 Review of Literature

1.2.1 Physician Prescribing Behavior

Physicians and patients have principal-agent relationship that arises under conditions of imperfect information. As agents, physicians play a huge role in deciding which medication or method of treatment best fits the patients' health condition. Physicians play an important role in the process by which patients would receive branded or generic drugs but these prescribing decisions were not explained by observable patients' characteristics (Hellerstein, 1998).

Physicians prescribing behavior is based largely on customary prescribing rather than on comparative effectiveness of prescription drugs (Caves et al., 1991). Not only is this explained by the limited information available about comparative effectiveness of drugs but because customary prescribing can be a very effective legal defense (Caves et al., 1991). Physicians might hesitate in switching treatment for subsequent prescriptions because of the risk associated with switching treatment especially if the original prescribed drug works for the patient (Gönül, Carter, Petrova, & Srinivasan, 2001:81) . Habit persistence in physicians' prescribing behavior can explain the persistent market shares of branded drugs (Coscelli, 2000:350-351).

1.2.2 ADVERTISING

The effect of direct-to-consumer advertising on the demand for prescription drugs is examined in this study. Direct-to-consumer advertising affects physicians' choice of drugs to prescribe through the patient's input during consultation. Patients are becoming more pro-active in planning and choosing their medication because of direct-to-consumer advertising. This section provides an overview of economic theories of advertising.

Bagwell (2007) presents a comprehensive review of literature on the economic theory and empirical studies of advertising. The author discussed the three main theories on the economic role of advertising on demand: the persuasive view, the informative view and the complementary view. Persuasive advertising influences consumer choice and creates spurious product differentiation and brand loyalty. It becomes an anti-competitive tool making the demand for the product more inelastic. This results in higher prices of goods but with no real value to consumers. Informative advertising promotes competition in the market by facilitating information. The

demand for the good becomes more elastic as the search cost for consumers are reduced. It facilitates entry of new firms through the publication of its existence, prices or products. The third view suggests that advertising is complementary to the advertised good. In Bagwell's example, if a consumer values social prestige, an advertised good may add more prestige thus complimenting the consumption of the good.

Other experts are in agreement that advertising can convey information if it can be easily verified. It brings about market power if producers can hamper consumers ability to gain information from other sources (Hurwitz & Caves, 1988). A survey of empirical analysis of advertising shows the effects of advertising to be industry –specific and vary on a case by case basis (Bagwell, 2007).

The effects of advertising would differ depending on whether the product is a search good or experience good. Search goods have objective features that consumers can easily understand and verify before making a decision to purchase. Experience goods have complex characteristics that can be verified only upon consumption of the good. Consumers only know the price prior to consumption and this is usually use as an indicator of quality. Experience goods tend to have lower price elasticity than search goods because of consumers' apprehension about unobservable characteristics of cheaper goods (Nelson, 1970).

Advertising may have direct information on the existence, location, price and function of a product. However, it may still have an indirect effect even if it does not have clear informative content (Bagwell, 2007). Advertising for experience goods are mostly indirect information and for search goods are dominantly direct information (Nelson, 1974). Indirect information has three

effects for experience goods: 1) signaling-efficiency effect in which firm signals that it is efficient and in turn implies that it offers good deals; 2) match-products-to-buyers effect which allows firms to direct its advertisement to consumers that values it the most and efficiently match products and buyers; and 3) repeat-business effect in which advertising reminds consumers of their previous experience with the product (Bagwell, 2007; Nelson, 1974).

Researches on the economic effects of advertising also looked at the distinction between its effect on "selective"(combative) and "primary" demands (Borden, 1942). Advertising is combative in nature if it is shifting consumer preference to the advertiser without any effect on the overall industry demand. Several studies support this theory (Alemson, 1970; Lambin, 1976; Metwally, 1975, 1976; L. A. Thomas, 1999). There are also studies examining the overall effect of advertising on primary/overall demand but the results of different studies show different outcomes in different industries (Bagwell, 2007).

Bagwell arrives at three major conclusions on the result of empirical studies on advertising and demand: (1) current advertising usually has positive short lived rather than long lived effect on sales; (2) advertising is combative in nature; and (3) advertising's effect on primary/overall demand varies across industries (Bagwell, 2007).

Advertising may also deter or facilitate the entry of new players and innovation of products in the market and the evidence in the literature is mixed (Bagwell, 2007). A relationship between advertising and prices also exists. Bagwell (2007) concludes that there is substantial evidence that retail advertising leads to lower retail prices and may encourage growth of low-price discount outlets.

With respect to advertising-quality relationship, a positive relationship is more likely when advertising conveys direct product-quality information to consumers (Bagwell, 2007). When consumers have insufficient information on the intrinsic quality of the products and markets or when there is no great variance in the nature of the product across brand names, price is used as a measure of quality (Agarwal & Teas, 2002; Gönül et al., 2001; Olson, 1977; Valarie A. Zeithaml, 1988; V.A. Zeithaml, 1991).

Advertising in the Pharmaceutical Industry

In 2008, the U.S. pharmaceutical industry spent around $18 billion dollars on advertising and promotion (IMS Health, 2008). This includes direct-to-consumer advertising, detailing and advertising in professional journals. But if we include spending on continuing medical education (CME), travel and lucrative honoraria to medical professionals, marketing expenditure directed to medical professionals alone could reach up to $25 billion each year (Donohue, Cevasco, & Rosenthal, 2007).

Pharmaceutical detailing is one of the most aggressive marketing strategies of the pharmaceutical industry. This involves regular visits from medical sales representatives which provide free meals, gifts and drug samples. The industry employed 87,892 detailers in 2001; a ratio of 1 medical sales representative for every 5 physicians (Chin, 2002). Industry spending on lunches for doctors is estimated at roughly $1 billion a year (Saul, 2006). Around 94% of physicians have accepted some form of gifts from the pharmaceutical industry (Campbell, 2007).

Spending on direct-to-consumer (DTC) advertising of prescription drugs has tripled in recent years. It has been the fastest growing marketing expense of the industry (Goozner, 2004:230). Between 1996 and 2005, spending on DTC advertising increased by 330% (Donohue et al., 2007). Pharmaceutical companies spent $4.4 billion on DTC advertising in 2008 (IMS Health, 2008). Overall, this is only a small portion (15.7%) of the industry's marketing expenditure. But if drug samples are excluded in the 2000 marketing expenditure of the industry, DTC advertising would account for 32% of the expenditure (National Institute of Health Care Management, 2001). Pharmaceutical companies promote their products directly to consumers through advertisements in magazines, newspapers, and consumer brochures; on the internet; and on radio and television (United States Government Accountability Office, 2002). Television advertising accounted for more than half (57%) of prescription drugs' DTC expenditure (National Institute of Health Care Management, 2001).

The Impact of Pharmaceutical Advertising

Physician detailing and journal advertising informs physicians about characteristics and uses of specific drugs (Leffler, 1981:47-48). When physicians and patients have no sufficient knowledge about the intrinsic qualities of competing products, brand names and level of advertising are cues usually use to measure the quality of a product (Agarwal & Teas, 2002; Valarie A. Zeithaml, 1988; V.A. Zeithaml, 1991). Pharmaceutical marketing, however, can be "uninformative and seem simply to harp the products' names in order to persuade doctors to select products out of habit rather than by evaluative choice (Leffler, 1981:47). It imposes social costs when it limits consumers' information on alternative sources (Hurwitz & Caves, 1988:299).

Physician detailing is considered persuasive in nature (Hurwitz & Caves, 1988; Leffler, 1981; Vernon, 1971).

There are mix opinions on the effect of direct-to-consumer advertising. Some experts criticize direct-to-consumer advertising to be misleading and increasing the demand for branded, more expensive drugs while others see the benefits of direct-to-consumer advertising as empowering to patients (Almasi, Stafford, Kravitz, & Mansfield, 2006; Auton, 2006). Direct-to-consumer advertising may have positive welfare effects depending on the disease types and patient characteristics (Bhattacharyya, 2005). Direct-to-consumer advertising encourages patients to visit the doctor for a particular illness, increasing the flow of patients treated by doctors for the particular illness. Direct-to-consumer advertising educate the patients about their undiagnosed medical conditions (Aikin, Swasy, & Braman, 2004; D. Bradford & Kleit, 2006; D. W. Bradford et al., 2006; Hosken & Wendling, 2009; Weissman et al., 2004). It has increased patients' role in the selection of medication by pressuring physicians to respond to independent requests as encouraged by prescription advertisements (Conrad & Leiter, 2004:170). A survey conducted by FDA reported that about half of the patient were prescribed with the medicine they asked about (Aikin et al., 2004). Direct-to-consumer advertising is also associated with increase in adherence to drug therapy (Calfee, Winston, & Stempski, 2002; Donohue, Berndt, Rosenthal, Epstein, & Frank, 2004; Wosinska, 2005). It averts underuse of medication by encouraging patients to talk to their doctors but at the same time it also promotes overuse of medication and increase use of advertised drugs when alternatives maybe more appropriate (Aikin et al., 2004; Kravitz et al., 2005; United States Government Accountability Office, 2006; Weissman et al., 2004). A majority of the physicians

in the FDA survey also felt that patients confuse the relative risks and benefits of the advertised drugs and patients tend to overestimate the efficacy of the medication(Aikin et al., 2004).

The concentration of physician prescribing is correlated with higher levels of advertising, low prices and larger lagged market shares (Stern & Trajtenberg, 1998). Physicians who have more exposure to pharmaceutical advertisements are also more open to DTC advertising of prescription drugs (Gönül, Carter, & Wind, 2000).

Consumers who have an ongoing need for health care -- those with children or with a chronic condition requiring medication, value prescription drug advertising more highly, while older consumers, consumers who have been sick recently or more educated consumers are more likely to trust their physicians instead (Gönül et al., 2000).

Pharmaceutical advertising has a market expansion effect rather than combative effect. It expands the market of the entire therapeutic class (Rosenthal, Berndt, Donohue, Epstein, & Frank, 2003). This is explained by increase awareness on diseases, brand of drugs available and compliance with drug therapy (Calfee et al., 2002; Rizzo, 1999; Rosenthal et al., 2003). Advertising also expands the market of prescription drugs because it encourages off-label uses of drugs and broadens the scope of disease (Gillman, 2006; Healy, 2006; Lacasse & Leo, 2006; Maggini, Vanacore, & Raschetti, 2006; Tiefer, 2006). Direct-to-consumer marketing has a greater effect on the sale of the entire therapeutic class while detailing has greater effect in expanding the market share of a brand (Narayanan, Desiraju, & Chintagunta, 2004).

A study showed that marketing has a positive effect on the sales of anti-ulcer drugs with detailing having the largest impact followed by journal advertising and direct-to-consumer advertising having the smallest (Berndt, Bui, Reiley, & Urban, 1995:104). A vast amount of literature shows the positive relationship between advertising and prescription of the marketed drugs (Adair & Holmgren, 2005; Boltri, Gordon, & Vogel, 2002; Bower & Burkett, 1987; Brewer, 1998; Chew et al., 2000; Chren & Landefeld, 1994; Iserson, Cerfolio, & Sade, 2007; Lurie & et al., 1990; Mizik & Jacobson, 2004; Orlowski & Wateska, 1992; Strong, 2003; Symm, Averitt, Forjuoh, & Preece, 2006; Wazana, 2000).

DTC increases drug consumption and favors heavily advertised drugs (Berndt, 2002:53; Berndt et al., 1995; United States Government Accountability Office, 2002). A government report states that "drugs that are promoted directly to consumers often are among the best-selling drugs, and sales for DTC-advertised drugs have increased faster than sales for drugs that are not heavily advertised to consumers" (United States Government Accountability Office, 2002:3). Between 1999 and 2000, the number of prescriptions dispensed for the most heavily advertised drugs rose 25 percent, as opposed to only 4 percent for drugs that were not heavily advertised (United States Government Accountability Office, 2002). Calfee, Winston and Stempski (2002), in a study of statin class, concluded however that direct-to-consumer advertising did not significantly affect demand for the new drug in the short run.

Advertising particularly detailing impedes price competition and lowers price elasticity which lead to higher equilibrium prices (Hurwitz & Caves, 1988; Leffler, 1981; Rizzo, 1999; Vernon, 1971). This is consistent with the observation that experience goods have lower price elasticity.

The inability of consumers to verify the quality of generic drugs in the market until they consume it makes it less attractive for some patients to shift to generic drugs. However, a recent study showed otherwise. Detailing increases price elasticity while other forms of marketing decreases price elasticity in the case of antihistamine drugs (Narayanan et al., 2004).

Advertising may facilitate the entry of new players in the pharmaceutical market. The pharmaceutical industry has historically favors first market entrants with later market entrants capturing substantially lower market shares, other things being equal (H. G. Grabowski & Vernon, 2000:24). Advertising produces brand-name recall effects that favor established products facing new competition (Leffler, 1981:47-48). Branded drugs are able to preserve their shares from competition from generic drug entrants through goodwill stock and loyalty build up while being marketed exclusively when the drugs were still on patent (Hurwitz & Caves, 1988). In a study by Ellison and Ellison (2007), they observed that incumbents in intermediate size markets have lower level of advertising and are more likely to reduce advertising before patent expiration to deter generic entry. The profitability of the drug of prior to patent expiration is an important determinant of generic entry (Reiffen & Ward, 2005b; Scott Morton, 2000). While some researches did not find any significant relationship between advertising and new product entry (Henry G. Grabowski & Vernon, 1992; Vernon, 1971), other studies found that advertising is not a barrier to entry for new products including generic drugs (Caves et al., 1991; Leffler, 1981; Scott Morton, 2000; Telser, Best, Egan, & Higinbotham, 1975).

1.2.3 PRICE

The price of the drug is not part of the information provided by medical detailers. Physicians have very limited information on prices of prescription drugs and may not have any incentive to prescribe cheaper medicines (Caves et al., 1991). Other experts suggest that there may be other factors that may make physicians sensitive to prices. Physicians may be affected by the patients' financial situation and the possibility that price-sensitive patients may switch to health care providers who prescribe lower-cost pharmaceuticals (S. F. Ellison et al., 1997; Gönül et al., 2001). However, "patients seem unlikely to select or change physicians simply because they do not prescribe the lowest cost drugs" (Caves et al., 1991:5). Physicians can infer patients' willingness to pay through the type of insurance held or through discussion with the patient (Gönül et al., 2001:80).

Patients are not directly sensitive to the price of prescription drugs because of insurance coverage on prescription drugs. Rather, consumer behavior is more sensitive on cost sharing schemes for prescription drug. Medicaid co-payments reduce prescription drug utilization. Increases in cost-sharing for prescription medicine among privately insured groups have negative significant effects on drug utilization (Coulson & Stuart, 1995:1147).

Doctors may also use price as a signal for quality. When drug efficacy is of prime consideration, physicians might prescribe the more expensive drug on the belief of higher efficacy (Gönül et al., 2001:81). Price are sometimes use as a measure of quality (Olson, 1977). This may happen when consumers have insufficient information about the intrinsic quality of the products or when there is no great variance in the nature of the product across brand names (Valarie A. Zeithaml, 1988; V.A. Zeithaml, 1991).

1.2.4 DRUG QUALITY

There is a lingering perception that generic drugs are inferior in quality and are not perfect substitutes for branded drugs. In 1989, FDA reviewers accepted bribes from generic drug manufacturers to facilitate the approval of their ANDAs. Some generic firms also violated manufacturing procedures and fabricated supporting documents for their application. This "generic scandal" impaired the reputation of generic drug manufacturers (Fernandez-Carol & Kaitin, 1991; Scott Morton, 1999).

Using survey data of pharmacists and physicians, Bearden and Mason concluded that confidence on regulatory control of FDA as a significant determinant of overall support to generic drugs (Bearden & Mason, 1980). A more recent survey showed that consumers perception that generic prescription drugs were riskier than brand name products varied depending on the medical condition being treated. More than half (53.8%) of the respondents thought that generic were riskier than brand name for heart problem. But for medical conditions like high blood pressure, strep throat, pain and cough, 50% or more of the respondents thought that generics were as riskier as brand name drugs. The study also concluded that significantly larger cost savings were required for consumers to purchase generic prescription drugs with higher perceived risk (Ganther & Kreling, 2000).

In the case of antidepressants, some patients experienced significant difference between the effectiveness of branded and generic drugs in addressing their concerns. A number of them experienced the symptoms of their mental condition when their doctors switched them to the generic version of their medication without their knowledge (Wax, 2007). A particular problem highlighted

by those who question the perfect substitutability of generic drugs is the FDA's policy to determine blood serum bioavailability. Bioavailability is "the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action"(Center for Drug Evaluation and Research, 2002). The approval for generic drugs require that "the rate and extent of absorption do not show a significant difference from listed drug or the extent of absorption does not show a significant difference and any difference in rate is intentional or not medically significant"(Sherwood, 2006). The FDA uses the plus-or-minus twenty percent test which implies that the amount of active ingredient in the blood over a period of time has to come within plus-or-minus twenty percent of that which is observed when the original branded drug is ingested (Mossinghoff, 1999). This requirement may not be significant for drugs that have a wide index of tolerance but not for drugs that have very narrow therapeutic band like anti-seizure medication (Mossinghoff, 1999:190-191).

Some drugs in the market have been reformulated to have delayed-release and extended-release characteristics. Delayed-release in drugs means "a formulation that has a coating to delay release of the drug until the product has passed through the stomach" while extended-release indicates "any formulation designed to deliver the dose over a longer interval than what is seen in immediate release products" (National Coordinating Council for Medication Error Reporting and Prevention, 2012).

Delayed or extended-release features of drugs are said to optimize and enhance the performance of the drug by avoiding the side effects "associated with high concentrations and the lack of activity associated with low concentrations" (Fyhr & Downie, 2003; Schaffler, 2007). This

feature also increases patient compliance by making it more convenient for patients to take the medication like reducing the number of times the patient has to take the medication in a day (Fyhr & Downie, 2003; Schaffler, 2007). Similarly, delayed or controlled-release formulations are said to optimize treatments and make treatment more convenient to patients (Schaffler, 2007). Studies show superiority of extended release drug over a "regular" drug for patients with major depressive disorder (Silverstone & Ravindran, 1999) and patients with high cholesterol (Fyhr & Downie, 2003). A study also noted the convenience of extended release formulation for patients with hypertension (Fyhr & Downie, 2003). However, studies failed to see the superiority of these features to a drug with flexible dosing regimen for patients with overactive bladder syndrome (Chapplea et al., 2005) or an established medication for depressed patients (Bielski, Ventura, & Chang, 2004).

1.2.5 HEALTH COVERAGE AND MEMBERSHIP IN MANAGE CARE ORGANIZATIONS

In general, patients with extensive insurance programs for prescription drugs are less sensitive to price of prescription drugs than patients with less comprehensive or no prescription drug coverage. In the study of the Canadian pharmaceutical consumption, deductible and co-payment schemes are important variables in the substitution of generic drugs to branded drugs (Anis, 1994). In a randomized controlled trial designed to determine the effect of cost-sharing on the demand for health services and the health status of individuals, individuals with more generous insurance buy more pharmaceuticals but the proportion of brand-name drugs among all drugs purchased in pharmacies was not a function of insurance plan (Leibowitz, Manning, Newhouse, United States Dept. of Health and Human Services, & Rand Corporation, 1985).

Membership to managed care organizations (MCOs) and formulary requirements of different organizations present constraints on the prescribing behavior of physicians and the pharmacists (S. F. Ellison et al., 1997; Gönül et al., 2001). Recent studies show that physicians contacted by managed care drug companies or affiliated with Health Maintenance Organizations (HMO) have a greater awareness of relative prices of prescription drugs (S. F. Ellison et al., 1997:427). Physicians whose patients belong to an HMO or other pre-paid plan are also more likely to prescribe generics to all their patients (Hellerstein, 1994, 1998). Pharmaceutical promotions like detailing and drug samples are less likely to influence physicians who see a higher percentage of HMO or Medicare patients (Gönül et al., 2001). Moral hazard is observed if physicians tend to differentiate the type of drugs they are prescribing to their patients based on their insurance coverage. Howard (1997) in his research found that "self-paying patients are significantly more likely than patients with Medicare or private insurance to be prescribed the generics that are cheapest relative to their brand-name counterparts."

MCOs try to control their expenditure on prescription drugs by controlling price and setting limits on drugs their members can use to treat specific conditions (Levy, 1999). To control the price, they negotiate discounts from drug manufacturers and pharmacies and use prescription drug capitation programs. To manage the use of drugs, they use drug formularies, generic substitution programs, therapeutic substitution programs, drug utilization review and step-care programs (Cook, 1998; Levy, 1999:31). Anis (1994) found that deductible and co-payment schemes are important variables in the substitution of generic drugs to branded drugs but formularies are not. The rise of generic drug market share is partly attributable to the increase in MCOs (Cook, 1998).

1.3 DISCRETE CHOICE MODEL OF DEMAND

This study uses the discrete choice model of demand in analyzing the relationship between physician prescribing behavior and variables that may influence it like price, direct-to-consumer advertising, quality of drugs, patient characteristics and physician characteristics. The discrete choice model of demand has been commonly used to examine the demand for differentiated products. It describes the decision makers' choices among alternative products, coarse of action or items (Train, 2008). It assumes that a consumer chooses a product that yield the highest utility based on product characteristics and some random components unobservable to outside observers/researchers (Anderson, de Palma, & Thisse, 1992).

The underlying utility function that determines the system of demand for differentiated products in a discrete choice model is the random utility function. Random utility represents a deterministic component which is a function of observable variables and a random component for which a variety of parametric assumptions have been made (Villas-Boas & Winer, 1999). The demand system is estimated in the discrete choice model by analyzing the random utility function as opposed to trying to estimate demand for each alternative product using a system of equation. The discrete choice model conveniently reduces the data requirements and the number of parameters estimated in a system of demand which makes it feasible to estimate coherent demand system for large and differentiated product markets (Salgado, 2008).

The issue of endogeneity of advertising and price arises in examining the relationship between demand and the said variables. Firms determine price and advertising based on market information and the unobservable variables that affect consumer choice. This brings about the issue

of endogeneity as prices and advertising will be correlated with these unobserved demand factors. Failure to account for the endogeneity of these variables could produce misleading results in the estimation process (S. T. Berry, 1994; Villas-Boas & Winer, 1999). The endogeneity of price and advertising are usually addressed using instrumental variables (Villas-Boas & Winer, 1999). Berry Lenvisohn and Pakes (1995) develop a method to estimate the discrete choice model using aggregated data taking into account the endogeneity of prices in the demand system. Aggregated or market level data and individual purchases have both been used to estimate the discrete choice model (Ackerberg, 2001; S. Berry et al., 1995; S. T. Berry, 1994; Chintagunta, Dube, & Goh, 2005; Goolsbee & Petrin, 2004; Nevo, 2000; Petrin, 2002; Train, 2008; Train & Winston, 2007; Villas-Boas & Winer, 1999). Individual level data were used to estimate the discrete choice model for prescription drugs in this study.

1.4 Analytical Framework

Previous studies developed utility models in analyzing physician prescribing behavior. Hellerstein's model (1994) hypothesizes that physician *j* will prescribe the generic form of the drug k to patient *i* if and only if

$$\boldsymbol{q}*_{\boldsymbol{k}}+\ \boldsymbol{c_j}+\boldsymbol{c_k}<\Delta\boldsymbol{P_k}(\mathbf{1}-\boldsymbol{\gamma\theta_{ij}}) \quad (1)$$

Where,

$q*_k$ is the quality difference between the brand-name drug and the generic substitute for the *k*th drug;

c_j is the physician-specific component of the prediction error the physician makes when assessing the quality difference (e.g. habit persistence in a physician's prescription decision);

c_k is the drug specific component of the prediction error the physician makes when assessing the quality difference (e.g. drug specific information diffusion);

ΔP_k is the price differential between the brand-name drug and the generic substitute;

γ is the proportion of the cost to the insurer that the physician does not internalize when deciding between brand-name and generic drugs (for example, if this parameter equals 1, the physician internalizes none of the cost to the insurer) which must be between 0 and 1 inclusive; and

θ_{ij} is the proportion of the cost of the drug covered by the patient's insurance, which must be between 0 and 1 inclusive.

Expressing the equation in probabilistic form, the theoretical model becomes equation (2).

$$\mathbf{Prob}\left[\boldsymbol{G_{ij}} = \mathbf{1}\middle|\Delta\boldsymbol{P_k}, \boldsymbol{q}*_{\boldsymbol{k}}, \boldsymbol{c_j}, \boldsymbol{c_k}, \boldsymbol{\theta_{ij}}\right] = \mathbf{Prob}[(\Delta\boldsymbol{P_k} - \boldsymbol{q}*_{\boldsymbol{k}} - \boldsymbol{c_k}) - \Delta\boldsymbol{P_k}\boldsymbol{\gamma}\boldsymbol{\theta_{ij}} - \boldsymbol{c_j} + \boldsymbol{\varepsilon_{ij}} > \mathbf{0}] \quad (2)$$

Where G_{ij} indicates whether physician *j* prescribed patient *i* the generic or brand-name form of drug *k*. Using the 1989 NAMCS data, the model was implemented as:

$\Delta P_k - q *_k - c_k$ Represents the price differential of branded and generic version of the drug minus the quality differential between the brand name and the generic forms of drug k and the physician's prediction error that is drug specific. Hellerstein's theoretical model assumes that the physician knows the price differential between branded and generic versions of the drug being prescribed. Price is not included in the model. Instead, a vector C of drug class dummy variable was used to represent the adjusted price. Hellerstein assumes that price and quality differences between branded and generic drugs do not vary within a given class of drugs.

$\Delta P_k \gamma \theta_{ij}$ Represents the price differential that is paid for by the patient's insurance but is not internalized by the prescribing physician. Hellerstein assumes that controlling for drug class, insurance covers the same proportion of drug costs for all patients who have the same type of coverage. Hellerstein represented this in her estimation equation as the interaction between the drug class dummy vector C and a vector X_2 of insurance dummy variables.

c_j Hellerstein estimates the physician-specific prediction error in the physician's assessment of the quality difference using observed characteristics of the physician and is represented by the following function:

$$\boldsymbol{S_j\pi_1 + M_j\pi_2 + T_j\pi_3 + R_j\pi_4 + X_j\pi_5 + v_j} \quad (3)$$

Where,

S is a dummy variable indicating whether the physician is a specialist (doctor who is not in general practice, family practice or general pediatrics) or a general practitioner

M is a dummy variable indicating whether the physician's practice is in a state with mandatory generic substitution laws

T mmy variable indicating whether the state uses two-line prescription pads

R is a vector of dummies used to identify the region of the country where the physician's practice is located

X is a vector of variables representing the physician's patients' characteristics: average age the percentage who are female, the percentage who are non-white; the percentage who are Hispanic; and for each type of insurance coverage recorded, in the NAMCS, the percentage of patients with that coverage.

Hence, Hellerstein arrives at the following estimation equation and implemented it using a fixed-effects probit specification:

$$P\left[G_{ij} = 1 \middle| C_k, X_{1i}, X_{2i,} S_j, M_j, T_j, R_j, X_j\right]$$

$$= \boldsymbol{P}[\boldsymbol{C_k\gamma} + \boldsymbol{X_{1i}\beta} + \boldsymbol{X_{2i}} \cdot \boldsymbol{C_k\gamma} + \boldsymbol{S_j\pi_1} + \boldsymbol{M_j\pi_2} + \boldsymbol{T_j\pi_3} + \boldsymbol{R_j\pi_4} + \boldsymbol{X_j\pi_5} + \boldsymbol{v_j} + \boldsymbol{\varepsilon_{ij}} > \boldsymbol{0}] \quad (4)$$

Howard (1997) implemented Hellerstein's theoretical model using the 1994 NAMCS data on antimicrobial drugs. He modified Hellerstein's model by adding the variable price and a measure of drug quality. These terms are explained as follows:

ΔP_k This is represented by L, the natural log of the ratio of the generic price to the brand-name price. Ratio of prices was use rather than their difference because the magnitude of the difference is heavily influenced by the dosage in which a drug is prescribed, which is not provided in the NAMCS data. Brand-name/generic price differentials vary considerably based on dosage and product-form, but the ratio of generic price to brand-name price is largely unaffected by these superficial characteristics. The natural log of the ratio is used so that equivalent percentage differences in the ratio will have equivalent impacts.

$q *_k + c_k$ interpreted as the consensus among physicians as to the quality differential between a brand-name drug and its generic substitute. Howard hypothesized that the medical community is risk-averse when faced with a new and untested product. The longer the generic drug has been in the market, the more it is perceived as a substitute for its branded counterpart.

Generic availability period was used as a proxy for consensus quality differential. This is represented as A, the natural log of the ratio of the number of days between the date the generic was approved by the FDA and June 30, 1994 (the mid date of the NAMCS survey) to the total number of days between December 31, 1981 and June 30,

1994. Generics approved prior to 1982 are assigned a ratio of 1. The generic availability ratio is measured in logarithmic terms.

$\Delta P_k \gamma \theta_{ij}$ This is represented by the interaction of a vector $\boldsymbol{P}$ of price differential dummy variables with the vector $\boldsymbol{X_2}$ of insurance dummy variables that Hellerstein developed. The vector P contains two dummy variables. The first indicates whether the ratio of the price of the generic form of the drug to the price of the brand-name form is above the median price ratio calculated from the drugs in the sample. The second dummy variable is the complement of the first: it indicates whether the drug's generic-to-brand-name price ratio is below the median price ratio for the drugs in the sample. This method presumes that drugs with similar generic-to-brand-name price ratios are equally likely to be prescribed as generics, ceteris paribus, but that drugs with below-median price ratios are more (or less) likely to be prescribed in generic form than drugs with above-median price ratios. On the other side of the interaction, the five dummy variables in X_2 record which of five types of medical insurance the patient used to pay for the physician visit at which the sampled prescription was written. The insurance types are HMO/other prepaid plan, Medicaid, Medicare, private/commercial insurance and self-pay (no insurance used). Howard hypothesized that drugs with low generic-to-brand-name price ratios and drugs prescribed to uninsured patients are more likely than their respective counterparts to be prescribed in generic form. Thus the below-median price ratio/self pay indicator was omitted for estimation purposes. The resulting coefficients on the other variables

in the $\boldsymbol{X_2 \cdot P}$ interaction reflect the impact, ceteris paribus, on the probability of a given drug being prescribed in generic form with respect to low-price-ratio drugs prescribed to self-pay patients. If one or more of these coefficients is significant it may be construed as evidence of moral hazard or the physicians are more likely to prescribe generics to uninsured patients than to patients holding certain types of insurance.

c_j This is represented by the same function developed by Hellerstein, except that M and T terms were dropped due to discontinuation of the variable Hellerstein used to determine the state in which a physician practices and the type of prescription pad the physician used in prescribing the medication.

In addition to the modification in the estimation equation, Howard (1997) also included other independent variables in his estimation equation. A dummy variable $\boldsymbol{O}$ was added to indicate prescriptions written for patients who received at least one other prescription for an antimicrobial drug during the same doctor visit. This was intended to capture variance caused by patients receiving multiple prescriptions. Howard also included a vector D of five individual drug dummy variables to flag prescriptions for five different antibiotics to introduce fixed effects for these five drugs. With this, Howard's estimation equation was as follows and was implemented using random effects probit model:

$$\mathrm{P}\left[G_{ij} = 1 \middle| L_k, A_k, X_{l1}, X_{2i}, P_k, S_j, R_j, X_j, O_i, D_k\right]$$

$$= \boldsymbol{P}[\boldsymbol{L_k\rho} + \boldsymbol{A_k v} + \boldsymbol{X_{1i}\beta} + \boldsymbol{X_{2i} \cdot P_k\gamma} + \boldsymbol{S_j\pi_1} + \boldsymbol{R_j\pi_2} + \boldsymbol{X_j\pi_3} + \boldsymbol{O_i\omega} + \boldsymbol{D_k\delta} + \boldsymbol{v_j} + \boldsymbol{\varepsilon_{ij}} > \boldsymbol{0}] \quad (5)$$

This study modifies Hellerstein's theoretical model by taking into account patient participation in the selection of prescription medication. Recent studies show how patients are playing a more active role in choosing the appropriate medication for them. Patients' exposure to direct-to-consumer advertisement of prescription drugs provided them with information which they may discuss with their doctors in selecting their medication. With this, Hellerstein's theoretical model was modified to incorporate the contribution the patients make in the decision process of selecting a medication.

$$\boldsymbol{q}*_{\boldsymbol{k}}+\ \boldsymbol{c_j}+\boldsymbol{c_k}+\boldsymbol{f_k}\ <\Delta\boldsymbol{P_k}(\mathbf{1}-\boldsymbol{\gamma\theta_{ij}}) \quad (6)$$

Where,

f_k is the quality assessment of the physician on the information provided by the patient about the prescription drug. It is assumed that the information the patient provided to the physician about an alternative prescription drug was most likely from direct-to-consumer advertisement of the prescription drug.

Furthermore, this study expanded the choices of prescription drugs from a choice between branded and generic drug to a choice between breakthrough, generic, me-too and generic me-too drugs.

To implement the model, the physician's choice of prescription drug is a function of the following variables where G_{ij} indicates whether physician *j* prescribed patient *i* the generic, breakthrough, me-too or generic me-too form of drug *k*.

$$\mathbf{Prob}\left[\boldsymbol{G_{ij}}=\mathbf{1}\middle|\Delta\boldsymbol{P_k},\boldsymbol{q}*_{\boldsymbol{k}},\boldsymbol{c_j},\boldsymbol{c_k},\boldsymbol{f_k},\boldsymbol{\gamma\theta_{ij}}\right] \quad (7)$$

$$\boldsymbol{P}\left[\boldsymbol{G_{ij}} = \mathbf{1} | \boldsymbol{C_k}, \boldsymbol{A_k}, \boldsymbol{E_k}, \boldsymbol{Q_{1k}}, \boldsymbol{Q_{1k}}, \boldsymbol{X_{1i}}, \boldsymbol{X_{2i}}, \boldsymbol{S_j}, \boldsymbol{R_j}, \widehat{\boldsymbol{X_j}}, \widehat{\boldsymbol{O}}_{\boldsymbol{i}}, \boldsymbol{V}\right] \qquad (8)$$

Where,

ΔP_k represented by C, the average cost of a month supply of the drug.

$q *_k + c_k$ similar to Howard's model, this represents the quality differential between the four types of drugs. In this model, the quality differential between the four types of drugs is represented by the following function:

$$\boldsymbol{A}_k\tau_1 + \boldsymbol{E}_k\tau_2 + \boldsymbol{Q}_{1k}\tau_3 + \boldsymbol{Q}_{2k}\tau_3 + z_k \qquad (9)$$

Where,

A is the length of time the drug was in the market following Howard's model. It is computed as the natural log of the ratio of the number of days between the date the drug was approved by the FDA and June 30, 2006 the date of the year when the survey was conducted to the total number of days between December 31, 1993 and June 30, 2006. Generics approved prior to 1994 are assigned a ratio of 1.

E Dummy variable indicating whether a drug has delayed-release or extended-release feature

Q_1 Dummy variable (only in the case of statins), indicating superiority of drug in reducing mortality.

Q_2 Dummy variable (only in the case of statins), indicating superiority of drug in reducing the risk of heart attack.

$\Delta P_k \gamma \theta_{ij}$ Operationalized by the vector $\boldsymbol{X_2}$ of insurance dummy variables following Hellerstein's assumption that after controlling for drug class, insurance covers the same proportion of drug costs for all patients who have the same type coverage. Since this study analyzes four different drug classes separately, there is no need for drug class dummy variable.

c_j Physician-specific prediction error in the physician's assessment of the quality difference using observed characteristics of the physician and represented by the following equation:

$$S_j\pi_1 + \boldsymbol{R}_j\pi_2 + \widehat{\boldsymbol{X}}_j\pi_3 + v_j \qquad (10)$$

Where,

S dummy variable indicating whether the physician is a specialist or a general practitioner

R vector of these dummies used to identify the region of the country where the physician's practice is located. The variables that were in Hellerstein's model to represent mandatory generic substitution laws and prescription pads were dropped because these variables were not available in the 2006 NAMCS.

$\hat{X}$ is a vector of variables representing the percentage of physician's patients' with each type of insurance coverage recorded in the NAMCS

f_k The information the patient provided during the doctor visit is represented by V, the natural log of the annual direct-to-consumer advertising expenditure of the prescription drug = ln (1+Direct-to-consumer advertising)

X_1 Vector of patient's characteristics which includes age of the patient and dummy variables for the patient's sex, race (white or non-white), and ethnicity (Hispanic or non-Hispanic).

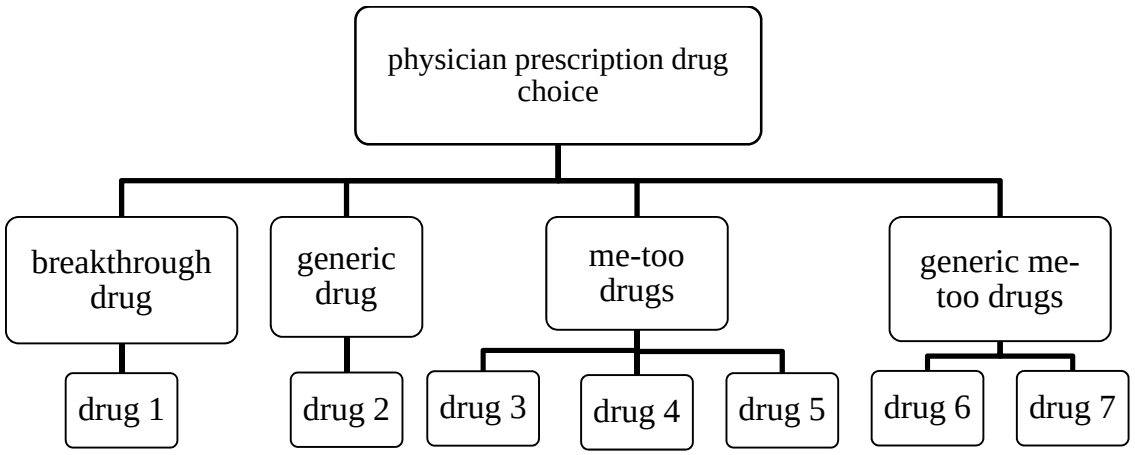
$\hat{O}$ still intended to capture variance caused by patients receiving multiple prescription (Howard, 1997) but the proxy used was the total number of medication of the patient

1.5 Model Structure

Most studies on physician's choice of prescription drug focus on the option between branded and its generic version. But physicians' options in choosing medication for their patients can further be differentiated by identifying the breakthrough drug, the generic version of the breakthrough drug, the me-too drugs and the generic versions of the me-too drugs in a specific class. A class of drug will have the breakthrough drug—the first drug under a drug class to be approved by the FDA, me-too drugs—branded drugs belonging in the same class that were approved by the FDA after the breakthrough drug, the generic drug which is the generic version of

the breakthrough drug and the generic me-too drugs which is the generic version of the me-too drugs. This study expands physicians' choice of prescription drugs between these types of drugs in a class. Figure 3 represents a non-sequential two-tiered structure for prescription choice by physician.

Figure 1. Non-sequential Two-tiered Nested Choice Structure



A non-sequential nested logit model, where the choices of drugs were classified into four nests, was used to estimate equation 8. Nested logit models are used when there are similarities among alternatives. It classifies the alternatives into nests which comprises the choice set, which in this study are the types of prescription drugs. This model relaxes the assumption of independently distributed errors and the independence of irrelevant alternatives inherent in conditional and multinomial logit models by clustering similar alternative into nests (StataCorp, 2007).

Assume J alternatives grouped into L nests. The physician's choice set for prescription drugs can be written as $[c_1,\ldots, c_j] = (c_{1|1},\ldots, c_{j1|1}),\ldots, (c_{1L},\ldots, c_{jL|L})$ (Green, 2000). The probabilistic form of the two-tiered nested logit model takes the forms

$$\boldsymbol{P_{j|l}} = \frac{e^{\beta' x_{j|l}}}{\sum_{j=1}^{J} e^{\beta' x_{j|l}}} \qquad (11)$$

$$\boldsymbol{P_{l}} = \frac{e^{\gamma' z_l + \tau_l I_l}}{\sum_{l=1}^{L} e^{\gamma' z_l + \tau_l I_l}} \qquad (12)$$

Where,

$P_{j|l}$ Probability physician *n* chooses prescription drug *j* given prescription drug nest *l* (e.g., me-too drugs)

P_l Probability physician *n* chooses prescription drug nest *l*

$\beta' x_{j|l}$ Measurable component of utility for physician *n* choosing prescription drug *j* given prescription drug nest *l*

$\gamma' z_l$ Measurable component of utility for physician *n* choosing prescription drug nest *l*

τ_l Estimated coefficient on inclusive term for prescription drug nest *l*

I_l Inclusive term that measures the correlation among random errors due to unobserved attributes of the choice set (Cervero & Duncan, 2008:11). The inclusive term is defined for the *l*th prescription drug nest as

$$\boldsymbol{I_l} = \ln \sum_{J=1}^{J_l} e^{\beta' x_{j|l}} \qquad (13)$$

The observed portion of utility can be decomposed into two parts (Train, 2008:86):

$$\boldsymbol{U_{ij} = Y_{ij} + W_{il} + \epsilon_{ij}} \qquad (9)$$

for $j \in B_l$, where

Y_{ij} depends on variables that describe alternative *j*. These variables vary over alternatives within nest *l*. The variables in this study include the following:

C the average cost of a month supply of a prescription drug

A the natural log of the ratio of the number of days between the date the drug was approved by the FDA and June 30, 2006 the date of the year when the survey was conducted to the total number of days between December 31, 1993 and June 30, 2006. Drugs approved prior to 1994 are assigned a ratio of 1.

E Dummy variable indicating whether a drug has delayed-release or extended-release feature

Q_1 Dummy variable (only in the case of statins), indicating superiority of drug in reducing mortality.

Q_2 Dummy variable (only in the case of statins), indicating superiority of drug in reducing the risk of heart attack.

V the natural log of the annual direct-to-consumer advertising expenditure of the prescription drug = *ln* (1+Direct-to-consumer advertising)

W_{il} depends only on variables that describe nest *l*. These variables differ over nests but not over alternatives within each nest. The variables in this study include the following:

X_1 vector of patient's characteristics which includes age of the patient and dummy variables for the patient's sex, race (white or non-white), and ethnicity (Hispanic or non-Hispanic).

$\hat{O}$ the total number of medication of the patient

X_2 insurance dummy variables

S dummy variable indicating whether the physician is a specialist or a general practitioner

R vector of dummies used to identify the region of the country where the physician's practice is located

$\hat{X}$ is a vector of dummy variables representing the percentage of physician's patients' with each type of insurance coverage recorded in the NAMCS

Given these variables, the utility function can be re-written as:

$$U = C_j\rho + A_j\tau_1 + \boldsymbol{E}_j\tau_2 + \boldsymbol{Q}_{1j}\tau_3 + \boldsymbol{Q}_{2j}\tau_3 + V_j\varphi + X_{1i}\beta + \hat{O}_i\omega + X_{2i}\gamma + S_i\pi_1 + R_i\pi_2 + \hat{X}_i\pi_3 + \epsilon_{ij} \quad (15)$$

1.6 ENDOGENEITY, MEASUREMENT ISSUES AND INSTRUMENTAL VARIABLES

The endogeneity of advertising and price is a concern in discrete choice estimations. Endogeneity of advertising may arise from the possible association between advertising and other variables like sales, elasticity of demand and profitability (Bagwell, 2007). Because firms determine price and advertising based on market information and other unobservable characteristics, prices and advertising will be correlated with these unobserved demand factors. The endogeneity of these two variables may produce misleading results in the estimation process.

The other issue on the empirical research of advertising is the identification of the proper measurement for advertising. An example pointed out by Bagwell is the possible effect of current and past advertising on sales and profit. He suggested that a measure of advertising that would take into account these temporal effects is necessary (Bagwell, 2007). However, studies arrived at different conclusions on the temporal effect of advertising on demand. Some studies find carry over effects of advertising on consumer demand (Lambin, 1976). Others see the effect of advertising lasting only about a year (Ashley, Granger, & Schmalensee, 1980; Boyd & Seldon, 1990; Leone, 1995). Nelson (1974) suggested that advertising has initial effects on sales but it is the firm-specific factors that have long term effects on sales. Kwoka's findings were consistent with Nelson's theory. He examined the factors affecting U.S. auto sales and found short term effect for advertising but longer effect for product styling (Kwoka, 1993). Landes and Rosenfield (1994) and Thomas (1989) had similar findings showing that brand loyalty is associated more with product quality than with

advertising. In the pharmaceutical industry, researchers found long run effects for pharmaceutical promotion particularly detailing (Hurwitz & Caves, 1988; Rizzo, 1999).

This study did not take into account the possible temporal effect of advertising. Recent studies show current advertising usually has positive short lived rather than long lived effect on sales (Bagwell, 2007). It also fails to identify an instrumental variable for direct-to-consumer advertising expenditure. Thus, the regression results of the direct-to-consumer advertising variable maybe underestimated and biased.

In the case of price, the parameter of price in the choice model "will be significantly underestimated if endogeneity is not taken into account" (Villas-Boas & Winer, 1999) . To address this, the price of the active pharmaceutical ingredient (API) of the drug was used as instrumental variable of the price of prescription drugs. APIs are the main chemicals used to produce the drug. The price of API was selected as instrumental variable because it makes up a large portion of the cost of producing a drug. It is directly correlated with price of drugs but has no direct or indirect effect on the physician's prescribing behavior as these data are unknown to prescribers. The price of API is a valid instrumental variable because it is related to price, has no direct effect on the dependent variable which is "choice" of prescription drug and is not correlated with the disturbance in the discrete choice model. However, one possible reason for "price of API" to be a weak instrument is that the cost of research is not taken into account in the model. Pharmaceutical companies include research and development as part of the costs of producing breakthrough drugs.

The price of prescription drugs C was regressed on the price of API, P_{API}. The estimated price of prescription drugs, $\hat{C}$, replaced the endogenous variable price, C, in the nested logit model.

$$U = \hat{C}_j\rho + A_j\tau_1 + \boldsymbol{E}_j\tau_2 + \boldsymbol{Q}_{1j}\tau_3 + \boldsymbol{Q}_{2j}\tau_3 + V_j\varphi + X_{1i}\beta + \hat{O}_i\omega + X_{2i}\gamma + S_i\pi_1 + R_i\pi_2 + \hat{X}_i\pi_3 + \epsilon_{ij} \quad (16)$$

1.7 Sample Frame and Summary Statistics

This study uses the 2006 National Ambulatory Medical Care Survey (NAMCS). This is a national probability sample survey of non-federal office-based physicians conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics, Division of Health Care Statistics. The survey was conducted from December 26, 2005, through December 24, 2006. Each physician is randomly assigned to a 1-week reporting period where data for a systematic random sample of visits are recorded by the physician or office staff on an encounter form provided for that purpose. Data are obtained on patients' symptoms, physicians' diagnoses, and medications ordered or provided. The survey also provides statistics on the demographic characteristics of patients and services provided, including information on diagnostic procedures, patient management, and planned future treatment (Center for Disease Control and Prevention). The NAMCS data were used in previous studies examining physician prescribing behavior (Hellerstein, 1998; Howard, 1997; Stern & Trajtenberg, 1998). For the 2006 sample, 1,455 physicians participated in the survey and 29,392 patient record forms were completed (Cherry, Hing, Woodwell, & Rechtsteiner, 2008). A drug mention data set was created from the 2006 NAMCS data making prescription choice by the physician the unit of analysis. Cases where the patients have other source of payment not identified in the survey, was not charged for the doctor's visit or have missing information on the source of payment were excluded in the study.

The sample in this study will be limited to the drugs belonging to the four of the top ten therapeutic classes based on the number of dispensed prescription (IMS Health).[3] These are: MHG-CoA reductase inhibitors (statins), selective serotonin reuptake inhibitors (SSRI), cardioselective beta blockers and proton pump inhibitors (PPI). Each therapeutic class was analyzed separately.

Price data are derived from the Consumer Reports Best Buy Drugs publication of Consumers Union (Consumers Union, 2006a, 2006b, 2007a, 2007b). The data were provided to Consumers Union by Wolters Kluwer Health, Pharmaceutical Audit Suite. These data reflect the nationwide retail average. The retail list price also referred to as the average wholesale price (AWP) is currently used by some public and private third-party payers as the basis for reimbursement (The Health Strategies Consultancy LLC, 2005). Different dosages have different corresponding prices. The average of the prices for the different dosages was computed and used in this study.

The 2006 expenditures on direct-to-consumer advertising were incorporated in the model to estimate the role of patients and the effect of pharmaceutical advertising in physician prescribing behavior. The DTC data were provided by TNS Media Intelligence (TNSMI), a leading provider of direct-to-consumer advertising expenditure and occurrence data (TNS Media Intelligence, 2009). The DTC advertising expenditure is composed of expenditure in the major types of media: television, radio, newspaper, magazine, internet and outdoors. Television expenditure includes cable television, network television, Spanish language network television, spot television, branded

[3] Available at http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/Top_Line_Data/2008_Top_Therapy_Classes_by_U.S._Sales.pdf

entertainment, syndication and local clearances of network television (including Spanish) and Syndication. Print includes business to business magazines, consumer magazines, Hispanic magazines, Hispanic newspapers, local magazines, national newspapers and Sunday magazines. Radio includes local radio, national spot radio and network radio. Outdoor advertising includes bulletins, painted walls, transit/bus shelters, in-store displays, convenience stores, shopping malls, airport, taxi displays and truck/mobile advertising. TNSMI tracks the occurrence of the brands or any marketing material associated with the product and collects the rates in doing the advertisement from networks, publishers, Standard Rate & Data Service (SRDS) Publications among others to compute the actual advertising expenditure (TNS Media Intelligence, 2009).

The 2006 price of the active pharmaceutical ingredient (API) which was used as the instrumental variable for the price of prescription drugs were acquired from IMS, a healthcare informatics organization. The data were collected from manufacturers of the API and were reported as the global average in US dollars of the manufacturers' average price per standard unit (USD/MNF/SHP).

The qualitative indicators on the superiority of some statin drugs in reducing mortality and risk of heart attack were from Consumer Report's Best Buy Drug. The data from this report were based on "an independent scientific review of 347 studies on statin drugs conducted by a team of physicians and researchers at the Oregon Health & Science University Evidence-Based Practice Center" (Cosumers Union of the United States Inc., 2010).

The prescription drugs in the sample were grouped according to the following typology—breakthrough drug, me-too drug, generic drugs and generic me-too drugs. The classification was

based on the date the FDA has approved the drug. This information is collected from the FDA Electronic Orange Book (Food and Drug Administration). The first to be approved in the class is labeled the breakthrough drug. The generic drug is the generic counterpart of breakthrough and generic me-too drugs are the generic counterpart of me-too drugs. Branded prescription drugs that were approved by FDA after the breakthrough drugs were the me-too drugs. The breakthrough drug in each therapeutic class has an existing generic counterpart and some of the me-too drugs also have generic counterparts.

1.7.1 SAMPLE: MHG-COA REDUCTASE INHIBITORS (STATIN DRUGS)

Statins are the newest class of cholesterol/lipid lowering drug. Randomized clinical trials report large reduction in cholesterol and evidence of benefit on stroke and total mortality (Hebert, Gaziano, Chan, & Hennekens, 1997). It has been the top selling class of prescription drugs since 2004 until 2008 when it placed second to antipsychotics via slim margin (IMS Health).

Table 1 summarizes the characteristics of the different statin drugs that were available in 2006. The statin class has eleven drugs in the market in 2006. The breakthrough drug Mevacor entered the market in 1987 and its generic counterpart lovastatin became available in 2001. There are two generic me-too drugs, pravastatin and simvastatin, that became available in the middle of 2006. This study does not include combination drug Vytorin.[4]

These two generic drugs engaged in direct-to-consumer advertising in that year. Four branded drugs (Lipitor, Crestor, Zocor and Pravachol) also engaged in direct-to-consumer

[4] Vytorin is a combination of statin and ezemtimibe.

advertising. The average costs of a month supply of these drugs were derived from the report of Consumer Reports Best Price Drugs (Consumers Union, 2007b, 2007c). These prices reflect the average (from June to December 2006) nationwide retail cost of a month supply of the prescription drug. It is the average price of all doses combined. Information on whether the prescription drug engaged in advertising from TNS Medial Intelligence is also summarized.

Table 1: Therapeutic Class: Statins

n=1833

Brand Name	Generic name	N	FDA approval	Type	Direct-to-consumer advertising	Extended release feature	Reduce mortality	Reduce the risk of heart attack	Price
Mevacor	lovastatin	30	8/31/1987	breakthrough drug	no	no	likely	yes	$94.00
Altoprev	lovastatin	0	6/26/2002	me-too drug	no	yes	likely	yes	$102.00
Pravachol	pravastatin	108	10/31/1991	me-too drug	yes	no	yes	yes	$136.00
Zocor	simvastatin	443	12/23/1991	me-too drug	yes	no	yes	yes	$144.00
Lescol	fluvastatin	29	12/31/1993	me-too drug	no	no	likely	likely	$67.00
Lescol XL	fluvastatin	10	10/6/2000	me-too drug	no	yes	likely	likely	$84.00
Lipitor	atorvastatin	906	12/17/1996	me-too drug	yes	no	yes	yes	$98.00
Crestor	rosuvastatin	141	8/12/2003	me-too drug	yes	no	likely	yes	$90.00
lovastatin		116	12/17/2001	generic drug	no	no	likely	yes	$58.00
pravastatin		7	4/24/2006	generic me-too	yes	no	yes	yes	$90.00
simvastatin		43	6/23/2006	generic me-too	yes	no	yes	yes	$109.00

Information on whether a certain drug has delayed or extended-release feature can be verified in the FDA's Orange book. With respect to reducing heart attacks, evaluation studies of the drugs showed that "atorvastatin , lovastatin, pravastatin and simvastatin have been proven to reduce the risk of heart attack over three to five years of use. Rosuvastatin has been shown to reduce the risk of heart attack over 1.9 years of use. The evidence of heart-attack prevention is less definitive for fluvastatin" (Cosumers Union of the United States Inc., 2010). The Consumer Report noted, however, that studies showing these findings only look at the short term rather than the long term impact of the drugs.

With respect to reduction of deaths, "atorvastatin, lovastatin, pravastatin and simvastatin have been found to reduce deaths from heart attacks among patients with a history of heart disease or risk factors for heart disease, such as diabetes and high blood pressure. Pravastatin and simvastatin were found to reduce the overall risk of dying among people considered to be at low risk of heart disease or heart attack." The report also noted that "lovastatin has not been proven to reduce deaths but the evidence points in that direction." Atorvastatin was tested and found to be effective in reducing deaths among high risk and would also be effective in reducing deaths among low risk people as well (Cosumers Union of the United States Inc., 2010).

Table 1 also includes the frequency of drug mention of the drugs in the 2006 National Ambulatory Care Survey. A total of n= 1,833 drugs in the statin class were included in this analysis. There were cases when the physician prescribed the generic names of Lipitor, Crestor, and Zocor even if the generic versions of these drugs were not available in the market when they were prescribed. In the case of Zocor, the generic simvastatin was approved by the FDA on June 23,

2006. All simvastatin prescriptions before July 2006 (n=28) were recoded as Zocor. Atorvastatin (n=5) were recoded as Lipitor and Rosuvastatin Calcium (n=1) was recoded as Crestor. It was assumed that physicians are aware of the availability of generic versions of drugs.

The succeeding table summarizes the descriptive statistics for the different variables included in this study in relation to the different types of prescription drugs.

Table 2: Summary Statistics for Prescription Drug Class Statins

n=1833

	Breakthrough drug	Generic drug	Me-too drugs	Generic me-too drugs
	n= 30	n=116	n=1637	n = 50
ALTERNATIVE SPECIFIC CHARACTERISTICS				
average nationwide retail cost of a month supply (in dollars) M(SD)	94.00 (0)	58.00 (0)	111.63 (22.50)	106.34 (6.66)
direct-to-consumer advertising expenditure (in dollars) M(SD)	0	0	95,074,053 (72171562)	280,416 (45776.584)
summary of length of time in the market[a] (in days) M(SD)	6884.63 (99.12)	1,638.90 (105.09)	3875.83 (1224.43)	106.12 (50.78)
CASE SPECIFIC CHARACTERISTICS				
Patient characteristics				
age of patient M(SD)	64.67 (14.83)	65.11 (14.02)	65.22 13.29)	72.26 (11.80)
sex of patient (female) n(%)	20 (66.67)	67 (57.76)	827 (50.52)	19 (38.00)
race of patient (non-white) n(%)	6 (20.00)	20 (17.24)	254 (15.52)	2 (4.00)
ethnicity of patient (Hispanic) n(%)	7 (23.33)	14 (12.07)	139 (8.49)	6 (12.00)
number of medication M(SD)	5.40 (2.31)	5.43 (2.23)	5.98 (2.07)	6.2 (1.82)
patient expected source of	16 (53.33)	62 (53.45)	974 (59.50)	32 (64.00)

payment- private coverage n(%)				
Patient expected source of payment- Medicare n(%)	16 (53.33)	54(46.55)	878 (53.63)	30 (60.00)
Patient expected source of payment- Medicaid n(%)	3 (10.00)	21 (18.10)	199(12.16)	1 (2.00)
Patient expected source of payment- Selfpay n(%)	2 (6.67)	5 (4.31)	67 (4.09)	0 (0.00)
Doctor characteristics				
doctor's specialization (specialized) n(%)	15 (50.00)	81 (69.83)	1217(74.34)	35(70.00)
practicing in the Midwest n(%)	1 (3.33)	25 (21.55)	370 (22.60)	12 (24.00)
practicing in the South n(%)	12 (40.00)	31 (26.72)	513 (31.34)	12 (24.00)
practicing in the West n(%)	9 (30.00)	47 (40.52)	343 (20.95)	10 (20.00)
percent of patient care revenue from Medicare (more than 50%) n(%)	13 (43.33)	47 (40.52)	579 (35.37)	22 (44.00)
percent of patient care revenue from Medicaid (more than 50%) n(%)	2 (6.67)	21 (18.10)	227 (13.87)	5 (10.00)
percent of patient care revenue from private insurance (more than 50%) n(%)	6 (20.00)	42 (36.21)	454 (27.73)	16 (32.00)
percent of patient care revenue from patient payment (more than 50%) n(%)	1 (3.33)	18 (15.52)	178 (10.87)	4 (8.00)

a. date the survey was conducted – date of FDA approval of the drug

The generic drug in the cheapest in the statins class ($58) followed by the breakthrough drug, the generic me-too drugs and the me-too drugs. On average, a month supply of generic me-too drugs cost $106.34 while a month supply of me-too drugs cost $111.63. Only the me-too drugs and the generic me-too drugs engaged in direct-to-consumer advertising.

Me-too drugs entered the market before the patent of the breakthrough drug expired. The breakthrough drug has been in the market for about 18 years in 2006 when NAMCS survey was done. The me-too drugs were about ten years in the market while the generic version of the breakthrough drug was about four years. The generic me-too drugs have been in the market for less than a year.

Patients who were prescribed with generic me-too drugs were older than the ones prescribed with generic, breakthrough or me-too drugs. Most patients were taking other medication aside from the statin drug prescribed by the physician. Majority of the patients pay using private coverage and Medicare.

1.7.2 SAMPLE: CARDIOSELECTIVE BETA BLOCKERS

Cardioselective beta blockers are common medication for high blood pressure as well as irregular heartbeat, angina, and symptoms of anxiety. There are eleven alternative prescription drugs in the therapeutic class of cardioselective beta blockers. Five of these drugs are me-too drugs and four are generic me-too drugs. One of the me-too drugs, Toprol-XL, was reformulated to have the extended-released feature. This is also the only drug in this class that engaged in direct-to-consumer advertising in 2006. Table 6 summarizes the descriptive statistics for cardioselective betablockers.

The prices of cardioselective beta blockers were the monthly cost of the prescription drugs based on the national average of its retail price as reported in the Consumer Reports Best Buy Drugs (Consumers Union, 2006b). The average price of the branded drugs is $90.22 (SD=71.40)

while the average price of generic drugs is $30.20 (SD=18.22). The overall average price for this class is $62.94 (SD=60.54).

Table 3: Therapeutic Class: Cardioselective Beta Blockers

n=1243

Brand name	Generic name	n	FDA approval	Type	Direct-to-consumer advertising	Extended release feature	Price
Lopressor	metoprolol tartrate	96	8/7/1978	breakthrough drug	no	no	$50.50
Kerlone	betaxolol	1	10/27/1989	me-too drug	no	no	$58.50
Toprol-XL	metoprolol succinate	483	1/10/1992	me-too drug	yes	yes	$54.67
Tenormin	atenolol	37	8/19/1981	me-too drug	no	no	$59.67
Sectral	acebutolol	2	12/28/1984	me-too drug	no	no	$234.00
Zebeta	bisoprolol	0	7/31/1992	me-too drug	no	no	$84.00
metoprolol tartrate		222	12/21/1993	generic drug	no	no	$10.50
betaxolol		0	10/22/1999	generic me-too	no	no	$37.00
atenolol		390	7/15/1988	generic me-too	no	no	$12.00
acebutolol		2	4/24/1995	generic me-too	no	no	$52.00
bisoprolol		10	11/16/2000	generic me-too	no	no	$39.50

There were 1,243 mentions of prescription drugs belonging to the cardioselective beta blockers class in the 2006 NAMCS data. Although the 25mg metropolol succinate was approved by the FDA in 2006, the drug did not become available in the market until 2007. There was one prescription of generic metropolol succinate in the dataset which was recoded as Toprol-XL, the branded version of the generic drug.

Table 4 summarizes the descriptive statistics of the key variables for the beta blockers.

Table 4. Summary Statistics for Beta Blockers

n=1,243

	Breakthrough drug	Generic drugs	Me-too drugs	Generic Me-too drugs
	n=96	n=222	n=523	n = 402
ALTERNATIVE SPECIFIC CHARACTERISTICS				
average nationwide retail cost of a month supply (in dollars) M(SD)	50.50 (0)	10.50 (0)	55.72 (11.13)	12.88 (5.11)
direct-to-consumer advertising expenditure (in dollars) M(SD)	0	0	13,838,181 (3986126)	0
summary of length of time in the market[a] (in days) M(SD)	10,150.54 (109.16)	4,557.08 (101.03)	5,532.64 (999.71)	6,404.87 (731.17)
CASE SPECIFIC CHARACTERISTICS				
Patient characteristics				
age of patient M(SD)	69.51 (11.17)	68.22 (13.81)	65.94 15.13)	64.17 (15.98)
sex of patient (female) n(%)	46 (47.92)	101 (45.50)	280 (53.54)	248 (61.69)
race of patient (non-white) n(%)	7 (7.29)	38 (17.12)	64 (12.24)	53 (13.18)
ethnicity of patient (Hispanic) n(%)	10 (10.42)	23 (10.36)	38 (7.27)	32 (7.96)
number of medication M(SD)	6.46 (1.76)	6.27 (1.83)	5.79 (2.10)	5.63 (2.15)

patient expected source of payment- private coverage n(%)	52 (54.17)	121 (54.50)	341 (65.20)	251 (62.44)
patient expected source of payment- Medicare n(%)	67 (69.79)	135 (60.81)	288 (55.07)	205 (51.00)
patient expected source of payment- Medicaid n(%)	13 (13.54)	28 (12.61)	34 (6.50)	45 (11.19)
patient expected source of payment- Selfpay n(%)	2 (2.08)	10 (4.50)	21 (4.02)	25 (6.22)
Doctor characteristics				
doctor's specialization (specialized) n(%)	68 (70.83)	162 (72.97)	401 (76.67)	276 (68.66)
practicing in the Midwest n(%)	29 (30.21)	52(23.42)	122 (23.33)	100 (23.88)
practicing in the South n(%)	25 (26.04)	54 (24.32)	175 (33.46)	102 (25.37)
practicing in the West n(%)	12 (12.50)	51 (22.97)	81 (15.49)	100 (24.88)
practicing in the North n(%)				
percent of patient care revenue from Medicare (more than 50%) n(%)	26 (27.08)	81 (36.49)	188 (35.95)	139 (34.58)
percent of patient care revenue from Medicaid (more than 50%) n(%)	8 (8.33)	28 (12.61)	38 (7.27)	81 (20.15)
percent of patient care revenue from private insurance (more than 50%) n(%)	30 (31.25)	60 (27.03)	128 (24.47)	141 (35.07)
percent of patient care revenue from patient payment (more than 50%) n(%)	7 (7.29)	22 (9.91)	32 (6.12)	62 (15.42)

a. date the survey was conducted – date of FDA approval of the drug

The cheapest drug in this class is the generic drug which only cost $10.50 for a month supply. This is followed by the generic versions of the me-too drugs which cost $12.88 a month. The price of the breakthrough drug and the me-too drugs were $50.50 and $55.72 respectively.

Only me-too drugs engaged in direct-to-consumer advertising. The drugs in the beta blockers class have been in the market in a while. The breakthrough drug Lopressor has been in the market for more than 27 years. The patients' primary sources of payment are private coverage and Medicare.

1.7.3 SAMPLE: PROTON PUMP INHIBITORS

Proton pump inhibitors (PPIs) are a class of drugs used to treat heartburn, gastroesophageal reflux disease (GERD) and ulcers by reducing gastric acid production (Consumers Union, 2007a). Tables 5 and 6 summarize the descriptive statistics of the class proton pump inhibitors. There are seven alternatives in the class of proton pump inhibitors: a breakthrough drug, a generic version of the breakthrough drug and five me-too drugs. All but Zegerid have delayed release features. Aciphex and generic omeprazole did not engage in direct-to-consumer advertising.

Table 5. Therapeutic Class: Proton Pump Inhibitors

n=1,346

Brand Name	Generic Name	N	FDA approval	Type	Direct-to-consumer advertising	Delayed release feature	Price
Prilosec	omeprazole	282	9/14/1989	breakthrough drug	yes	yes	$181.00
Prevacid	lansoprazole	254	5/10/1995	me-too drug	yes	yes	$161.50
Aciphex	rabeprazole	100	8/19/1999	me-too drug	no	yes	$189.00
Protonix	pantoprazole	240	2/2/2000	me-too drug	yes	yes	$152.50
Nexium	esomeprazole	376	2/20/2001	me-too drug	yes	yes	$187.00
Zegerid	omeprazole/sodium bicarbonate	11	6/15/2004	me-too drug	yes	no	$157.50
omeprazole		83	10/18/2002	generic	no	yes	$102.50

The price of the proton pump inhibitors were the average cost of a month supply of the medication based on the average retail prices of all the doses of the drugs. These prices were reported in the Consumer Reports Best Buy Drugs (Consumers Union, 2007a). The price of generic is $102.50 and the average price of the branded drugs is $171.42 (SD=16.09).

There were 1346 mentions of prescription drugs belonging in the proton pump inhibitors class in the 2006 NAMCS. Pysician prescriptions of Rabeprazole sodium (n=1), Esomeprazole magnesium (n=4), and Pantroprazole sodium (n=2), were recoded as Aciphex, Nexium and Protonix as there were no generic versions of these drugs in 2006. There are no generic versions of the me-too drugs when the survey was conducted in 2006.

Table 6 summarizes the descriptive statistics of the key variables for the proton pump inhibitors.

Table 6. Summary statistics for Proton Pump Inhibitors

n= 1,346

	Breakthrough drug	Generic drug	Me-too drugs
	n=282	n=83	n=981
ALTERNATIVE SPECIFIC CHARACTERISTICS			
Average nationwide retail cost of a month supply (in dollars) M(SD)	181 (0)	102.50 (0)	171.83 (15.49)
Direct-to-consumer advertising expenditure (in dollars) M(SD)	1,032,800 (0)	0	73,560,914 (84091542)
Summary of length of time in the market[a] (in days) M(SD)	6118.82 (100.19)	1358.57 (103.38)	2621.61 (878.23)

CASE SPECIFIC CHARACTERISTICS			
Patient characteristics			
age of patient M(SD)	61.56 (17.60)	62.84 (15.80)	59.59 (17.05)
sex of patient (female) n(%)	176 (62.41)	48 (57.83)	598 (60.96)
race of patient (non-white) n(%)	38 (13.48)	14 (16.87)	114(11.62)
ethnicity of patient (Hispanic) n(%)	30 (10.64)	5 (6.02)	84 (8.56)
number of medication M(SD)	5.46 (2.48)	5.94 (2.38)	5.44 (2.48)
Patient expected source of payment- private coverage n(%)	157 (55.67)	49 (59.04)	625 (63.71)
Patient expected source of payment- Medicare n(%)	128 (45.39)	42 (50.60)	438 (44.65)
Patient expected source of payment- Medicaid n(%)	54 (19.15)	10 (12.05)	132 (13.46)
Patient expected source of payment- Selfpay n(%)	13 (4.61)	2 (2.41)	35 (3.57)
Doctor characteristics			
doctor's specialization (specialized) n(%)	189 (67.02)	60 (72.29)	716 (72.99)
Practicing in the Midwest n(%)	72 (25.53)	27 (32.53)	245 (24.97)
Practicing in the South n(%)	80 (28.37)	18 (21.69)	366 (37.31)
Practicing in the West n(%)	63 (22.34)	20 (24.10)	152 (15.49)
Practicing in the North n(%)			
Percent of patient care revenue from Medicare (more than 50%) n(%)	22 (26.51)	88 (31.21)	294 (29.97)
Percent of patient care revenue from Medicaid (more than 50%) n(%)	39 (13.83)	9 (10.84)	98 (9.99)
Percent of patient care revenue from private insurance (more than 50%) n(%)	72 (25.53)	30 (36.14)	278 (28.34)
Percent of patient care revenue from patient payment (more than 50%) n(%)	31 (10.99)	8 (9.64)	84 (8.56)

a. date the survey was conducted – date of FDA approval of the drug

The generic drug omeprazole is the cheapest drug in the proton pump inhibitors' class. This is followed by the me-too drugs with an average monthly cost of $171.83. The most expensive drug in this class, Aciphex, is a me-too drug. A month supply of Aciphex costs $189. There are me-too drugs that are cheaper than the breakthrough drug, Prilosec, which caused the average price of me-too drugs to be lower than the price of the breakthrough drug.

Both the breakthrough drug and the me-too drugs spent for direct-to-consumer advertising in 2006. The breakthrough drug spent $1,032,800 on direct-to-consumer advertising while the me-too drugs spent an average of $73,560,914. The breakthrough drug has been in the market for more than six years when the survey was conducted in 2006. Me-too drugs entered the market before the generic version of the breakthrough drug Prilosec became available.

Patients who received me-too drugs were slightly younger compared to those prescribed with the breakthrough drug or generic drug. The patients who were in proton pump inhibitors have, on average, five other medications. The expected sources of payment for majority of the patients were private coverage and Medicare.

1.7.4 SAMPLE: SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI)

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants. They have simpler dosing and less toxic effects compared to other anti-

depressants. A study showed that paroxetine, fluoxetine and sertraline were similar in effectiveness for depressive symptoms (Kroenke et al., 2001).

Prozac has been marketed by Eli Lilly as the breakthrough drug in the SSRI class of antidepressant drugs. There were eight me-too drugs in this class and four of them have generic counterparts. Two were reformulated to be delayed released and extended released. Sarafem, coded as a me-too drug, is a rebranded Prozac. One generic drug (sertraline) and two me-too drugs (Zoloft and Lexapro) spent for direct-to-consumer advertising in 2006. Table 7 summarizes the information on the SSRIs.

Table 7.Therapeutic Class: Selective Seratonin Reuptake Inhibitors

n=1308

Brand name	Generic name	N	FDA approval	Type	Direct-to-consumer advertising	Delayed release/ controlled-release feature	Price
Sarafem	fluoxetine	6	7/6/2000	me-too drug	no	no	$191.00
Prozac	fluoxetine	188	12/29/1987	breakthrough drug	no	no	$225.33
Celexa	citalopram	123	7/17/1998	me-too drug	no	no	$107.00
Lexapro	escitalopram	333	8/14/2002	me-too drug	yes	no	$97.67
Paxil	paroxetine	168	12/29/1992	me-too drug	no	no	$118.25
Paxil CR	paroxetine	14	2/16/1999	me-too drug	no	yes	$114.67
Prozac Weekly	fluoxetine	0	2/26/2001	me-too drug	no	yes	$139.00
Zoloft	sertraline	319	12/30/1991	me-too drug	yes	no	$104.33
Pexeva	paroxetine	4	7/3/2003	me-too drug	no	no	$112.00
Fluoxetine		77	8/2/2001	generic drug	no	no	$49.50
Citalopram		34	10/28/2004	generic me-too	no	no	$45.00
Paroxetine		37	7/30/2003	generic me-too	no	no	$63.75
Sertraline		5	6/30/2006	generic me-too	yes	no	$85.67
Fluvoxamine		0	11/29/2000	generic me-too	no	no	$94.00

Prices of the SSRIs were based on the average cost of a month supply of SSRI based on the average retail price in September, 2006. These information were published by Consumers Union through the Consumer Reports Best Buy Drugs (Consumers Union, 2006a). The average price for branded drug under this class is $134.36 (SD=44.23) while the average price for generic drugs is $67.58 (SD=21.66). The overall average price is $110.51 (SD=49.50).

There were a total of n=1308 drug mention in the 2006 National Ambulatory Care Survey that belonged to the SSRI class that were included in this analysis. There were 13 mentions of the prescription drug Luvox. Although this drug was approved by the FDA in 1997, it was not available in the market in 2006. These cases were excluded in the analysis. There were also mentions of sertraline prior to its approval and release in the market on June 30, 2006. These four cases were recoded as Zoloft which is the brand name version of sertraline.

Table 8. Summary statistics for prescription drug class SSRI

n=1,308

	Breakthrough drug	Generic drugs	Me-too drugs	Generic Me-too drugs
	n= 188	n= 77	n= 967	n = 76
ALTERNATIVE SPECIFIC CHARACTERISTICS				
average nationwide retail cost of a month supply (in dollars) M(SD)	213.50 (0)	47.60 (0)	105.52 (9.85)	56.80 (11.94)
direct-to-consumer advertising expenditure (in dollars) M(SD)	0	0	4,980,014.40 (5389297.40)	28,085.53 (106537.6)
summary of length of time in the market[a] (in days) M(SD)	6,737.53 (99.04)	1,789.07 (94.46)	3,524.56 (1746.73)	771.62 (300.10)

CASE SPECIFIC CHARACTERISTICS				
Patient characteristics				
age of patient M(SD)	45.59 (17.78)	52.30 (15.57)	49.56 (19.14)	59.05 (17.06)
sex of patient (female) n(%)	131 (69.68)	49 (63.64)	666 (68.87)	44 (57.89)
race of patient (non-white) n(%)	16 (8.51)	6 (7.79)	108 (11.17)	4 (5.26)
ethnicity of patient (Hispanic) n(%)	11 (5.85)	16 (20.78)	89 (9.20)	10 (13.16)
number of medication M(SD)	4.14 (2.49)	4.31 (2.51)	4.40 (2.55)	5 (2.40)
patient expected source of payment- private coverage n(%)	106 (56.38)	41 (53.25)	609 (62.98)	45 (59.21)
patient expected source of payment- Medicare n(%)	38 (20.21)	22 (28.57)	279 (28.85)	32 (42.11)
patient expected source of payment- Medicaid n(%)	17 (22.08)	38 (20.21)	148 (15.31)	7 (9.21)
patient expected source of payment- Selfpay n(%)	26 (13.83)	9 (11.69)	110 (11.38)	12 (15.79)
Doctor characteristics				
doctor's specialization (specialized) n(%)	125 (66.49)	58 (75.32)	731 (75.59)	56 (73.68)
practicing in the Midwest n(%)	54 (28.72)	28 (36.36)	227 (23.47)	12 (15.79)
practicing in the South n(%)	51 (27.13)	7 (9.09)	291 (30.09)	21 (27.63)
practicing in the West n(%)	35 (18.62)	29 (37.66)	197 (20.37)	23 (30.26)
practicing in the North n(%)				
percent of patient care revenue from Medicare (more than 50%) n(%)	38 (20.21)	18 (23.38)	227 (23.47)	20 (26.32)
percent of patient care revenue from Medicaid (more than	28 (14.89)	20 (25.97)	143 (14.79)	17 (22.37)

50%) n(%)				
percent of patient care revenue from private insurance (more than 50%) n(%)	78 (41.49)	35 (45.45)	350 (36.19)	24 (31.58)
percent of patient care revenue from patient payment (more than 50%) n(%)	29 (15.43)	13 (16.88)	151 (15.62)	11 (14.47)

a. date the survey was conducted – date of FDA approval of the drug

1.8 EMPIRICAL RESULTS AND DISCUSSION

Prior to implementing the nested logit models of the four classes of drugs, the estimated value of the price of prescription drugs was derived using the price of active pharmaceutical ingredient (API) of the prescription drug as an instrumental variable (IV) for price, [C = fn (P_{API})].

A single first stage regression was used to estimate the value of price for all four second stage regressions. The sample is composed of all the drugs in the four classes examined in this study (n=41). The n is too small for inclusion of other independent variables in the first stage regression. The sample size of the drugs in each class is also too small to allow for separate first stage regression for the instrumental variable of each drug class. The result of the regression estimation is as follows:

Table 9. First –stage regression of the variable price on the instrumental variable API price

n = 41

		Coef.	t	*p*>|t|	
P_{API}		31.859	2.02	0.051	*
Cons		82.927	5.98	0.000	
Summary Statistics					
Number of obs	=	41			
F(1,39)	=	4.07			
Prob>F	=	0.05			
R^2	=	0.09			
Adjusted R^2	=	0.07			

*Significant at .05 level

The regression results show that the API has a statistically significant effect on price ($F_{1,39}$= 4.07, p =.05). This may suggest that API is a weak instrument for price. However, the low F and the weak statistical significance can be attributed to the small sample size. The estimated value of price, $\hat{C}$ =E(P|P_{API}), was included in the nested logit model. Note that the estimation was done manually by running two separate regressions. The standard errors were not manually adjusted. This will make the standard errors of the nested logit models incorrect. The coefficients of the model are still correctly estimated but this may overestimate the statistical significance of the variables.

The results of the nested logit models for statins, beta blockers, proton pump inhibitors (PPIs) and selected serotonin reuptake inhibitors (SSRIs) are summarized in the following sections. The estimates were derived using full information maximum-likelihood estimation. Nested logit model clusters alternatives into nests thus relaxing the assumption of independently distributed errors and the independence of irrelevant alternatives inherent in standard multinomial and conditional logit models. The results of this study are limited to the analysis of factors that may

affect the prescription of the specific type of drug and not the specific drug in the class. The results presented are limited to first level probabilities and coefficients.

1.8.1 STATINS

The non-sequential two-tiered tree structure for the statins is presented below. The first level presents the four nests which correspond to the types of prescription drugs (generic, breakthrough, me-too and generic me-too drugs). The second level presents the different alternatives in each nest.

Figure 2: Tree Structure Specified for the Nested Logit Model of Statins

Type	N	Alternatives	N	k
Generic drug	1,833	lovastatin	1,833	116
Breakthrough drug	1,833	Mevacor	1,833	30
Me-too drugs	12,831	Lescol XL	1,833	10
		Crestor	1,833	141
		Altoprev	1,833	0
		Pravachol	1,833	108
		Zocor	1,833	443
		Lescol	1,833	29
		Lipitor	1,833	906
Generic me-too drugs	2,077	simvastatin	885	43
		pravastatin	1,192	7
Total			18,574	1,833

k = number of times alternative is chosen
n = number of observations at each level

Nested Logit Model Results for Drug Class Statins

The following table summarizes the result of the nested logit model for drug class statin.

Table 10. Nested Logit Model with IV Results on Prescribing Choice of Physicians for Statins

Parameters		Coef.	z	P>|z|	
Predicted price, $\hat{C}$		-0.013	-2.62	0.009	**
Length of time ratio, A		1.024	4.27	0.000	***
Direct-to-consumer advertising expenditure, V		0.176	6.82	0.000	***
Reduces mortality		0.114	0.34	0.734	
Prevents heart attack		-0.589	-1.60	0.109	
Delayed/extended release feature		-0.171	-0.58	0.563	
Generic drug (base)					
Patient characteristics					
Age x	breakthrough drugs	-0.024	-1.78	0.075	
	me-too drugs	-0.021	-2.36	0.018	*
	generic me-too drugs	-0.004	-0.28	0.779	
Sex x	breakthrough drugs	0.396	0.89	0.376	
(male)[a]	me-too drugs	-0.310	-1.52	0.128	
	generic me-too drugs	-0.863	-2.39	0.017	*
Race x	breakthrough drugs	0.563	1.02	0.307	
(white)	me-too drugs	0.163	0.59	0.557	
	generic me-too drugs	-0.945	-1.20	0.229	
Ethnicity x	breakthrough drugs	0.784	1.41	0.160	
(non-hispanic)	me-too drugs	-0.131	-0.41	0.680	
	generic me-too drugs	1.038	1.79	0.073	
Number of medication x	breakthrough drugs	0.026	0.28	0.778	
	me-too drugs	0.116	2.50	0.012	*
	generic me-too drugs	0.121	1.41	0.159	

Patient expected source of payment (self pay)					
Private Insurance x	breakthrough drugs	0.306	0.57	0.572	
	me-too drugs	0.372	1.40	0.162	
	generic me-too drugs	0.384	0.82	0.415	
Medicare x	breakthrough drugs	0.562	0.95	0.344	
	me-too drugs	0.643	2.36	0.018	*
	generic me-too drugs	0.723	1.41	0.157	
Medicaid x	breakthrough drugs	-1.049	-1.41	0.159	
	me-too drugs	-0.445	-1.38	0.168	
	generic me-too drugs	-2.189	-2.01	0.045	*
Doctor characteristics					
Doctor specialization x	breakthrough drugs	-1.129	-2.44	0.015	*
(general practice)	me-too drugs	0.231	0.99	0.322	
	generic me-too drugs	-0.430	-1.06	0.289	
Region of practice (Northeast)					
Midwest x	breakthrough drugs	-2.855	-2.55	0.011	*
	me-too drugs	-0.941	-2.60	0.009	**
	generic me-too drugs	-1.025	-1.90	0.058	
South x	breakthrough drugs	-0.828	-1.47	0.141	
	me-too drugs	-0.843	-2.44	0.015	*
	generic me-too drugs	-1.387	-2.72	0.007	*
West x	breakthrough drugs	-1.284	-2.16	0.031	*
	me-too drugs	-1.594	-4.74	0.000	***
	generic me-too drugs	-1.897	-3.57	0.000	***
Percentage of patient care revenue from Medicare greater than 50% x	breakthrough drugs	0.614	1.23	0.221	
	me-too drugs	-0.369	-1.49	0.136	
	generic me-too drugs	0.208	0.48	0.633	
Percentage of patient care revenue from Medicaid greater	breakthrough drugs	-0.588	-0.55	0.579	
	me-too drugs	0.363	0.77	0.440	

than 50% x	generic me-too drugs	0.301	0.33	0.742
Percentage of patient care revenue from private insurance greater than 50% x	breakthrough drugs	-0.333	-0.56	0.574
	me-too drugs	-0.489	-1.88	0.060
	generic me-too drugs	-0.067	-0.14	0.888
Percentage of patient care revenue from self-payment greater than 50% x	breakthrough drugs	-1.018	-0.69	0.488
	me-too drugs	-0.026	-0.05	0.962
	generic me-too drugs	-1.072	-0.97	0.333
Dissimilarity parameters				
τ generic drug	— [b]			
τ breakthrough drugs	— [b]			
τ me-too drugs	0.676			
τ generic me-too drugs	2.591			
Summary Statistics				
No. of cases	1,833			
Log likelihood	-2672.376			
Wald chi^2	1021.05 (0.000)			
LR test for IIA = χ^2 (prob.)	13.32 (0.001)			

a. Reference category in parentheses

b. Degenerate nest. Parameter not defined.

*Significant at .05 level

**Significant at .01 level

***Significant at .001 level

The results show that increase in price decreases the likelihood that a drug will be prescribed relative to other drugs in the same class. This is significant at $p \leq .01$. On the other hand, increase in the length of time in the market and direct-to-consumer advertising expenditure increase the likelihood that a drug will be prescribed relative to other drugs in the same class. These findings are significant at $p \leq .001$ level. Indicators of drug quality like possible effects on

mortality and heart attack and extended feature are not significant predictors of prescribing behavior of physicians in the class of statins.

In terms of patient characteristics, an increase in age decreases the probability of being prescribed me-too drugs relative to the probability of being prescribed generic drug ($p \leq .05$). Females are also more likely to be prescribed generic drugs than generic me-too drugs compared to males ($p \leq .05$). An increase in the number of medication increases the probability of being prescribed me-too drugs relative to the probability of being prescribed generic drugs ($p \leq .05$). Medicare as an expected source of payment also increases the probability that a patient will be prescribed me-too drugs relative to the probability of being prescribed a generic drug ($p \leq .05$). On the other hand, Medicaid as an expected source of payment increases the probability of a patient being prescribed generic drug relative to being prescribed generic me-too drugs ($p \leq .05$).

In terms of physician characteristics, physicians with specialized practice are less likely to prescribe breakthrough drugs than generic drug compared to those with general practice ($p \leq .05$). Physicians who are practicing in the Midwest are less likely to prescribe breakthrough and me-too drugs than the generic drug compared to physicians in the Northeast ($p \leq .01$). Physicians in the South are less likely to prescribe me-too drugs and generic me-too drugs than generic drugs compared to physicians in the Northeast ($p \leq .05$; $p \leq .01$). Physicians in the West are less likely to prescribe breakthrough, me-too and generic me-too drugs than generic drug compared to physicians in the Northeast ($p \leq .05$; $p \leq .001$; $p \leq .001$).

The dissimilarity parameter (τ) is a measure of the degree of correlation of random shocks within each nest (StataCorp, 2007:443). The value of the dissimilarity parameters (τ) ≤ 1 indicates

whether the model is consistent with the random utility model. In this case, the dissimilarity parameters for generic drugs and breakthrough drugs are undefined because these are degenerate nests; each branch has only one alternative. The dissimilarity parameter of me-too drugs is 0.676 but the dissimilarity parameter for generic me-too drugs is slightly higher than 1.0. This value makes this model inconsistent with the random utility model. While this is so, the model is still mathematically correct and gives well behaved probabilities between 0 and 1 and that sum to 1 (Cameron & Trivedi, 2010:515). The likelihood ratio test for independence of irrelevant alternatives (IIA) is significant at $p. \leq 001$ indicating that we can reject the null hypothesis that the IIA requirement holds. This implies that nested logit model maybe more appropriate than conditional logit or standard multinomial logit model.

The results of the alternative-specific variables for the nested logit model without the instrumental variable on price are presented for comparison with the nested logit model with IV.

Table 11. Nested Logit Model Results for Alternative-Specific Variables on Prescribing Choice of Physicians for Statins

Parameters	Coef.	z	P>|z|	
Price, C	0.006	3.17	0.002	**
Length of time ratio, A	0.979	4.20	0.000	***
Direct-to-consumer advertising expenditure, V	0.157	7.51	0.000	***
Reduces mortality	-0.111	-0.41	0.684	
Prevents heart attack	-0.589	-1.60	0.040	
Delayed/extended release feature	-0.171	-0.58	0.789	

The results show that the use of instrumental variable on price has resulted to the reversal of the sign of the price coefficient from positive to negative. The price coefficient on the model with the IV is more consistent with the hypothesis of this study that an increase in price will reduce the likelihood of a drug from being prescribed. This suggests that the price was indeed endogenous and using the instrumental variable was helpful in addressing endogeneity. Accordingly, the inclusion of the IV in the model has also reversed the sign of the coefficients for length of time in the market, direct-to-consumer advertising and the qualitative measure for the reduction of mortality. The inclusion of the IV also made the effects of these variables more consistent with the hypotheses of the model that increase in length of time in the market and increase in advertising expenditure will also increase the likelihood of a drug from being prescribed.

1.8.2 CARDIOSELECTIVE BETA BLOCKERS

The following figure presents the non-sequential two-tiered tree structure for cardioselective beta blockers. The first level are the four nests which represent the types of prescription drugs while the second level presents the alternatives in each nest.

Figure 3. Tree Structure Specified for the Nested Logit Model of Cardioselective Beta Blockers

Type	N	Alternatives	n	k
Generic drug	1,242	metoprolol	1,242	222
Breakthrough drug	1,242	Lopressor	1,242	96
Me-too drugs	4,968	Zebeta	1,242	0
		Tenormin	1,242	37
		Spectral	1,242	2
		Toprol XL	1,242	483
Generic me-too drugs	3,726	bisoprolol	1,242	10
		atenolol	1,242	390
		acebutolol	1,242	2
		betaxolol	1,242	0
Total			11,178	1,242

k = number of times alternative is chosen
n = number of observations at each level

Nested Logit Model Results for Drug Class Cardioselective Beta Blockers

The following table summarizes the result of the nested logit regression model for the drug class cardioselective beta blockers.

Table 12. Nested Logit Model Results for Prescribing Choice of Physicians for Cardioselective Beta Blockers

Parameters		Coef.	z	P>|z|	
Predicted price, $\hat{C}$		-0.334	-4.75	0.000	***
Length of time ratio, A		-0.473	-3.12	0.002	**
Direct-to-consumer advertising expenditure, V		0.136	5.00	0.000	***
Generic drug (base)					
Patient characteristics					
Age x	breakthrough drugs	-0.011	-1.35	0.178	
	me-too drugs	-0.015	-2.18	0.029	*

	generic me-too drugs	-0.013	-2.08	0.038	*
Sex x	breakthrough drugs	0.051	0.20	0.838	
(male)[a]	me-too drugs	0.397	2.38	0.017	*
	generic me-too drugs	0.764	4.36	0.000	***
Race x	breakthrough drugs	-1.013	-2.24	0.025	*
(white)	me-too drugs	-0.340	-1.39	0.163	
	generic me-too drugs	-0.466	-1.85	0.064	
Ethnicity x	breakthrough drugs	0.063	0.15	0.879	
(non-hispanic)	me-too drugs	-0.498	-1.71	0.088	
	generic me-too drugs	-0.481	-1.59	0.111	
Number of medication x	breakthrough drugs	0.012	0.19	0.846	
	me-too drugs	-0.142	-3.30	0.001	**
	generic me-too drugs	-0.142	-3.23	0.001	**
Patient expected source of payment (self pay)					
Private Insurance x	breakthrough drugs	0.058	0.20	0.844	
	me-too drugs	0.257	1.27	0.205	
	generic me-too drugs	0.323	1.51	0.130	
Medicare x	breakthrough drugs	0.634	1.83	0.067	
	me-too drugs	0.079	0.34	0.730	
	generic me-too drugs	0.029	0.12	0.901	
Medicaid x	breakthrough drugs	0.488	1.18	0.238	
	me-too drugs	-0.547	-1.75	0.080	
	generic me-too drugs	-0.103	-0.34	0.737	
Doctor characteristics					
Doctor specialization x	breakthrough drugs	-0.042	-0.15	0.881	
(general practice)	me-too drugs	0.140	0.71	0.476	
	generic me-too drugs	-0.106	-0.53	0.594	
Region of practice (Northeast)					
Midwest x	breakthrough drugs	0.119	0.36	0.716	

	me-too drugs	0.104	0.45	0.654	
	generic me-too drugs	0.107	0.44	0.661	
South x	breakthrough drugs	-0.034	-0.10	0.918	
	me-too drugs	0.443	2.00	0.046	*
	generic me-too drugs	0.296	1.25	0.212	
West x	breakthrough drugs	-0.650	-1.64	0.101	
	me-too drugs	-0.246	-1.02	0.310	
	generic me-too drugs	0.262	1.07	0.286	
Percentage of patient care revenue from Medicare greater than 50% x	breakthrough drugs	-0.423	-1.34	0.179	
	me-too drugs	0.150	0.76	0.447	
	generic me-too drugs	-0.120	-0.56	0.576	
Percentage of patient care revenue from Medicaid greater than 50% x	breakthrough drugs	-0.489	-0.74	0.460	
	me-too drugs	-0.349	-0.82	0.409	
	generic me-too drugs	0.609	1.54	0.125	
Percentage of patient care revenue from private insurance greater than 50% x	breakthrough drugs	0.261	0.83	0.407	
	me-too drugs	-0.099	-0.44	0.657	
	generic me-too drugs	0.085	0.37	0.713	
Percentage of patient care revenue from self-payment greater than 50% x	breakthrough drugs	0.226	0.29	0.768	
	me-too drugs	-0.159	-0.32	0.753	
	generic me-too drugs	0.007	0.01	0.988	
Dissimilarity parameters					
τ generic drug	— [b]				
τ breakthrough drugs	— [b]				
τ me-too drugs	0.284				
τ generic me-too drugs	0.216				
Summary Statistics					
No. of cases	1,242				
Log likelihood	-1664.7571				
Wald chi^2 (51)	382.08				

Prob>chi^2	0.000
LR test for IIA $= \chi^2$ (prob.)	115.33 (0.000)

a. Reference category in parentheses

b. Degenerate nest. Parameter not defined.

*Significant at .05 level

**Significant at .01 level

***Significant at .001 level

The results of the nested logit model show that an increase in the price of the prescription drug will result in the decrease the likelihood of a drug from being prescribed. This is statistically significant at $p \leq .001$. The length of time the drug has been in the market is a significant determinant of physician prescribing behavior for cardioselective beta blockers at $p \leq .01$. An increase in the length of time in the market decreases the likelihood of a drug from being prescribed. An increase in the spending on direct-to-consumer advertising will increase the likelihood of a type of drug from being prescribed and this is significant at $p \leq .001$.

In terms of patient characteristics, older patients are more likely to be prescribed generic drugs than me-too and generic me-too drugs ($p<.05$). Females are more likely to be prescribed me-too and generic me-too drugs than generic drugs compared to males. These findings are statistically significant at $p<.05$ and $p<.001$ respectively. Non-whites are less likely to be prescribed the breakthrough drug than the generic drug compared to whites ($p<.05$). As the patient's number of medication increases, the likelihood that patient will be prescribed a me-too or generic me-too drugs than a generic drug decreases ($p<.01$). In the cardioselective beta blockers class, the patient's expected source of payment is not a significant determinant of the physician's prescribing decision.

Physicians practicing in the South are more likely to prescribe me-too drugs than generic drugs compared to physicians practicing in the Northeast (p<.05).

The dissimilarity parameters τ for generic and breakthrough drugs were undefined because they are degenerate nests. The dissimilarity parameter for me-too drugs and generic me-too drugs are 0.284 and 0.216. These values are less than 1 which implies that this model is consistent with the random utility model. The likelihood ratio test for independence of irrelevant alternatives (IIA) is significant at p <.001. The hypothesis that the IIA assumption holds can be rejected which implies that the nested logit model is more appropriate than conditional or multinomial logit model.

The results of the nested logit model without the IV for alternative-specific variables are presented for comparison to the model with IV.

Table 13. Nested Logit Model Results for Alternative-Specific Variables on Prescribing Choice of Physicians for Beta Blockers

Parameters	Coef.	z	P>|z|	
Price, C	-0.044	-2.27	0.023	*
Length of time ratio, A	-0.111	-0.52	0.606	
Direct-to-consumer advertising expenditure, V	0.164	3.29	0.001	**

Unlike the effect of the IV in the statin class, the inclusion of IV in the model did not change the directionality of the coefficient for beta blockers. Price has remained negative. The results on price for both models are consistent with the hypothesis that increase in price will reduce the likelihood of a drug from being prescribed. Direct-to-consumer advertising has also remained

positive and consistent with the hypothesis of this research. As explained in the previous section, the sign of the coefficient for length of time is not consistent with the hypothesis that length of time in the market increases the likelihood of a drug from being prescribed.

1.8.3 PROTON PUMP INHIBITORS

There were no generic me-too drugs at the time the NAMCS survey was conducted in 2006. Hence, there are only three nests in the first level of the nested logit model. The following table presents the non-sequential two-tiered tree structure for the nested logit model.

Figure 4. Tree Structure Specified for the Nested Logit Model for Proton Pump Inhibitors

Type	N	Alternatives	n	k
Generic drug	1,346	omeprazole	1,346	83
Breakthrough drug	1,346	Prilosec	1,346	282
Me-too drugs	6,730	Protonix	1,346	240
		Zegerid	1,346	11
		Aciphex	1,346	100
		Nexium	1,346	376
		Prevacid	1,346	254
Total			9,422	1,346

k = number of times alternative is chosen
n = number of observations at each level

Nested Logit Model Results for Prescription Drug Class Proton Pump Inhibitors

The following table summarizes the results of the nested logit regression model for the drug class proton pump inhibitors.

Table 14. Nested Logit Model with IV Results on Prescribing Choice of Physicians for Proton Pump Inhibitors

Parameters		Coef.	z	P>|z|	
Predicted price, $\hat{C}$		0.012	3.26	0.001	**
Length of time, A		0.105	0.83	0.408	
Direct-to-consumer advertising expenditure, V		0.051	3.88	0.000	***
Drug has extended/delayed release feature		2.572	4.00	0.000	***
Generic drug (base)					
Patient characteristics					
Age x	breakthrough drug	0.013	1.57	0.117	
	me-too drugs	-0.005	-0.53	0.593	
Sex x	breakthrough drug	0.237	0.94	0.349	
(male)[a]	me-too drugs	0.143	0.61	0.541	
Race x	breakthrough drug	-0.485	-1.35	0.176	
(white)	me-too drugs	-0.547	-1.68	0.093	
Ethnicity x	breakthrough drug	0.496	0.97	0.331	
(non-hispanic)	me-too drugs	0.379	0.78	0.435	
Number of medication x	breakthrough drug	-0.088	-1.58	0.114	
	me-too drugs	-0.069	-1.35	0.176	
Patient expected source of payment (self pay)					
Private Insurance x	breakthrough drug	0.183	0.57	0.567	
	me-too drugs	0.371	1.24	0.214	
Medicare x	breakthrough drug	-0.294	-0.81	0.416	
	me-too drugs	0.031	0.09	0.925	
Medicaid x	breakthrough drug	0.691	1.61	0.107	
	me-too drugs	0.430	1.04	0.298	
Doctor characteristics					
Doctor specialization x	breakthrough drug	-0.196	-0.68	0.500	
(general practice)	me-too drugs	0.069	0.26	0.797	
Region of practice (Northeast)					

Midwest x	breakthrough drug	-0.186	-0.55	0.580	
	me-too drugs	-0.180	0.57	0.566	
South x	breakthrough drug	0.463	1.30	0.195	
	me-too drugs	0.700	2.07	0.038	*
West x	breakthrough drug	0.019	0.05	0.959	
	me-too drugs	-0.349	-1.03	0.304	
Percentage of patient care revenue from Medicare greater than 50% x	breakthrough drug	0.292	0.84	0.402	
	me-too drugs	0.390	1.21	0.228	
Percentage of patient care revenue from Medicaid greater than 50% x	breakthrough drug	0.519	0.72	0.470	
	me-too drugs	0.218	0.32	0.752	
Percentage of patient care revenue from private insurance greater than 50% x	breakthrough drug	-0.610	-1.95	0.052	
	me-too drugs	-0.378	-1.36	0.175	
Percentage of patient care revenue from self-payment greater than 50% x	breakthrough drugs	0.042	0.05	0.958	
	me-too drugs	-0.133	-0.17	0.863	
Dissimilarity parameters					
τ breakthrough drug	— [b]				
τ generic drug	— [b]				
τ me-too drugs	1.032				
Summary Statistics					
No. of cases	1,346				
Log likelihood	-2275.2117				
LR test for IIA = χ^2 (prob.)	0.03 (0.986)				

a. Reference category in parentheses

b. Degenerate nest. Parameter not defined.

*Significant at .05 level

**Significant at .01 level

***Significant at .001 level

The results of the nested logit model show that price, direct-to-consumer advertising expenditure and the extended/delayed release feature of the prescription drug are all significant determinants of physician prescribing behavior. Price, direct-to-consumer advertising expenditure and extended/delayed release feature increases the likelihood of a drug to be prescribed by a physician. These variables are significant at $p<.01$, $p<.000$ and $p<.000$, respectively. The prescription drug's length of time in the market is not a significant determinant of physician prescribing behavior in the PPI class.

None of the patient characteristics are statistically significant to influence physician prescribing behavior in the proton pump inhibitors class. With respect to physician characteristics, practicing in the South increases the likelihood of a physician to prescribe me-too drugs than the generic drug in the class compared to practicing in the Northeast ($p<.05$).

The dissimilarity parameters for τ breakthrough drug and generic drug were undefined as these are degenerate nests. The dissimilarity parameter for me-too drugs is 1.032. This value is slightly higher than 1.0 which may challenge the consistency of the nested logit model with the random utility model. But like the previous results, the model is still mathematically correct and gives well behaved probabilities between 0 and 1 and that sum to 1 (Cameron & Trivedi, 2010:515). The likelihood ratio test for independence of irrelevant alternatives (IIA) is not statistically significant indicating that the null hypothesis that the IIA assumption holds. It may indicate that conditional logit or standard multinomial logit model may work in the class of PPI.

The results of the nested logit model without the IV for alternative-specific variables for the proton pump inhibitors are presented for comparison with the nested logit model with IV:

Table 15. Nested Logit Model Results for Alternative-Specific Variables on Prescribing Choice of Physicians for Proton Pump Inhibitors

Parameters	Coef.	z	P>|z|	
Price, *C*	0.009	3.30	0.001	**
Length of time, *A*	0.141	1.01	0.310	
Direct-to-consumer advertising expenditure, *V*	0.079	5.37	0.000	***
Drug has extended/delayed release feature	3.010	4.27	0.000	***

In the case of proton pump inhibitors, the effect of the inclusion of IV in the nested logit model did not result in the change of the sign of the alternative-specific coefficients. The sign of the price coefficient remained positive and is inconsistent with the hypothesis of this study. This suggests that the IV was a weak instrument for this class of prescription drugs. The signs of other variables in both models are consistent with the hypothesis that they will increase the likelihood of being prescribed.

1.8.4 SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI)

The following figure presents the non-sequential two-tiered tree structure for SSRIs. The first level are the four nests which represent the types of prescription drugs while the second level presents the alternatives in each nest.

Figure 5. Tree Structure Specified for the Nested Logit Model of SSRI

Type	N	Alternatives	n	k
Generic drug	1,308	Fluoxetine	1,308	77
Breakthrough drug	1,308	Prozac	1,308	188
Me-too drugs	10,464	Sarafem	1,308	6
		Lexapro	1,308	333
		Paxil CR	1,308	14
		Pexeva	1,308	4
		Zoloft	1,308	319
		Paxil	1,308	168
		Celexa	1,308	123
		Prozac weekly	1,308	0
Generic me-too drugs	4,543	Sertraline	619	5
		Paroxetine	1,308	37
		Fluvoxamine	1,308	0
		Citalopram	1,308	34
Total			17,623	1,308

k = number of times alternative is chosen
n = number of observations at each level

Nested Logit Model Results for Prescription Drug Class Selective Serotonin Reuptake Inhibitors (SSRI)

Table 16. Nested Logit Model Results for Prescribing Choice of Physicians for SSRIs

Parameters		Coef.	z	P>|z|	
Predicted price, $\hat{L}$		0.044	5.05	0.000	***
Length of time ratio, A		0.393	4.79	0.000	***
Direct-to-consumer advertising expenditure, V		-0.013	-1.78	0.075	
Drug has delayed/extended release feature		-1.362	-4.46	0.000	***
Generic drug (base)					
Patient characteristics					
Age x	breakthrough drugs	-0.008	-0.99	0.321	
	me-too drugs	-0.011	-1.41	0.159	

	generic me-too drugs	-0.005	-0.49	0.622	
Sex x	breakthrough drugs	0.664	2.30	0.022	*
(male)[a]	me-too drugs	0.478	1.93	0.053	
	generic me-too drugs	-0.261	-0.80	0.421	
Race x	breakthrough drugs	0.041	0.08	0.937	
(white)	me-too drugs	0.478	1.05	0.295	
	generic me-too drugs	-0.278	-0.41	0.685	
Ethnicity x	breakthrough drugs	-1.253	-2.89	0.004	**
(non-hispanic)	me-too drugs	-0.724	-2.27	0.023	*
	generic me-too drugs	-0.475	-1.04	0.299	
Number of medication x	breakthrough drugs	0.067	1.05	0.294	
	me-too drugs	0.065	1.16	0.244	
	generic me-too drugs	0.044	0.61	0.543	
Patient expected source of payment (self pay)					
Private Insurance x	breakthrough drugs	0.423	1.19	0.235	
	me-too drugs	0.765	2.44	0.015	*
	generic me-too drugs	0.111	0.28	0.778	
Medicare x	breakthrough drugs	-0.140	-0.33	0.743	
	me-too drugs	0.382	1.04	0.300	
	generic me-too drugs	0.392	0.80	0.421	
Medicaid x	breakthrough drugs	0.541	1.27	0.203	
	me-too drugs	0.196	0.51	0.608	
	generic me-too drugs	-1.205	-2.11	0.035	*
Doctor characteristics					
Doctor specialization x	breakthrough drugs	-0.002	-0.01	0.995	
(general practice)	me-too drugs	0.278	1.04	0.298	
	generic me-too drugs	-0.319	-0.93	0.355	
Region of practice (Northeast)					
Midwest x	breakthrough drugs	-0.160	-0.44	0.661	

	me-too drugs	-0.561	-1.73	0.084	
	generic me-too drugs	-1.539	-3.31	0.001	**
South x	breakthrough drugs	1.209	2.49	0.013	*
	me-too drugs	0.994	2.18	0.029	*
	generic me-too drugs	0.497	0.94	0.345	
West x	breakthrough drugs	-0.603	-1.60	0.109	
	me-too drugs	-0.824	-2.57	0.010	*
	generic me-too drugs	-0.755	-1.83	0.067	
Percentage of patient care revenue from Medicare greater than 50% x	breakthrough drugs	-0.006	-0.01	0.989	
	me-too drugs	-0.045	-0.12	0.904	
	generic me-too drugs	-0.142	-0.30	0.764	
Percentage of patient care revenue from Medicaid greater than 50% x	breakthrough drugs	-0.760	-1.67	0.094	
	me-too drugs	-0.502	-1.33	0.182	
	generic me-too drugs	0.561	1.13	0.260	
Percentage of patient care revenue from private insurance greater than 50% x	breakthrough drugs	0.028	0.09	0.926	
	me-too drugs	-0.435	-1.63	0.104	
	generic me-too drugs	-0.766	-2.06	0.039	*
Percentage of patient care revenue from self-payment greater than 50% x	breakthrough drugs	0.546	1.05	0.295	
	me-too drugs	0.542	1.17	0.240	
	generic me-too drugs	-0.145	-0.24	0.813	

Dissimilarity parameters	
τ generic drug	— [b]
τ breakthrough drugs	— [b]
τ me-too drugs	0.602
τ generic me-too drugs	0.929
Summary Statistics	
No. of cases	1,308
Log likelihood	-2644.0724
Wald chi^2 (52)	698.18

Prob>chi^2	0.000
LR test for IIA $= \chi^2$ (prob.)	14.91 (0.001)

a. Reference category in parentheses

b. Degenerate nest. Parameter not defined.

*Significant at .05 level

**Significant at .01 level

***Significant at .001 level

Price, length of time in the market, and the delayed/extended release feature are all significant variables. An increase in the price of prescription drugs will increase the likelihood of the physician prescribing the drug (p<.001). An increase of the length of time in the market will also increase the likelihood of the drug being prescribed by the physician (p<.001). Having the delayed/extended release feature will reduce the likelihood of the physician to prescribe the drug (p<.001).

With respect to patient characteristics, physicians in the study are more likely to prescribe breakthrough drugs than generic drugs to female than male patients (p<.05). Hispanics are more likely to be prescribed generic than breakthrough or me-too drugs (p<.01, p<.05). Breakthrough and me-too drugs are both branded drugs. Physicians in this sample were more likely to prescribe me-too drugs than generic drugs to patients who are expected to pay through private insurance compared to self-pay patients (p<.05). Patients who are expected to pay through Medicaid were more likely to receive generic drugs than generic me-too drugs compared to patients who were expected to self-pay (p<.05).

Physicians practicing in the Midwest were more likely to prescribe the generic drug in the class than generic me-too drugs compared with physicians in the Northeast (p<.01). Physicians in the South were more likely to prescribe the breakthrough and me-too drugs than the generic drug compared with physicians in the Northeast (p<.05). Physicians practicing in the West are less likely to prescribe me-too drugs than the generic drug compared to physicians in the Northeast (p<.05). Physicians whose percentage of patient care revenue from private insurance is greater than 50% were more likely to prescribe the generic drug than the generic me-too drugs in the SSRI class (p<.05).

The dissimilarity parameters for τ breakthrough drug and generic drug were undefined as these are degenerate nests. The dissimilarity parameters for me-too drugs and generic me-too drugs are 0.602 and 0.929. These values are less than 1.0 which suggests that this nested logit model is consistent with the random utility model. The likelihood ratio test for independence of irrelevant alternatives (IIA) is statistically significant at (p<.01) indicating that the null hypothesis that the IIA assumption holds can be rejected. It suggests that the use of the nested logit model is appropriate.

The results of the nested logit model with the actual price variable are presented for comparison to the model with instrumental variable on price:

Table 17. Nested Logit Model Results for Alternative-Specific Variables on Prescribing Choice of Physicians for SSRIs

Parameters	Coef.	z	P>|z|	
Price, C	-0.001	-7.85	0.000	***
Length of time ratio, A	0.008	7.56	0.000	***
Direct-to-consumer advertising expenditure, V	0.001	-6.60	0.000	***
Drug has delayed/extended release feature	-0.034	-7.67	0.000	***

The results show that the instrumental variable reversed the sign of the price coefficient to the direction that is not consistent with the hypothesis of the study. While the nested logit model without the instrumental variable resulted in a negative coefficient indicating the negative relationship between price and choice of prescription drugs, the inclusion of the instrumental variable resulted in the positive relationship between price and choice of prescription drugs. The sign of the coefficient for direct-to-consumer advertising expenditure was also reversed to the direction that is also not consistent with the hypothesis of the study. In the nested logit model without the IV, direct-to-consumer advertising is statistically significant and increases the likelihood for a drug from being prescribed. In the model with IV, direct-to-consumer advertising expenditure negatively affects the likelihood of choosing a particular type of prescription drug. The delayed/extended release feature has remained negative in both models.

1.9 Summary of Findings

Based on the results of the nested logit models with IV for the four classes of drugs, price influences physician prescribing behavior. However, the relationship between price and physician

prescribing behavior is not consistent across the four classes of drugs. In the classes of statins and cardioselective beta blockers, an increase in price decreases the likelihood that a drug will be prescribed. Both were statistically significant at $p<.01$. In the case of SSRIs and PPIs, an increase in price will increase the likelihood that the drug will be prescribed. Both were also statistically significant at $p<.001$.

Older studies suggest that physicians are not price sensitive. Price is not part of the information provided by medical detailers. Physicians have very limited information on prices of prescription drugs and may not have any incentive to prescribe cheaper medicines (Caves et al., 1991). This study suggests otherwise. The findings suggest that physicians' may have some level of awareness on the price of prescription drugs. Some literature explains that there may be other factors that may make physicians sensitive to prices. Physicians may be sensitive to patients' financial situation (S. F. Ellison et al., 1997; Gönül et al., 2001). A recent study shows that physicians contacted by managed care drug companies or who are affiliated with Health Maintenance Organizations (HMO) have a greater awareness of relative prices of prescription drugs (S. F. Ellison et al., 1997:427). A positive relationship between price and demand for prescription drugs may be explained by the use of price as an indicator of quality (Gönül, Carter, Petrova, & Srinivasan, 2001; Olson, 1977; Valarie A. Zeithaml, 1988; V.A. Zeithaml, 1991). This study supports previous findings that price significantly influences physician prescribing behavior. The directionality of the relationship depends on the class of prescription drugs.

The regression results for the four classes of drugs show different relationships between the length of time in the market and the physician prescribing behavior. The results of statin and

SRRIs validate our hypothesis that an increase in the length of time in the market will increase the likelihood that a drug will be prescribed. In the case of beta blockers, an increase in the length of time in the market reduces the likelihood of a drug from being prescribed. For PPIs, the variable is not statistically significant. The difference in the results of the length of time variable maybe explained by the sensitivity of patients to the quality of drugs, which varies depending on the class of drugs. It should be recalled that the older drugs in the class are the breakthrough drugs and some me-too drugs. Generic drugs usually enter the market 15 to 20 years after the branded drugs were introduced in the market. The lingering perception that generic drugs are inferior than branded drugs may influence the preference for established branded drugs in the class of statin and SSRIs. The concerns with respect to the difference in the "bioavailability" of active ingredient between branded and generic drugs particularly for drugs with very narrow therapeutic band like SSRIs can also explain the preference for established drugs in the market.

The positive relationship between the drug's length of time in the market and physician prescribing behavior in the statins, and SSRIs is also consistent with the theory that physicians prescribing behavior was a result of customary prescribing or habit persistence (Caves et al., 1991). Not only is this explained by the limited information available about comparative effectiveness of drugs but because customary prescribing can be a very effective legal defense (Caves et al., 1991). Physicians might hesitate in switching treatment for subsequent prescriptions because of the risk associated with switching treatment especially if the original prescribed drug works for the patient (Gönül et al., 2001:81). Habit persistence in physicians' prescribing behavior can explain the persistent market shares of branded drugs (Coscelli, 2000:350-351).

In the case of cardioselective beta blockers, the negative correlation between length of time and physician preference supports the view that generic drugs are as riskier as brand name drugs. Furthermore, since most of these cardioselective betablockers are maintenance medication. Patients are expected to regularly take them in the long term. This has implication on costs. The generic drugs have been in the market for a fairly shorter period of time than the branded drugs. Preference to prescribe generic drugs is consistent with the previous finding that physicians favor cheaper drugs among cardioselective beta blockers.

In the case of PPIs, length of time in the market is not s significant determinant of physician prescribing behavior. Similar to price, the effect of the drug's length of time in the market on physician prescribing behavior depends on the class of drugs.

Other quality indicators of prescription drugs were included in the model. In the class of statins, indicators on the drug's ability to reduce the likelihood of heart attack, mortality or if it has the extended-release feature were included in the model but none of these variables were statistically significant. For the three other classes of drugs, the indicator on whether the drug has the extended-release or delayed-release feature was included. In the case of cardioselective beta blockers, the indicator was dropped because it was correlated with advertising. The only drug that spent on the direct-to-consumer advertising is also the only drug that has the extended-release feature. For proton-pump inhibitors, the delayed-release feature increases the likelihood that the drug will be prescribed. The positive relationship may support concerns of doctors about patient compliance to medication regimen or patient sensitivity to side effects associated with fluctuations in the concentration of drugs in the body system.

For SSRIs, the delayed-release/controlled-release feature reduces the likelihood that the drug will be prescribed (p<.01). Studies were mix on the superiority of extended release over regular drugs in the SSRI class. Drugs with extended-release feature maybe superior for patients with major depressive disorder but not for depressed patients with established medication. Like the other variables, the effect of this indicator on the prescribing behavior of physicians seems to be class specific.

The statistically significant positive relationship between direct-to-consumer advertising and physician prescribing behavior is consistent in the three classes of drugs – statin, cardioselective beta blockers and PPIs. This variable is not statistically significant in the class of SSRIs. An increase in direct-to-consumer advertising expenditure increases the likelihood that the prescription drug will be prescribed by a physician. The significance of direct-to-consumer advertising expenditure in the physician's choice of prescription drug may suggest that patients play a role in the selection of their prescription drugs. Information gathered by patients from direct-to-consumer advertising empowered patients to play a role in the selection of their medication. The significant effect of direct-to-consumer advertising in the prescribing behavior of physicians may also be explained by the correlation between higher levels of advertising and concentration of physician prescribing (Stern & Trajtenberg, 1998).

This research found some patient characteristics to be statistically significant in influencing physician prescribing behavior. In the case of statins, an increase in age increases the likelihood that a physician will prescribe a generic drug than a me-too drug (p<.05). Older persons tend to be prescribed generic drug than me-too drug. The same observation applies to cardioselective beta

blockers. An increase in age increases the likelihood that a person will be prescribed a generic drug than a me-too drug or generic me-too drugs. Both are significant at $p<.05$. This suggests that physicians are more likely to prescribe the generic drug to older patients. Age is not a statistically significant variable for SSRIs and PPIs.

Sex is also a statistically significant determinant of physician prescribing behavior in statins, cardioselective beta blockers and SSRIs. In the case of statins, females are less likely to be prescribed generic me-too drugs than the generic drug compared to males. The opposite is true with cardioselective beta blockers. Females are more likely to be prescribed me-too and generic me-too drugs than the generic drug compared to males. For SSRIs, females are more likely to be prescribed the breakthrough drug than the generic drug compared to males. The findings suggest that the sex of the patient is likely to influence physician prescribing behavior, depending on the class of drugs.

Race was also a significant determinant in the case of cardioselective beta blockers. Being non-white decreases the physician's likelihood of prescribing breakthrough drug than the generic drug compared to being white ($p\leq.05$). Race is not significant in the other classes of drugs. Ethnicity is statistically significant in the SSRIs. Hispanics are more likely to be prescribed a generic drug than breakthrough or me-too drugs compared to non-hispanics. Both the breakthrough and me-too drugs are branded drugs.

The patient's number of medication is a statistically significant determinant of physician prescribing behavior in statins and cardioselective beta blockers. In the statins class, an increase in the number of medication increases the probability of a physician prescribing me-too drugs relative

to the probability of prescribing generic drug. In the case of cardioselective beta blockers, an increase in the number of medication decreases the probability of the physician prescribing me-too and generic me-too drugs relative to the probability of prescribing generic drug. Again, the nature of the relationship depends on the class of drugs.

For SSRIs and statins, the patient's source of payment is also a statistically significant predictor of physician prescribing behavior. In the class of statins, Medicare as an expected source of payment increases the probability of a physician prescribing me-too drugs than generic drug compared to self-paying patients ($p<.05$). In the class of SSRIs, patients with private insurance are more likely than self-paying patients to be prescribed me-too drugs than generic drug ($p<.05$). In both statins and SSRIs, patients with Medicaid are more likely than self-paying patients to receive a generic drug prescription than generic me-too drugs prescription ($p \leq .05$).

This finding that some types of patients' source of payment are statistically significant in influencing physician prescribing behavior suggests moral hazard. The observation that patients with Medicare or private insurance are more likely than self-paying patients to receive a prescription of me-too drugs than generic drug and patients with Medicaid are more likely than self-paying patients to receive a prescription for generic drug than me-too drug is consistent with the theory of moral hazard and previous findings that patients with more generous insurance coverage tent to receive more expensive drugs. Howard's findings on moral hazard when he examined the antibacterial drug class using the 1994 NAMCS data showed that self-paying patients are significantly more likely than patients with Medicare or private insurance to be prescribed the generics (Howard, 1997).

There are some physician characteristics that are statistically significant in this study. These findings suggest that some physicians have the propensity to prescribe generic drugs while others tend to prescribe the breakthrough drug or me-too drugs, consistent with Hellerstein's findings (Hellerstein, 1994). In the case of statins, physicians with specialized practice are less likely than physicians with general practice to prescribe breakthrough drugs than generic drug ($p<.05$). This variable is not statistically significant in the other classes of drugs examined in this research.

In addition, there are regional differences in physician prescribing behavior. In the statins class, physicians who are practicing in the Midwest are less likely than physicians in the Northeast to prescribe breakthrough and me-too drugs than the generic drug ($p<.05$). Physicians in the West are more likely than physicians in the Northeast to prescribe generic drug than breakthrough, me-too and generic me-too drugs ($p<.05$). Physicians in the South are more likely than physicians in the Northeast to prescribe generic drug than me-too drugs and generic me-too drugs ($p<.05$). On the contrary, in the case of cardioselective beta blockers and PPIs, physicians who practice in the South are more likely than physicians in the Northeast to prescribe me-too than generic drugs ($p<.05$). In the case of SSRIs, physicians from the Midwest are more likely than the physicians from the Northeast to prescribe generic than generic me-too drugs ($p<.01$). Physicians from the South are more likely than patients in the northeast to prescribe branded drugs (breakthrough and me-too drugs) than generic drug ($p<.05$). Physicians from the West are more likely than physicians from the Northeast to prescribe generic drug than me-too drugs ($p<.05$). These may be explained by different state policies influencing physician prescribing behavior. However, because of limited

data, this study was not able to test that. Further studies can be done on regional/state level differences in prescribing patterns of physicians.

In proton pump inhibitors, physicians with greater than 50% patient care revenue from private insurance are more likely to prescribe the generic drug than the breakthrough drug compared to physicians with less than 50% patient care revenue from private insurance ($p<.05$). Similarly, in the SSRI class, physicians with greater than 50% patient care revenue from private insurance are more likely to prescribe the generic drug than generic me-too drugs compared to physicians with less than 50% patient care revenue from private insurance ($p<.05$). Further studies can be done in establishing the relationship between physician characteristics and the propensity to prescribe certain types of drugs.

1.10 Conclusion

This research concludes that price, direct-to–consumer adverting and certain characteristics of drugs that may indicate quality affects the likelihood of a drug to be prescribed. The effects of price, the drug's length of time in the market and the delayed/extended release feature of the drug are class specific. Sometimes, an increase in price increases the likelihood of being prescribed. In other times, it decreases. It suggests that physicians have certain level of awareness on price of drugs. An increase in drug's length of time in the market is likely to increase the prescription of the drug but in the class of proton pump inhibitors, physicians are more likely to prescribe newer drugs. In all the classes of drugs, an increase in direct-to-consumer advertising increases the likelihood that the drug will be prescribed. This supports previous findings on the

increasing role of patients in selecting their medication and the effect of advertising on the demand for prescription drugs.

Certain patient characteristics like age, sex, race, ethnicity and number of current medication influences physician prescribing behavior. The trend differs in each class. There is an indication of moral hazard when the patient's expected source of payment increases the likelihood of the patient from receiving one type of the drug over the other. More generous insurance coverage is associated with more expensive drugs.

There is also evidence that some physicians tends to prescribe one type of drug over the other. Significant physician characteristics include the region of practice, specialization and primary source of revenue. Further studies can be done to verify regional or stated differences in physician prescribing behavior taking into account the differences in state policies.

THE EFFECT OF THE ENTRY OF ME-TOO DRUGS ON THE DEMAND FOR GENERIC DRUGS

2.1 CHAPTER INTRODUCTION

The previous section presented the discrete choice analysis of physician prescribing behavior. It showed the relationship between physicians' choice of drugs and the price of drugs, direct-to-consumer advertising, drug quality, patient and physician characteristics. Most of the relationships between physician prescribing behavior and the variables examine were class specific. The results vary between classes. However, there is one relationship that is consistent in all the four classes of drugs examined in this study. Direct-to-consumer advertising increases the likelihood of a drug to be prescribed by a physician. It suggests that patients have increasing role in determining their medication. It also suggests that direct-to-consumer advertising may increase the demand for such drug. Data shows that drugs that spent heavily on direct-to-consumer marketing are me-too drugs.

In section 2, we mentioned the proliferation of me-too drugs in the pharmaceutical market. Me-too drugs are reformulated drugs which have only marginal new benefits for conditions for which treatments are already available (Shtilerman, 2006b). They are drugs that did not present significant clinical improvement and modified versions of older highly profitable drugs. Me-too drugs are further discussed in this section.

The entry of me-too drugs in the market has implications on research and development of new drugs as they tend to reduce the monopoly profit of breakthrough drugs. Me-too drugs

compete with breakthrough drugs when introduced during patent exclusivity (J. A. DiMasi, 2000; Lee, 2004; Lu & Comanor, 1998). The period of marketing exclusivity for breakthrough drugs have fallen overtime from a median of 10.2 in the 1970s to 1.2 years in the late 1990s (Joseph A. DiMasi & Paquette, 2004).

Me-too drugs also have implications on drug spending. Some me-too drugs are produced by the same company that manufactured the breakthrough drug. In some instances, they are introduced in the market when the patent of the breakthrough drug is about to end and generic versions of the breakthrough drug will soon be available in the market. It may be seen as a strategy of the pharmaceutical company to prevent patients from shifting to generic drugs, enabling the company to keep its market share and profit. However, this may result in overall increase in prescription drug spending but with little associated quality gain. The entry of new drugs in the market in the 1990s is a major driver of drug-spending growth (Danzon & Pauly, 2002). According to the Center for Medicare and Medicaid Services, spending for prescription drugs grew at an average annual rate of 14.5 percent from 1997 to 2002. About $162 billion was spent for prescription drugs in 2002. The growth of drug spending is faster than other spending on medical goods and services.

Using the regression results in the previous section, the effect of me-too drugs on the demand for the different types of prescription drugs is examined. This is done by looking at average marginal effects of price, direct-to-consumer advertising and drug's length of time in the market. The average marginal effect "measures the instantaneous rate of change" in the demand for

prescription drug with a unit change in the independent variable (price, DTC advertising and length of time in the market).

2.2 OVERVIEW: ME-TOO DRUGS

"Once the first breakthrough discovery is made of a new pharmacological activity for a new molecule, subsequent years saw the emergence of a host of new molecules or 'me-too' drugs from the same chemical class and possessing the same pharmacological profile" (Nair, 2003). Me-too drugs have similar chemical structure or mechanism of action with a drug that is already in the market which usually referred to as the breakthrough drug (Joseph A. DiMasi & Paquette, 2004). The breakthrough drug and me-too drugs are assumed to belong to the same class and may have the same therapeutic activity or class effect. Because patent is based on specific chemical structure and not on mechanism, many drugs in the market are "functionally similar"(Cook, 1998). This allowed the marketing of me-too drugs as substitute of proven drugs in the same class (Furberg & Pitt, 2001:1456-1457).

The production of me-too drugs has been part of the evolution of the pharmaceutical industry. Goozner (2010) narrated the history of me-too drugs. Immediately after Gerhard Domagk published his discovery of the anti-bacterial properties of one of his red dyes at Bayer laboratories, every drug company began creating and peddling their own version of sulfanilamide. These are the first me-too drugs (Goozner, 2004:210). The entry of other drug companies in the production of sulfanilamide resulted in intense competition driving the price of the drug to fall. Similar patterns happened in the development of the first two generation of antibiotics. The government developed the procedure to mass produce penicillin and licensed five companies to sell

the drug. These companies engaged in fierce competition. Selman Waksman discovered and patented streptomycin in the late 1940s. But since the drug was developed in a research conducted at a public university, the drug was eventually licensed broadly and sold generically even though he initially licensed the drug to Merck Research Laboratories (Goozner, 2004:211-212).

Other drug companies began scouring for new antibiotics. They patented new medicines comparable to streptomycin. The price of the new drugs soared as the pharmaceutical companies marketed them to be improved versions of the generic antibiotic predecessors, despite the fact that the new drugs were very similar in outcomes to the generic antibiotics penicillin and streptomycin (Goozner, 2004:212). The Federal Trade Commission discovered that the drug companies refused to engage in price competition and argued that competition took place in the quality of the drug – in terms of frequency of dosage and method of getting the drug into the body. This is the beginning of the me-too drugs as we know it today (Goozner, 2004:213).

In the early 1960s, a series of Congressional hearings headed by Senator Kefauver investigated the industry's penchant in spending much of its time and resources in producing me-too drugs that rarely resulted in price competition. This resulted in the 1962 amendments to the Food and Drug Act requiring drug companies to prove that their drugs were not only safe but effective. It did little though to reduce me-too drugs. From then on, the introduction of comparable or similar drugs in the market resulted in vicious marketing competition between drug companies (Goozner, 2004:214).

The Hatch-Waxman Act extended the patent of branded drugs to three years for improvements of existing products that requires additional research. This provision resulted in the

reformulations of existing products like the delayed-release and extended-release versions of already marketed drugs (Levy, 1999). The development of these drugs usually cost about one-fourth of the cost to develop new molecular entities especially if clinical trials are no longer required (Congressional Budget Office, 2006). These reformulated drugs will have longer patent life (greater than the three year extension provided by the Hatch-Waxman Act) if new patent is obtained (Reiffen & Ward, 2005a).

The early 1990s is characterized by soaring drug prices and health care cost. The industry claimed me-too drugs have fewer side effects and provide choice to some patients who responded differently to drugs (Goozner, 2004). David Kessler, then Commissioner of the FDA stated that many of the drugs approved by the FDA between 1989 and 1993 are me-too drugs. "Only a minority offered a clear clinical advantage over existing therapies" (Kessler, Rose, Temple, Schapiro, & Griffin, 1994). A report by the National Institute of Health Care Management also agrees to this observation. Although there was an increase in the number of drugs that entered the market in the 1990s, most of these drugs only provide modest innovation. They are also responsible for driving the increase in drug spending between 1995 and 2000 (National Institute of Health Care Management, 2002).

An update of the data from the U.S. Food and Drug Administration shows that from 1990 to 2006, 77% of the 1,135 drugs approved by the FDA are classified for standard review (CDER, 2004, 2007). Standard review is granted to drugs that "appears to have therapeutic qualities similar to those of one or more already marketed drugs" in contrast to priority review which is granted to drugs which present "significant improvement compared to marketed products in the treatment,

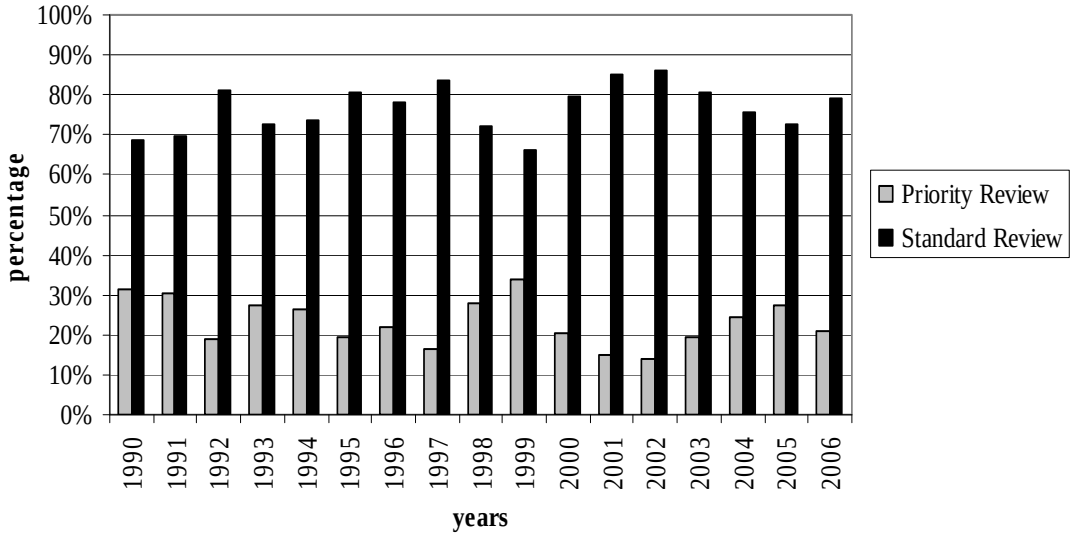
diagnosis, or prevention of a disease" (CDER, 2004). Most of the growth in new drugs seeking FDA approval between 1989 to 2000 are me-too drugs (National Institute of Health Care Management, 2002).

Table 18. FDA approved new drugs 1990-2006

Calendar Year	Priority Number Approved	Standard Number Approved
1990	20	44
1991	19	44
1992	17	74
1993	19	51
1994	16	45
1995	16	67
1996	29	102
1997	20	101
1998	25	65
1999	28	55
2000	20	78
2001	10	56
2002	11	67
2003	14	58
2004	29	90
2005	22	58
2006	21	80
TOTAL	336	1135
Percentage (%)	22.84%	77.16%

Source: US Food and Drug Administration

Figure 6. New Drug Application Approved 1990-2006



The pharmaceutical industry spent billions of dollars in researching for alternatives that will bring renewed patent life to their top selling drugs whose patents are about to expire. Forty-two of the fifty-two drugs with more than $1 billion in sales in 2000 lose their patent protection in 2007. Most of these alternatives were me-too or just copy of the original drugs intended to be marketed as "new and improved medicines" (Goozner, 2004:222). Between 1996 and 2001, the pharmaceutical companies' spending on research and development increased by 40 percent, but the number of new drugs reaching the market decreased by 50 percent (Lansbury, 2003). Almost 75% (23 out of 31) of the blockbuster drugs (those with annual sales of $1 billion or more) launched between 1992 and 2001 were me-too drugs for common conditions such as allergies and inflammation (Lansbury, 2003). There is a mismatch in the amount of investments allocated in drugs that have only marginal new benefits for conditions for which treatments are already

available and chronic and emerging diseases that present substantial social burden (Croghan & Pittman, 2004; Shtilerman, 2006a). The increase in me-too drugs is expected to continue given the financial, legal, technological and regulatory environments (National Institute of Health Care Management, 2002).

This aggressive search for me-too drugs is coupled by the rapid rise of drug companies marketing expenses. The pharmaceutical companies conduct seeding trials to entice doctors to prescribe the new product, make false and misleading claims about superiority of their products and switch campaigns (Kessler et al., 1994). Between 1996 and 2000, marketing expenses rose by 71.4 percent to $15.7 billion with direct-to-consumer advertising representing the fastest growing expense (Goozner, 2004:230). Advertisements are being used to change physicians' behavior and differentiate among products that are "virtually indistinguishable" (Kessler et al., 1994). Many of these advertisements have incomplete or misleading information about their respective products in areas which the FDA has set explicit standards of quality (Wilkes, Doblin, & Shapiro, 1992).

Me-too drugs enable pharmaceutical companies to keep their business afloat until another profitable blockbuster drug is discovered (Opderbeck, 2005:519). However, competition in the same therapeutic class means competing for the same market. Pharmaceutical companies engage in intensive marketing and advertising to expand their profit. Examining the data submitted to the Securities and Exchange Commission (SEC) by nine U.S pharmaceutical companies that market the top selling 50 drugs for seniors, Families USA concluded that:

> Eight of those companies—Merck, Pfizer, Bristol-Myers Squibb, Pharmacia, Abbott Laboratories, American Home Products, Schering-Plough, and Allergan—

> spent more than twice as much on marketing, advertising, and administration as they did on R&D. The remaining company, Eli Lilly, spent more than one and one-half times as much on marketing, advertising, and administration as it did on R&D (Families USA, 2001:3)

2.3 EFFECTS OF ME-TOO DRUGS ON PRICE, QUALITY, INNOVATION AND CHOICE

Experts have analyzed the impact of me-too drugs in three areas: price and quality of drugs in the same class, innovation in the pharmaceutical industry and consumer choice. Researches about price competition between me-too drugs and breakthrough drugs have mix results. In some cases, the average list price of branded drugs continues to increase faster than inflation after the introduction of me-too competitors (Cook, 1998; Lu & Comanor, 1998). Lu and Comanor (1998) observed that the rate of price increase is slower for drugs with brand name competitors and the introductory price of drugs tended to be lower when several me-too drugs are already in the market. Similar studies found that me-too drugs compete with breakthrough drugs and lower the price of drugs in the same class (Dao, 1984; J. A. DiMasi, 2000; Lee, 2004). On the other hand, an examination of a dozen of latest entrants introduced between 1995 and 1999 showed no price break for eight drugs and a price differential within 10 percent of the median price of existing drugs in the class for the remaining drugs (Goozner, 2004:232).

Doctors tend to prescribe customarily which may give breakthrough drugs some advantage over me-too drugs. Doctors have experience with it first and are usually hesitant to switch to new drugs unless they were proven more effective (Cook, 1998). However with aggressive advertising

(switch campaigns, seeding trials, etc.), physicians' incomplete information about the comparative price of prescription drugs and the notion that new drugs are better, enable pharmaceutical companies to sell and charge higher prices for me-too drugs (Kessler et al., 1994). Me-too drugs with small advantages over existing medication may have lower introductory price but once they become widely accepted, their prices rise rapidly (Cook, 1998; Lu & Comanor, 1998).

Me-too drugs tend to have a negative effect on innovation as pharmaceutical companies expend more energy in the advertising of me-too drugs and less on research and development of new drugs (Families USA, 2001; Hollis, 2005). Breakthrough drugs are estimated to have only one to six years of pure market exclusivity before a me-too drug enters the market (Cook, 1998). This reduces the incentive to engage in research as the potential return on investment is threatened by competition from me-too drugs.

Me-too drugs give patients and doctors options in finding a drug that works well for the individual patient (Blochl-Daum, 2006; Joseph A. DiMasi & Paquette, 2004; Furberg, Herrington, & Psaty, 1999; M. Thomas & Mann, 1998). The availability of different drugs of similar therapeutic effects may have varied side effects and efficacy profiles to different individuals. Some me-too drugs may have lesser side effects and better treatment effect to some patients (Cook, 1998). Reformulated drugs or incrementally modified drugs can result in better health of patients due to increase adherence to treatment (Congressional Budget Office, 2006). However, there is insufficient evidence that they differ in effect (Angell, 2004; Goozner, 2004; Hollis, 2005:1991; Kessler et al., 1994).

The impact of me-too drugs on the market may not be limited to the demand for breakthrough drugs. The perceived improvement of me-too drugs from breakthrough drugs, although untested, may further reduce the potential market share of generic drugs. The literature shows that the generic price discount has no significant effect in their market share (Hurwitz & Caves, 1988). Furthermore, there is a lingering perception that generic drugs are riskier than branded drugs (Fernandez-Carol & Kaitin, 1991; Ganther & Kreling, 2000; Scott Morton, 1999). When consumers have insufficient information on the intrinsic quality of the products and markets or when there is no great variance in the nature of the product across brand names, price is used as a measure of quality (Gönül et al., 2001; Olson, 1977; Valarie A. Zeithaml, 1988; V.A. Zeithaml, 1991). Physicians lack information on the effectiveness of and risks entailed by substitutable drugs that their choice is based strongly on customary prescribing which not only minimizes effort but also provides a legal defense (Caves et al., 1991:5 citing Temin 1980.) Physicians may also hesitate to switch treatment for subsequent prescriptions because of the risk associated with it especially if the original prescribed drug works for the patient (Gönül et al., 2001:81). Habit persistence in physicians' prescribing behavior can explain the persistent market shares of branded drugs (Coscelli, 2000:350-351). All these factors may play a role in favoring branded or me-too over generic drugs.

2.4 Post Estimation Analysis

The post estimation analysis using the regression results in the previous chapter are presented. The results show the effect of the changes in the significant alternative-specific predictors in the models on the demand of the other drugs in the market. The subsequent tables

show the average marginal effect of changes in price,[5] length of time in the market and direct-to-consumer advertising[6]. The average marginal effects show the change in the estimated probabilities of the different types of drugs as predictors change.

2.4.1. POST ESTIMATION ANALYSIS FOR DRUG CLASS STATIN

Predicted Probabilities

The predicted probabilities of each type of drug were computed based on the estimated nested logit model for drug class Statin. The predicted probabilities were interpreted as the market shares of generic, breakthrough, me-too and generic me-too drugs.

Table 19: Summary of Predicted Probabilities for Statin

Classification of prescription drug	Mean	Std. Dev.
Generic drug	0.062	0.044
Breakthrough drug	0.016	0.022
Me-too drug	0.892	0.069
Generic me-too drug	0.050	0.056

The results suggest that me-too drugs have the biggest predicted share of the market at 89%. The generic drug has 6.2% predicted share, the generic me-too drug has 5% predicted share and the breakthrough drug has 1.6% predicted share of the market.

[5] "Price" refers to the average cost of a month supply of the drug.
[6] "Direct-to-consumer advertising" refers to annual spending on direct-to-consumer advertising.

Marginal Effects

The average marginal effects of each of the statistically significant alternative-specific predictors (price, length of time in the market and direct-to-consumer advertising expenditure) were computed. The average marginal effects show the change in the estimated probabilities of the different types of drugs with the change in the predictors.

Table 20 shows the average marginal effects of a unit change in the price of prescription drug. A dollar increase in the price of the drug has a negative effect on the probability of the drug being prescribed and positive effect on the probabilities of the other alternatives.

Table 20. Summary of Average Marginal Effect of Change in Price for Statin

Classification of prescription drug	AME	Std. Dev.
Δ generic drug		
Generic drug	-0.001	0.000
Breakthrough drug	0.000	0.000
Me-too drug	0.001	0.000
Generic me-too drug	0.000	0.000
Δ breakthrough drug		
Generic drug	0.000	0.000
Breakthrough drug	-0.000	0.000
Me-too drug	0.000	0.000
Generic me-too drug	0.000	0.000
Δ me-too drug		
Generic drug	0.001	0.000
Breakthrough drug	0.000	0.000

Me-too drug	-0.001	0.001
Generic me-too drug	0.001	0.001
Δ generic me-too drug		
Generic drug	0.000	0.000
Breakthrough drug	0.000	0.000
Me-too drug	0.000	0.001
Generic me-too drug	-0.001	0.001

A dollar change in the price of generic drug will decrease its market share by 0.1%. This will have a minimal negative effect on the market shares of breakthrough and generic me-too drug but will increase the market share of me-too drugs by 0.1%. The effect of a dollar change in the price of me-too drug will decrease its market share by almost 0.2% and will increase of both the market shares of generic and me-too generic drugs by 0.1%.

The change in the length of time for statin has similar effect. A unit change of the length of time of the drug has been in the market will have a positive effect on the probability of the drug to be prescribed and negative effect on the probability of the other drugs to be prescribed.

Table 21.-Summary of Average Marginal Effects of Change in Length of Time for Statin

Classification of prescription drug	Mean	Std. Dev
Δ generic drug		
Generic drug	0.058	0.037
Breakthrough drug	-0.001	0.002
Me-too drug	-0.055	0.035
Generic me-too drug	-0.003	0.004
Δ breakthrough drug		

Generic drug	-0.001	0.002
Breakthrough drug	0.016	0.020
Me-too drug	-0.014	0.017
Generic me-too drug	-0.001	0.002
Δ me-too drug		
Generic drug	-0.055	0.035
Breakthrough drug	-0.014	0.017
Me-too drug	0.093	0.049
Generic me-too drug	-0.042	0.042
Δ generic me-too drug		
Generic drug	-0.002	0.003
Breakthrough drug	-0.000	0.001
Me-too drug	-0.024	0.039
Generic me-too drug	0.046	0.046

* Note that the predictor variable "length of time" is in natural log form

A 10% increase in the length of time of a generic drug will increase its market share by 0.6% and will reduce the market share of me-too drug by about 0.5%. Both breakthrough drug and generic me-too drugs predicted market share will be reduced by very small percentage. A 10% increase in the length of time in the market of the breakthrough drug will result in the increase in market share of the breakthrough drug by 0.15% and a decrease in the market share of the generic drug by 0.01%, me-too drug by .13% and generic me-too drug by 0.01%. A 10% increase in the length of time the me-too drugs are in the market will increase the market share of me-too drugs by about 0.89% and will reduce the market share of generic drugs by 0.52%, breakthrough drug by 0.13% and generic me-too drugs by 0.40%. A 10% increase of the length of time the generic me-too

drug is in the market will result in an increase in its market share by 0.44% and a decrease of about 0.02% in market share of generic drugs, 0% of breakthrough drugs and 0.23% of me-too drugs.

The next table summarizes the average marginal effects of a unit change in direct-to-consumer advertising expenditure to the probabilities of the different classification of drugs for the drug class Statin. A unit increase in direct-to-consumer advertising expenditure has positive effect on the probability of that drug from being prescribed and negative effect on the probabilities of the other alternatives.

Table 22. Summary of Average Marginal Effects of Change in Direct-to-Consumer Advertising Expenditure for Statin

Classification of prescription drug	Mean	Std. Dev
Δ generic drug		
Generic drug	0.010	0.006
Breakthrough drug	-0.000	0.000
Me-too drug	-0.009	0.006
Generic me-too drug	-0.000	0.001
Δ breakthrough drug		
Generic drug	-0.000	0.000
Breakthrough drug	0.003	0.003
Me-too drug	-0.002	0.003
Generic me-too drug	-0.000	0.000
Δ me-too drugs		
Generic drug	-0.009	0.006
Breakthrough drug	-0.002	0.003
Me-too drug	0.016	0.008
Generic me-too drug	-0.007	0.007
Δ generic me-too drugs		

Generic drug	-0.000	0.000
Breakthrough drug	-0.000	0.000
Me-too drug	-0.004	0.007
Generic me-too drug	0.008	0.008

* Note that the predictor variable "direct-to-consumer advertising" is in natural log form

A 10% increase in direct-to-consumer advertising expenditure increases the predicted market share of generic drug by 0.10% and decreases the market share of me-too drugs by 0.10%. A 10% increase in the direct-to-consumer advertising of breakthrough drug increases market share of breakthrough drug by 0.03% and decreases the market share of me-too drugs by 0.02%. A 10% increase in me-too drug's direct-to-consumer advertising results in an increase in me-too drug's market share by 0.15% and a decrease in the market shares of generic drug by 0.09%, breakthrough drug by 0.02% and the generic me-too drug by 0.07%. A 10% increase in the direct-to-consumer marketing expenditure of generic me-too drug increases the predicted market share of generic me-too drug by 0.08% and decreases the market share of me-too drug by 0.04%.

2.4.2. POST ESTIMATION ANALYSIS FOR DRUG CLASS BETA BLOCKERS

Predicted Probabilities

The estimated nested logit model for the drug class beta blockers was used to estimate the probabilities of generic, breakthrough, me-too and generic me-too drugs. The probabilities are interpreted as the predicted market shares of the drugs.

Table 23. Summary of Predicted Probabilities for Beta Blockers

Classification of prescription drug	Mean	Std. Dev.
Generic drug	0.179	0.071
Breakthrough drug	0.078	0.048
Me-too drug	0.423	0.108
Generic me-too drug	0.321	0.112

The results show that me-too drugs have a predicted market share of 42.3%. The generic drug has a predicted market share of 17.9%. The breakthrough drug has a predicted market share of 7.8% and the generic me-too drugs have a predicted market share of 32.1%.

Marginal Effects

The average marginal effects of changes in price and direct-to-consumer advertising expenditure were computed. The length of time the drug has been in the market is not a significant predictor variable in the model. Table 20 shows the average marginal effect of a unit change in the price on the market share of the drugs. An increase in price decreases the predicted market share of the drug and increases the predicted market shares of the alternative drugs in the drug class Beta Blockers.

Table 24. Summary of Average Marginal Effects (AME)of Change in Price for Beta Blockers

Classification of prescription drug	Mean	Std. Dev.
Δ generic drug		
Generic drug	-0.047	0.014
Breakthrough drug	0.005	0.004

Me-too drug	0.024	0.009
Generic me-too drug	0.018	0.008
Δ breakthrough drug		
Generic drug	0.005	0.004
Breakthrough drug	-0.023	0.012
Me-too drug	0.011	0.006
Generic me-too drug	0.008	0.004
Δ me-too drugs		
Generic drug	0.024	0.009
Breakthrough drug	0.011	0.006
Me-too drug	-0.078	0.009
Generic me-too drug	0.043	0.012
Δ generic me-too drugs		
Generic drug	0.018	0.008
Breakthrough drug	0.008	0.004
Me-too drug	0.043	0.012
Generic me-too drug	-0.069	0.011

A dollar increase in the price of the generic drug decreases the predicted market share of the generic drug by 4.7%. The biggest gainer in an increase in price of the generic drug is the me-too drug with an increase in predicted market share of 2.4%. This also increases the predicted market shares of breakthrough drug by 0.5%and generic me-too drugs by 1.8%. A dollar increase in the price of breakthrough drug decreases the predicted market share of the breakthrough drug by 2.3%. This increases the predicted market share of me-too drug by 1.1%, the generic drug by 0.5% and generic me-too drugs by 0.8%. A similar increase in the price of me-too drugs results in the decrease of me-too drug's predicted market share by 7.8%. This increases the generic drug

market share by 2.4%, breakthrough drug by 1.1% and generic me-too drug by 4.3%. A dollar increase in the price of generic me-too drugs will decrease its market share by 6.9%. This will increase the market share of the generic drug by 1.8%, the breakthrough drug by 0.8% and the me-too drug by 4.3%.

The succeeding table shows the average marginal effect of a unit change in the length of time the drug has been in the market on the predicted market shares of the respective drugs. A unit increase in the length of time a particular drug has been in the market will have a negative effect on the predicted market share of that drug and positive effects on the predicted market shares of the other drugs in the beta blockers class of drugs.

Table 25. Summary of Average Marginal Effects of Change in Length of Time for Beta Blockers

Classification of prescription drug	Mean	Std. Dev.
Δ generic drug		
Generic drug	-0.067	0.020
Breakthrough drug	0.007	0.006
Me-too drug	0.034	0.012
Generic me-too drug	0.026	0.011
Δ breakthrough drug		
Generic drug	0.007	0.006
Breakthrough drug	-0.033	0.018
Me-too drug	0.015	0.008
Generic me-too drug	0.011	0.006
Δ me-too drug		
Generic drug	0.034	0.012
Breakthrough drug	0.015	0.008
Me-too drug	-0.110	0.012

Generic me-too drug	0.061	0.016
Δ generic me-too drug		
Generic drug	0.026	0.011
Breakthrough drug	0.011	0.006
Me-too drug	0.061	0.016
Generic me-too drug	-0.097	0.015

* Note that the predictor variable "length of time in the market" is in natural log form

A 10% increase in the length of time the generic drug has been in the market will decrease its predicted market share by 0.64%. It will increase the predicted market shares of breakthrough drugs by 0.07%, me-too drugs by 0.32% and the me-too drug market share by 0.25%. A 10% increase in the length of time the breakthrough drug has been in the market will reduce its predicted market share by 0.31% and will increase the predicted market share of generic drug by 0.07%, the predicted me-too drug market share by 0.14% and the predicted generic me-too drug market share by 0.10%. A 10% increase in the length of time the me-too drug has been in the market will reduce its predicted market share by 1.05% and will increase the predicted market shares of generic drug by 0.32%, breakthrough drug by 0.14% and the generic me-too drug by 0.58%. A 10% increase in the length of time the generic me-too drug has been in the market will reduce the generic me-too drug market share by 0.92% and will increase the predicted market share of generic drug by 0.25%, the breakthrough drug by 0.10% and the me-too drug market share by 0.58%.

The next table summarizes the average marginal effects of the change in direct-to-consumer advertising expenditure of prescription drugs in the class of beta blockers. A unit change in direct-to-consumer advertising expenditure of a respective drug will have a positive effect on its predicted

market share and a negative effect on the predicted market shares of other drugs. Table 22 summarizes the results.

Table 26. Summary of the Average Marginal Effects of Change in Direct-to-Consumer Advertising Expenditure for Beta Blockers

Classification of prescription drug	Mean	Std. Dev.
Δ generic drug		
Generic drug	0.019	0.006
Breakthrough drug	-0.002	0.002
Me-too drug	-0.010	0.004
Generic me-too drug	-0.007	0.003
Δ breakthrough drug		
Generic drug	-0.002	0.002
Breakthrough drug	0.010	0.005
Me-too drug	-0.004	0.002
Generic me-too drug	-0.003	0.002
Δ me-too drugs		
Generic drug	-0.010	0.004
Breakthrough drug	-0.004	0.002
Me-too drug	0.032	0.004
Generic me-too drug	-0.018	0.005
Δ generic me-too drugs		
Generic drug	-0.007	0.003
Breakthrough drug	-0.003	0.002
Me-too drug	-0.018	0.005
Generic me-too drug	0.028	0.004

* Note that the predictor variable “direct-to-consumer advertising” is in natural log form

A 10% increase in direct-to-consumer advertising expenditure of the generic drug will result in a 0.18% increase in its predicted market share. This will also result in a slight decrease in market shares of breakthrough drug by 0.02% and the me-too drug by 0.1% and the generic me-too drug by 0.07%. A 10% increase in direct-to-consumer advertising expenditure of breakthrough drug will increase the predicted market share of the breakthrough drug by 0.10% and will decrease the predicted market shares of generic drug by 0.20%, me-too drug by 0.04% and generic me-too drug by 0.03%. A 10% increase in direct-to-consumer advertising expenditure of me-too drugs increases the market share of me-too drugs by 0.30% and decreases the market shares of generic drug by 0.1%, breakthrough drug by 0.04% and generic me-too drugs by 0.17%. Finally, a 10% increase in direct-to-consumer advertising expenditure of generic me-too drugs increases the predicted market share of generic me-too drugs by 0.27% and decreases the predicted market share of generic drug by 0.07%, breakthrough drug by 0.03% and me-too drug by 0.17%.

2.4.3. POST ESTIMATION ANALYSIS FOR DRUG CLASS PROTON PUMP INHIBITORS

Predicted Probabilities

The estimated nested logit model for the drug class proton pump inhibitors was used to estimate the probabilities for generic, breakthrough and me-too drugs. There are no generic me-too drugs in this class when the NAMCS survey was conducted in 2006. The estimated probabilities are interpreted as the predicted market shares of the drugs.

Table 27. Summary of Predicted Probabilities for Proton Pump Inhibitors

Classification of prescription drug	Mean	Std. Dev
Generic drug	0.063	0.032
Breakthrough drug	0.208	0.063
Me-too drug	0.729	0.073

The predicted probabilities show that me-too drugs have the largest predicted market share for proton pump inhibitors at 72.9%. This is followed by the breakthrough drug with a predicted market share of 20.8% and the generic drug with the predicted market share of 6.3%.

Marginal Effects

The average marginal effects of price and direct-to-consumer advertising expenditure are presented in the succeeding tables. The results show the change in the predicted probabilities of the different types of drugs with a unit change in the predictor.

The following table shows the average marginal effect of a dollar change in the price of prescription drugs. A dollar increase in the price of prescription drug increases the predicted market share of the drug and decreases the predicted market shares of the alternative drugs.

Table 28. Summary of the Average Marginal Effects of Change in Price for Proton Pump Inhibitors

Classification of prescription drug	Mean	Std. Dev
Δ generic drug		
Generic drug	0.001	0.000
Breakthrough drug	-0.000	0.000

Me-too drug	-0.001	0.000
Δ breakthrough drug		
Generic drug	-0.000	0.000
Breakthrough drug	0.002	0.000
Me-too drug	-0.002	0.000
Δ me-too drugs		
Generic drug	-0.001	0.000
Breakthrough drug	-0.002	0.000
Me-too drug	0.002	0.000

A dollar increase in price of generic drug increases the predicted market share for the generic drug by 0.1% and slightly decreases the predicted market share for the breakthrough drug and me-too drug by 0.1%. A dollar increase in the price of breakthrough drug results in an increase in the predicted market share of breakthrough drug by 0.2%. The predicted market share of me-too drug will decrease by 0.2%. A dollar increase in the price of me-too drugs will increase the predicted market share of me-too drugs by 0.2% and decrease the predicted market share of the breakthrough drug by 0.2%.

Table 25 shows the average marginal effect of a unit change in direct-to-consumer advertising expenditure. A unit increase in direct-to-consumer advertising expenditure will have a positive effect on the predicted market share of that drug and a negative effect on the predicted shares of the alternative drugs in the PPI market.

Table 29. Summary of Average Marginal Effects of Change in Direct-to-Consumer Advertising Expenditure for Proton Pump Inhibitors

Classification of prescription drug	Mean	Std. Dev
Δ generic drug		
Generic drug	0.003	0.001
Breakthrough drug	-0.001	0.000
Me-too drug	-0.002	0.001
Δ breakthrough drug		
Generic drug	-0.001	0.000
Breakthrough drug	0.008	0.002
Me-too drug	-0.007	0.002
Δ me-too drugs		
Generic drug	-0.002	0.001
Breakthrough drug	-0.008	0.002
Me-too drug	0.010	0.002

* Note that the predictor variable "length of time in the market" is in natural log form

A 10% increase in the direct-to-consumer advertising expenditure of the generic drug increases the predicted market share of that drug by 0.03%. This decreases the predicted market shares of breakthrough drug by 0.01% and the me-too drugs by 0.02%. A 10% increase in the direct-to-consumer advertising expenditure of the breakthrough drug increases its predicted market share by 0.08% and decreases the predicted market shares of generic drug by 0.01% and the me-too drug by 0.07%. Increasing the direct-to-consumer advertising expenditure of me-too drugs by 10% increases the predicted market share of me-too drugs by 0.10% and decreases the predicted market shares of generic drug by 0.02% and breakthrough drug by 0.08%.

2.4.4. POST ESTIMATION ANALYSIS FOR DRUG CLASS SELECTIVE SEROTONIN REUPTAKE INHIBITORS

Predicted Probabilities

The estimated nested logit model for the drug class SSRI was used to estimate the probabilities for generic, breakthrough, me-too and generic me-too drugs. The estimated probabilities are interpreted as the predicted market shares of the drugs.

Table 30. Summary of Predicted Probabilities for SSRIs

Classification of prescription drug	Mean	Std. Dev
Generic drug	0.062	0.049
Breakthrough drug	0.137	0.051
Me-too drug	0.736	0.079
Generic me-too drug	0.066	0.054

The predicted probabilities show that me-too drugs have the largest predicted market share for SSRI at 73.6%. The breakthrough drug has a predicted market share of 13.7%. The generic drug's predicted market share is 6.2% while the predicted market share of generic me-too drugs is 6.6%.

Marginal Effects

The average marginal effects of price and length of time in the market are presented in tables 31 & 32. Direct-to-consumer advertising expenditure is not a significant predictor of physician prescribing behavior in the PPI class. The results show the change in the predicted

probabilities of the different types of drugs with a unit change in the predictor. The following table shows the marginal effect at mean of a unit change in the price of prescription drugs. A dollar increase in the price of prescription drug increases the predicted market share of the drug and decreases the predicted market shares of the alternative drugs.

Table 31. Summary of the Average Marginal Effects of Change in Price for SSRIs

Classification of prescription drug	Mean	Std. Dev
Δ generic drug		
Generic drug	0.002	0.002
Breakthrough drug	-0.000	0.000
Me-too drug	-0.002	0.001
Generic me-too drug	-0.000	0.000
Δ breakthrough drug		
Generic drug	-0.000	0.000
Breakthrough drug	0.005	0.002
Me-too drug	-0.004	0.002
Generic me-too drug	-0.000	0.000
Δ me-too drugs		
Generic drug	-0.002	0.001
Breakthrough drug	-0.004	0.002
Me-too drug	0.008	0.002
Generic me-too drug	-0.002	0.001
Δ generic me-too drugs		
Generic drug	-0.000	0.000
Breakthrough drug	-0.000	0.000
Me-too drug	-0.002	0.001
Generic me-too drug	0.003	0.002

A dollar increase in the price of generic drug will increase its predicted market share by 0.2%. This will result in the corresponding decrease in the market share of me-too drugs by 0.2%. A unit increase in the price of breakthrough drug will result in the increase in its predicted market share by 0.5% and a decrease in the predicted market share of me-too drugs by 0.4%. A dollar increase in the price of me-too drugs will result in the increase of its predicted market share by 0.8% and a decrease in the predicted market shares of generic drug by 0.2%, breakthrough drug by 0.4% and generic me-too drugs by 0.2%. A dollar increase in the price of generic me-too drugs will result in the increase of its predicted market share by 0.3% and a decrease in the predicted market share of me-too drugs by 0.2%.

Table 32 shows the average marginal effect of a unit change in the length of time the drug was in the market. A unit change on a drug's length of time in the market has a positive effect on the predicted market share of that drug and negative effect on the predicted market shares of the alternative drugs in the market.

Table 32. Summary of the Average Marginal Effects of Change in Length of Time in the Market for SSRIs

Classification of prescription drug	Mean	Std. Dev.
Δ generic drug		
Generic drug	0.022	0.015
Breakthrough drug	-0.003	0.003
Me-too drug	-0.017	0.011
Generic me-too drug	-0.002	0.003
Δ breakthrough drug		
Generic drug	-0.003	0.003

Breakthrough drug	0.045	0.014
Me-too drug	-0.039	0.013
Generic me-too drug	-0.003	0.002
Δ me-too drugs		
Generic drug	-0.017	0.011
Breakthrough drug	-0.039	0.013
Me-too drug	0.074	0.013
Generic me-too drug	-0.018	0.013
Δ generic me-too drugs		
Generic drug	-0.002	0.003
Breakthrough drug	-0.003	0.002
Me-too drug	-0.018	0.013
Generic me-too drug	0.023	0.016

* Note that the predictor variable "length of time in the market" is in natural log form

A 10% increase in the length of time in the market of the generic drug will increase its predicted market share by 0.21% and will decrease the predicted market shares of breakthrough drug by 0.03%, me-too drugs by 0.16% and generic me-too drug by 0.02%. A 10% increase in the length of time in the market of the breakthrough drug will increase its predicted market share by 0.43% and will decrease the predicted market shares of generic drug by 0.03%, me-too drug by 0.37% and generic me-too drug by 0.03%. A 10% increase in the length of time in the market of the me-too drug will increase its predicted market share by 0.71% and will decrease the predicted market shares of generic drug by 0.16%, breakthrough drug by 0.37% and generic me-too drug by 0.17%. A 10% increase in the length of time in the market of generic me-too drug will increase its market share by 0.22% and will reduce the predicted market share of me-too drug by 0.17%, breakthrough drug by 0.03% and generic drug by 0.02%.

2.5 ANALYSIS

Me-too drugs have the largest predicted market shares in the four classes of drugs. The market share of me-too drugs is biggest in the statin class, with 89% of the market. This is followed by the predicted market share of me-too drugs in the SSRIs with 74% share. Me-too drugs are predicted to have a market share of 73% in the class of proton pump inhibitors. For the beta blockers, the market share of me-too drugs is 42%.

The breakthrough drug has the lowest market share in statin (2%) and beta blockers (8%). In the case of proton pump inhibitors, the breakthrough drug has a higher market share than the generic drug, 21% compared to 6%. Branded drugs (me-too and breakthrough drug) has around 90% of the predicted market share of proton pump inhibitors. The generic drug has a slightly higher market share than the generic me-too drugs in the statin class, 6% compared to 5%. But they have a much lower market share than the generic me-too drugs in the beta blockers class, 18% compared to 32%. Non-branded drugs (generic and generic me-too drugs) have the largest combined predicted market share in the beta blockers (50%). The predicted market shares of generic drug and generic me-too drug in SSRIs is 6% and 7% respectively. Breakthrough drug has predicted market share of 14%.

The effect of price is the same for statin and beta blockers. An increase in price decreases the market share of the drug and increases the market shares of the alternative drugs in these two classes of drugs. For statins, a dollar increase in the price of generic drug will decrease its predicted market share by 0.1% and will increase the predicted market share of me-too drugs by the same amount and vice versa. In the beta blockers, a dollar increase in the price of generic drug will

reduce its market share by 4.7% and will increase the predicted market share of me-too drugs by 2.4%, the breakthrough drug by 0.5% and the generic me-too drugs by 1.8%. A dollar increase in the price of me-too drug will decrease its market share by 7.8%. The biggest gainer in the increase in price of beta blockers are the generic me-too drugs with an increase of predicted market share by 4.3% followed by the generic drugs by 2.4% and breakthrough drug by 1.1%.s

For SSRIs and PPIs, the increase in the price of drug will have a positive effect on the predicted market share of that drug. For SSRIs, a dollar increase in the price of generic drug will result in the increase in its predicted market share by 0.2%. This will result in the decrease in the market shares of me-too drug by 0.2%. A similar increase in the price of breakthrough drugs will cause the predicted market share of breakthrough drug to increase by 0.5% and for the predicted market share of me-too drugs by 0.4%. An increase in the price of me-too drugs will cause its predicted market share to increase by 0.8% and for the breakthrough drug to decrease by 0.4%, the generic and generic me-too drugs by 0.2% each. In the case of PPIs, a dollar increase in the price of generic drug will increase the predicted share of generic drug and decrease the share of me-too drugs by 0.1%. An increase in the price of breakthrough drug will affect the market share of me-too drugs more than the generic drug and vice versa.

The length of time the drug has been in the market is not a significant determinant of demand for PPIs. The length of time the drug has been in the market has positive effects on the market share of drugs in statin and SSRI classes. The longer the drug has been in the market, the larger its predicted market share is. However, the opposite is the effect of length of time in beta blockers. The longer the drug is in the market, the less its market share is. In the statins, a 10%

increase in the length of time in the market for generic drugs will result in the increase in its predicted market share by about 0.6%. This will reduce the market share of me-too drugs by 0.5%. Similarly, an increase in the length of time in the market of breakthrough and generic me-too drugs will negatively affect the market share of me-too drugs more than the generic drugs. An increase in the me-too drugs length of time in the market will negatively affect the market share of generic drug and generic me-too drugs more than the breakthrough drug predicted market share. Similar observations can be made in the case of SSRIs except that the increase in the length of time in the market of me-too will negatively affect the predicted market share of breakthrough drugs more than the generic and generic me-too drugs.

In the case of beta blockers, an increase in the length of time in the market for generic drugs will reduce its market share and will increase the market share of the other types of drugs. Me-too drugs get the biggest increase in market share with the increase in length of time of generic, breakthrough and generic me-too drugs. An increase in me-too drugs length of time in the market reduces its market share and increases the market share of generic me-too drugs more than the increase in the market share of generic and breakthrough drugs.

Direct-to-consumer advertising is a significant determinant of predicted market share in drug classes statin, beta blockers and PPIs. It has positive effect on the predicted market share of the advertised drug and negative effect on the probabilities of the other alternatives. Increasing the direct-to-consumer advertising of generic drug will increase its market share and reduce the market shares of the other drugs. In the case of statin, a 10% increase in direct-to-consumer advertising of generic drug, breakthrough drug or the generic me-too drugs will increase its share

and will reduce the market share of me-too drug by almost same amount as the increase in share of the respective drug. If me-too drug increases its direct-to-consumer advertising by 10%, its market share will increase by 0.15%. The increase in the market share of me-too drugs will have greater negative effects on the market shares of generic and generic me-too drugs than the market share of breakthrough drug.

In the case of beta blockers, a 10% increase in the direct-to-consumer advertising expenditure of generic drug will increase its predicted market share and will reduce the predicted market share of me-too drugs more than breakthrough drugs and generic me-too drugs. Same observation can be seen when breakthrough and generic me-too drugs' direct-to-consumer advertising expenditure increases. Me-too drugs' market share is most negatively affected by the increase in advertising expenditure of the other types of drugs. If me-too drugs' direct-to-consumer advertising expenditure increases, generic me-too drugs loose more than generic and breakthrough drugs in terms of predicted market share.

Similar observations can be made with the PPI class where an increase in direct-to-consumer advertising expenditure of generic or breakthrough drug will have the most negative impact on the market share of me-too drugs. An increase in the direct-to consumer marketing of me-too drugs will increase its market share and will reduce the predicted market share of breakthrough drugs more than the decrease in market share of generic drug.

2.6 CONCLUSION

This study showed how changes in in price, length of time in the market and direct-to-consumer advertising expenditure will affect the predicted market share of the different types of drugs in the market. The effects of price and length of time in the market on predicted market shares are mixed. They depend on the drug class. However, the effect of an increase in direct-to-consumer advertising expenditure is consistent across classes. It increases the market share of the advertised drug and decreases the market shares of the other drugs. This suggests that direct-to-consumer advertising can have combative effect in the pharmaceutical industry, shifting consumer preference to the advertised products. This should be tested further, controlling for the overall industry demand.

Among these types of drugs, me-too drugs frequently engage and invest huge amount of money on direct-to-consumer advertising. In the drug classes' statins and beta blockers, an increase in direct-to-consumer advertising expenditure of me-too drugs negatively affects the predicted market shares of generic drugs (both the generic and generic me-too drugs combined) more than the breakthrough drug. In PPIs, increase in direct-to-consumer advertising of me-too drugs negatively affects the predicted market share of the breakthrough drug more than the generic drug. This section showed that the spending of me-too drugs on direct-to-consumer advertising greatly contributes in the increase in its market share. In most cases, the increase in market share of me-too drugs because of direct-to-consumer advertising negatively affects the market share of generic drugs. The effects of the changes in direct-to-consumer advertising of me-too drugs on the market share of breakthrough drugs and generic drugs support previous findings that the entry of me-too

drugs in the market reduces the incentives to conduct research of new drugs as it reduces the market exclusivity of breakthrough drugs. Me-too drugs also increase drug spending. An increase in the direct-to-consumer advertising expenditure of me-too drugs reduces the market share of generic drugs, which usually are the cheaper drugs in the market.

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