ESSAYS ON PHARMACEUTICALS AND HEALTH CARE EXPENDITURES

A Dissertation

by

ZEYNAL KARACA

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

August 2007

Major Subject: Economics

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Approved by:

Chair of Committee,	Steven N. Wiggins
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ABSTRACT

Essays on Pharmaceuticals and Health Care Expenditures. (August 2007)

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The U.S. pharmaceutical industry has been remarkably successful in developing new treatments for many of the leading causes of morbidity and mortality. These new treatments and their high prices lead government and private parties to increase spending and raise the issue of access. Price and cost increases have stimulated insurance costs, raising questions about the value of new technologies. A key way to address the increase in pharmaceutical prices is to investigate the impact of newer therapies on overall health expenditure.

There is a conflict among researchers about the benefits and costs of newer and better drugs. Some researchers argue that newer and better drugs keep people out of hospitals and provide significant cost savings. Another group of researchers argue in their work that newer drugs do not really provide significant cost savings. This dissertation investigates the impacts of break-through drug classes on overall health care expenditures. Empirical evidence presented in this dissertation shows that drugs belonging to new drug classes provide significant advances in treatment of conditions compared to other drugs. The results indicate that all new drug classes except Fluoroquinolones provide substantial cost savings on overall health care expenditures.

This dissertation also explores the relations between FDA Therapeutic Drug Classification and total health care expenditures. It offers a better methodology by incorporating both the quality and the age of the drugs to capture their effects on total health care expenditures.

It studies the impacts of the quality and the age of the drugs on the diseases of following therapeutic classes: musculoskeletal system and connective tissue, skin and subcutaneous tissue, neoplasm, mental disorders, nervous system and sense organs, circulatory system, respiratory system, digestive system, genitourinary system. The nature of therapeutic conditions coupled with their duration lead us to conclude that for some therapeutic categories newer priority drugs are preferable, for others newer standard drugs are better. The results suggest that there is no general rule to state that newer priority drugs decrease health care expenditures.

DEDICATION

To my wife, Pervin, my daughter Ezo Helin and my son Baran Ekin

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TABLE OF CONTENTS

CHAPTER Page

LIST OF TABLES

TABLE Page

CHAPTER I

INTRODUCTION

This dissertation is composed of a detailed examination of the impact of new drugs on the cost of prescriptions and on the overall cost of healthcare. The impact of new drugs and drug classes on overall healthcare expenditures is an important medical and economic question. Pharmaceutical firms spend billions of dollars developing new therapies. These therapies are typically sold at a substantial premium over older therapies and the use of these drugs is controversial. Some claim that there are few therapeutic advantages of these newer drugs and they simply drive up costs. This position has found its way into certain policies as public and private insurers restrict the inclusion of certain drugs in their formularies. Health plan and Medicare/Medicaid often restrict the use of newer therapies pointing to associated cost savings. These policies may lead to prescription cost savings, but run the risk of excluding therapies that lower total healthcare spending.

In an important paper, Lichtenberg (2001a and 2001b) shows that people taking newer drugs pay more, but experience even larger nondrug cost savings, and fewer lost work-days than people using older drugs. His results indicate that newer drugs reduce overall medical costs and improve health. Lichtenberg (2002) updates the original study by incorporating new observations from 1997 and 1998 MEPS dataset and by analyzing the sample for the entire population and for just the Medicare population. The new results support his previous findings with higher effects of drug age on medical expenditures, showing that newer drugs decrease nondrug expenditures by about seven times more than the increase in drug expenditures.

This dissertation follows the style of Journal of Health Economics.

Lichtenberg (2002) also found that the mean age of drugs used by Medicare enrollees with private prescription insurance is about 9 percent lower than the mean age of drugs used by Medicare enrollees without either private or public prescription insurance.

Duggan (2005) has criticized the argument that the "replacement of older drugs by newer drugs may lower health care spending by reducing the demand for hospitalizations and other health care services". Duggan investigates antipsychotic drugs and shows that newer antipsychotic drugs increase prescription drug expenditures by 610 percent, but do not reduce spending on other types of medical care services.

These results call into question certain of Lichtenberg's conclusions. Lichtenberg's study was subject to a number of data and computational limitations. First, to obtain precise estimates of effect of drug age on outcomes and spending for specific conditions, larger samples are required. Second, he analyzed only one indicator of drug quality: years since FDA approval. Other indicators, such as FDA evaluation of therapeutic potential were not investigated. Third, the most important, Lichtenberg assumes that all newer drugs of a similar age represent comparable improvements compared to older drugs of a similar age. That is, drug improvement is linear in time and the rate of improvement is the same across all classes. This assumption is strong and potentially could lead to biased estimation of the impact of drug age on drug and nondrug expenditures.

This dissertation addresses these issues by using an improved set of methodologies. First, we have increased the sample size by incorporating additional panels from 1999, 2000 and 2001 from Medical Expenditure Panel Surveys. Second, we added the FDA evaluation of therapeutic potential as quality measurement of the drugs. Third, the most important one is the methodological change regarding the identification of drug innovation. The available evidence

indicates that drug innovation often consists of significant breakthroughs where varied firms introduce similar new therapies that replace numerous pre-existing therapies. These new drugs are often comparable to each other even though they are introduced years apart. Further, these waves do not hit all classes. A wave of major innovation in one class may occur during a period when innovation is relatively static in another.

Our approach to measure innovation builds on these facts by examining the cost savings associated with major groups of new drugs. More specifically, between the late 1970s and early to mid-1990s, there were several widely noted breakthroughs in pharmaceutical research that led to new substantial classes of drugs. These breakthroughs included the Selective Serotonin Reuptake Inhibitors, Statins, Ace Inhibitors, H2 Antagonists, Proton Pump Inhibitors Calcium Channel Blockers, and Fluoroquinolones. These classes of drugs are important because each class represents a novel approach to therapy or a unique mode of action. Further, if newer drugs have a significant impact on medical expenditures, as suggested by Lichtenberg and challenged by Duggan (2005), then the effects ought to show up strongly for these important new classes of drugs.

The impact of the quality and the age of the drugs may differ across therapeutic conditions. For instance, drugs prescribed for infectious diseases may totally have different impacts on health care expenditures than the drugs prescribed for mental disorders. The former one is usually prescribed for the treatment of very short-term infections and patients usually end up purchasing one or two prescriptions. However, drugs prescribed for mental disorders are mostly prescribed for longer terms. We analyzed the impacts of the quality and the age of the drugs on each therapeutic class separately based on their clinical modification of the 9th edition of International Classes of Diseases prepared by United States and adopted in 1979 (ICD-9-CM).

ICD-9-CM categorizes diseases and injuries broadly into 18 categories. Availability of the data from Medical Expenditure Panel Survey (MEPS) allowed us to create unique data sets for only nine of them, namely; neoplasm, mental disorders, diseases of the nervous system and sense organs, diseases of the circulatory system, diseases of the respiratory system, diseases of the digestive system, diseases of the genitourinary system, diseases of the skin and subcutaneous tissue, and diseases of the musculoskeletal system and connective tissue.

The policy implications of this dissertation are especially crucial for Medicare and Medicaid enrollees. They have experienced firm restrictions from policymakers to have access to newer drugs due to the high cost associated with usage of new drugs. Medicaid drug access restriction programs have increased the age of prescribed drugs for Medicaid patients versus non-Medicaid patients. Since, previous researches have suggested that using newer drugs decrease the overall spending on health care use and morbidity and mortality rates, this restriction can make Medicaid beneficiaries worse off.

The remaining of the dissertation is as follows: Chapter II reviews the literature review. Chapter III presents the study regarding the impacts of breakthrough drug classes on health care expenditures. Chapter IV presents the FDA Drug Evaluations and health care expenditures and Chapter V conclude the remarks.

CHAPTER II

LITERATURE REVIEW

This dissertation explores the main waves of pharmacoeconomics and health economics. This dissertation is connected to the existing literature in three broad categories. The first category regards to the impact of newer drugs on overall health care expenditures. The second category relates our work to the access of Medicaid and Medicare enrollees to newer, expensive drugs. The last category of this dissertation in existing literature is related to the analysis of FDA drug approval and therapeutic classification.

II.1. Literature on Cost and Benefit of Newer Drugs

Spending on prescription drugs in the United States from 1996 to 2001 grew at a 15% annual rate, accounting for more than 10% of all health care expenditures. This growth was mainly driven by an increase in the average price of a prescription, which rose by more than 10% per year from 1996 to 2001 (Berndt, 2000). Price increases were caused both by an increase in the price of existing drugs and by a shift to newly approved drugs, which tend to be more expensive than the drugs that preceded them in the same therapeutic category.

Determining how optimally to respond to the growth in prescription drug spending is a highly sophisticated problem. It will be very hard to capture the effects of severity of conditions, the interaction among the conditions, the prescription behavior of doctors and the behavior of insurance providers in regards to payments simultaneously. It will be very hard to remove the adverse selection and moral hazard impacts while determining the optimal response of patients and/or institutions to the growth in prescription drug expenditures.

Recent researchers have noted, the difference between two drug prices may not accurately reflect the difference in health care spending that would result if a patient were to choose one treatment over another (Lichtenberg 1996, 2001a, 2001b and 2002). A more expensive drug may deliver health benefits that reduce the patient's demand for other health care services, to some extent offsetting its higher price. A similar offset effect could occur for individuals who otherwise would take no treatment. Even with no offset effect, a more expensive treatment may deliver health or quality of life benefits that are sufficiently large to pass a cost–benefit test. In measuring the value of any drug treatment, one would like to know its effect on both spending and health, with these effects potentially varying across individuals. The results of Lichtenberg (1996) show that the number of hospital bed-days decreased most rapidly for those diagnoses with the greatest increase in the total number of drugs prescribed and the biggest change in the distribution of the drugs.

Lichtenberg (2001a and 2001b) investigates the new drugs and measures the effect of new drug treatment on both spending and health utilization indicator, with these effects potentially varying across individuals. In his paper, he has analyzed prescribed medicine event-level data from the 1996 Medical Expenditure Panel Survey (MEPS), which provide evidence about the effect of drug age on mortality, morbidity and total medical expenditures. His results indicate that people consuming new drugs had significantly fewer hospital stays than people consuming the old drugs. The increase in expenditures because of using new drugs is around $18 per prescription while the reduction in total nondrug expenditures, $70 per prescription, is much larger than increase in new drug prices. The empirical results of this study indicate that people taking newer drugs are likely to have significantly lower medical expenditures and fewer work-loss days than people who are consuming the old drugs.

Lichtenberg (2002) has updated the previous study by incorporating the extra observations from 1997 and 1998 MEPS and by analyzing the sample for the entire population and for Medicare population. He used the medical condition as unit of analysis rather than a prescription in this updated version of the paper. The new results are stronger than the existing ones. Additionally, the results in this paper show that Medicare enrollees with private prescription insurance use newer drugs more than Medicare enrollees without either private or public prescription insurance. The age of the drugs in the former group is 8.6% lower than in the latter group. A reduction in the age of drugs decreases nondrug expenditures around seven times higher than increase in drug expenditures. Two-third of the decrease in total nondrug expenditures comes from hospital costs.

The introduction of new drugs has increased society's ability to produce goods and services by increasing the number of hours worked per member of the working-age population. Lichtenberg (2005) shows that under very conservative assumptions, the value of the increase in ability to work attributable to new drugs is 2.5 times as great as expenditure on new drugs. This suggests that the potential of drugs to increase employee productivity should be considered in the design of drug-reimbursement policies. Conversely, policies that broadly reduce the development and utilization of new drugs may ultimately reduce our ability to produce other goods and services.

Advances in medical care have led to sustained increases in medical spending over time. An evaluation of whether increased medical spending is useful requires the valuation of the increase in care. The enormous growth in spending has led many to argue that the increasing costs are excessive. Others, however, suggest that spending more may provide good value, whether measured in costs per year of life gained or in overall measures of economic benefit.

The vast literature on the cost-effectiveness of specific medical treatments and other interventions suggests that many medical treatments provide reasonable value. However, there has been comparatively little effort to understand the value of the medical system as a whole: Is the increase in spending by more than a factor of eight worth it? Cutler et al. (2006) addressed this question by examining how medical spending has translated into medical gain in survivals. They analyzed the value of medical spending in the United States from 1960 to 2000. They compared the adjusted increases in life expectancy with the lifetime cost of medical care in the same years. Their results show that the life expectancy for newborns increased by 6.97 years from 1960 through 2000. They pointed out that, on average, the increases in medical spending since 1960 have provided reasonable value. However, the spending increases in medical care for the elderly since 1980 are associated with a high cost per year of life gained. They concluded that the national focus on the rise in medical spending should be balanced by attention to the health benefits of this increased spending.

The potential role of new drugs in reducing expenditures for nondrug health services has also received considerable attention in recent policy debates. Miller, Moeller and Stafford (2005) studied the patterns of use and association with nondrug health expenditures for new cardiovascular drugs. They estimate expenditure models to determine whether the use of newer drugs to treat cardiovascular conditions is of associated with lower (or higher) nondrug expenditures for these conditions. They fail to confirm the findings of previous research that newer drugs are associated with reductions in nondrug expenditures. They find, however, that increases in the number of drugs used, or the mix of drugs of different ages, are associated with increased nondrug expenditures and find that the number or mix of drugs used are important confounders in the estimated association between drug age and nondrug expenditures.

Duggan (2005) has criticized the argument that the "replacement of older drugs by newer drugs may lower health care spending by reducing the demand for hospitalizations and other health care services". Duggan investigates antipsychotic drugs and shows that newer antipsychotic drugs increase prescription drug expenditures by 610 percent, but do not reduce spending on other types of medical care services. The results presented in this paper generalize to other categories of prescription drugs or to individuals with other types of health insurance is of course not obvious. The paper points out that the incentives for Medicaid recipients are not much different from those that exist in many private insurance plans, which often have small co-pay that may differ slightly between brand and generic drugs. Besides, antipsychotics are very different from the typical drug category given that Medicaid accounts for the vast majority of spending on the drugs. The author concludes that Medicaid's experience with antipsychotics during the last decade may shed some light on what can occur when the government becomes the dominant purchaser for one category of prescription drugs.

II.2. Literature on Prescription Drug Cost Sharing

Prescription drug expenditures are one of the fastest growing components of national health expenditures. To control prescription drug costs, health plans and employers have increased prescription drug cost-sharing amounts for patients. Gibson, Ozminkowski and Goetzel (2005) analyzed the effects of prescription drug cost sharing. They analyzed patients respond to increased cost sharing by substituting less expensive alternatives for medications with higher levels of co-payments or coinsurance, and examined the body of evidence on the relationships between cost sharing and use of essential or maintenance medications, health outcomes, process-of-cue measures (such as medication adherence and discontinuation), and costs. They used healthcare reference databases and key journals to identify peer-reviewed empirical studies that

examined the effects of variation in the amount of prescription drug co-payments or coinsurance on healthcare utilization patterns. Their results show that higher levels of prescription drug cost sharing generally produce intended effects, namely, decreasing the consumption of prescription drugs and steering patients away from nonpreferred to preferred brand-name drugs. However, patients do not always switch to generic drugs. Although not consistently reported, the most troublesome effects associated with higher levels of cost sharing are treatment disruptions (such as lower levels of treatment adherence, continuation, and initiation) for chronically ill patients. At times, higher levels of cost sharing can affect the use of essential, medications and outcomes of care. They conclude that cost sharing reduces the consumption of prescription drugs but may have unintended effects on the process and outcomes of therapy.

Many managed care organization use some managerial mechanism to increase drug utilization and decrease its associated cost. Some efforts have focused on monitoring clinical conditions, drug use, and compliance, whereas other efforts have focused on consumer cost sharing and changing product-mix. Efforts focusing on improving quality of care by identifying untreated patients or by enhancing compliance can lead to appropriately increased drug costs, although perhaps with reduced overall medical expenditures (Fendrick et al., 2001). In contrast, the mechanisms implemented to constrain drug costs have raised concerns regarding missed opportunities to enhance clinical outcomes, and the possibility of higher medical expenditures. To balance the demands for access to pharmaceuticals with pressures to constrain costs, levels of cost sharing could be set in a manner that achieves appropriate clinical and financial outcomes. Modern multitier systems often base patient contributions on drug acquisition cost, and often do not consider medical necessity as a coverage criterion. Fendrick et al. (2001) have also used the benefit-based copay approach and determined that patient contributions are based on the

potential for clinical benefit, taking into consideration the patient's clinical condition. For any given drug, patients with a high potential benefit would have lower copays than patients with a low potential benefit. Implementation of such a system would provide a financial incentive for individuals to prioritize their out-of-pocket drug expenditures based on the value of their medications, not their price.

Trends in drug spending over time closely paralleled the growth in drug coverage. Danzon and Pauly (2001) examines the contribution of insurance coverage to the recent growth in spending on pharmaceuticals. The authors find that most of the coverage growth reflects an increase in the number of people with coverage, 65 percent from 1987 to 1996, rather than increased depth of coverage. The direct moral hazard effect of this insurance growth accounts for between one-fourth and one-half of the increase in drug spending. The authors also point out that technological improvements contributed to these changes, because both the flow of new drugs increased the demand for insurance and information technologies enabled the development of pharmacy benefit management, which reduced the real price of drug coverage.

II.3. Literature on Access to Newer Therapies

The economic and human impact of new drugs is an important issue for both public and private policymakers. The benefits of new drugs to society exceed their cost by a substantial margin. These benefits include net decrease in overall medical expenditures, reduced limitations on work and other activities contributing to quality of life, and increased longevity. Further, new drugs contribute to health and economic growth in the United States. Formularies, to the extent that they restrict drug choices, restrict access to new drugs (Lichtenberg, 2003).

Majority of Medicaid and Medicare enrollees experience some restrictions on their prescription medication use because of associated higher costs. Heisler et al. (2004) analyzed

data from two prospective cohort studies of adults who reported regularly taking prescription medications using two waves of the Health and Retirement Study, a national survey of adults aged 51 to 61 in 1992, and the Asset and Health Dynamics Among the Oldest Old Study, a national survey of adults aged 70 or older in 1993. They assessed the independent effect on health outcomes over two to three years of follow up of reporting in 1995-1996 having taken less medicine than prescribed because of cost during the prior two years. After adjusting for differences in socio demographic characteristics, health status, alcohol consumption, smoking, body mass index (BMI), and comorbid chronic conditions, they determined the risk of a significant decline in overall health among respondents in good to excellent health at baseline and of developing new disease-related adverse outcomes among respondents with cardiovascular disease, diabetes, arthritis, and depression. Their results show that 32.1% of those who had restricted medications because of cost reported a significant decline in their health status compared with 21.2% of those who had not. An important outcome of this study shows that cost-related medication restriction among middle-aged and elderly Americans is associated with an increased risk of a subsequent decline in their self-reported health status, and among those with preexisting cardiovascular disease with higher rates of angina and nonfatal heart attacks or strokes.

Increase in pharmacy costs and demand for prescription drug coverage for broader populations of seniors have resulted in the implementation of generic-only pharmacy benefits in Medicare health maintenance organizations (HMOs). Christian-Herman, Emons and George (2004) studied the effects of generic-only drug coverage in a Medicare HMO. The impact on cost and quality of care is unknown. They examined data for members of a California Medicare HMO whose coverage changed to a generic-only benefit and found that the change was associated with

reduced health plan pharmacy cost, increased out-of-pocket pharmacy costs for members, increased overall hospital admissions, changed drug-use patterns, and a negative impact on quality metrics for certain conditions. Banthin and Miller (2006) analyzed recent trends in Medicaid prescription drug expenditures by therapeutic classes and subclasses. They identified the fastest growing categories of drugs, where drugs are grouped into clinically relevant classes and subclasses. They used data from the Medical Expenditure Panel Survey linked to a prescription drug therapeutic classification system, to examine trends between 1996/1997 and 2001/2002 in utilization and expenditures for the noninstitutionalized Medicaid population. They found rapid growth in expenditures for antidepressants, antipsychotics, antihyperlipidemics, antidiabetic agents, antihistamines, COX-2 inhibitors, and proton pump inhibitors. Their results point that Medicaid programs may want to reassess their cost-containment policies in light of the rapid take-up of new drugs.

Murawski and Abdelgawad (2005) explore of the impact of preferred drug lists on hospital and physician visits and the costs to Medicaid. They conduct an exploratory investigation of the possible effects of the implementation of a state Medicaid preferred drug list on the average number of visits by Medicaid patients to hospitals and physicians, and to provide preliminary estimates of the Medicaid reimbursement costs of these additional visits. They design a regression-based, difference-in-differences retrospective analysis using anonymized patient-level data on cardiovascular-related inpatient and outpatient hospital visits and procedures, and physician visits and procedures. The empirical results indicate that there is a statistically significant increase in the number of outpatient hospital visits and physician visits for the test group compared with the control group in the first 6 months after preferred drug list implementation. The results also show that there is a positive but statistically insignificant

increase in the number of inpatient hospital visits. All increases in visits for the test group compared with the control group in the second 6 months after preferred drug list implementation were positive but statistically insignificant. As a result, estimated average Medicaid reimbursement costs for cardiovascular patients in the state increased during that year. The authors state that the observed range of increases in hospital and physician visits is evidence for the possible existence of an unintended consequence of preferred drug list implementation by state Medicaid programs.

Recently, some policymakers questioned the Medicare policy in regard to prescription drug coverage. In late 2003, US Congress passed the new law and approved Medicare Prescription Drug Improvement and Modernization Act (MMA), which provides universally available prescription drug benefits to elderly and disabled Medicare beneficiaries for the first time. Frencher and Glied (2006) discusses the form of the prescription drug benefit package, the use of competing private plans and the uncertainty about the future cost of the new prescription drug benefit. The paper then evaluates the implications for academic medicine of the prescription drug benefit and other MMA legislative provisions aimed at improving the quality of medical practice and shifting away from acute care. The authors find that the health of seniors and the efficient use of public funds in the new prescription drug benefit depend centrally on the prescribing practices of physicians. Academic medicine should turn its attention to training the next generation of physicians to be more effective agents and advocates for their patients in their use of pharmaceuticals.

Pauly (2004) studied Medicare drug coverage and moral hazard. This paper explores the effect of more extensive drug coverage in Medicare on the use of and spending for prescription drugs and considers whether any additional use is likely to represent satisfaction of previously

unmet needs or whether it represents yet more overuse. Reasonable estimates of the effect on spending strongly suggest that the spending increase will be small and that some of it will go to beneficiaries who do not face high financial barriers at present. Thus, from the viewpoint of improvements in health, national spending on drugs, or pharmaceutical firm revenues, effects is small. The effects of such programs on Medicare's fiscal future are much more important.

The access to new treatments and health care may differ across different demographic groups. Few studies address racial and ethnic disparities in essential new drug use and whether disparities decrease through time. Wang et al. (2006) studied the disparities in access to essential new prescription drugs between Hispanic whites, non-hispanic whites and non-Hispanic blacks. The paper examined racial and ethnic disparities separately by comparing respectively non-Hispanic whites to non-Hispanic blacks and Hispanic whites using the Medical Expenditure Panel Survey (1996-2001). New drugs were defined as approved within the past 5 years, and an expert panel identified essential drugs. They stated that disparities exist in new, essential drug acquisition between non-Hispanic whites and non-Hispanic blacks and they contribute this outcome to socioeconomic and health characteristics of the population.

Headen and Masia (2005) also studied the Medicaid restrictions to the novel drugs by quantifying its affects on physician location and health disparities. Their results suggest that non-white residents are more likely to be affected than the white residents living in a zip code where Medicaid prescribing rules affect the drug choice of physicians.

The patterns of pharmaceutical consumption may also differ across groups based on their characteristics such as age, sex, socioeconomic status, and region of residence. Metge et al**.** (1999) made a population-based analysis to explore the pattern of the population’s use of pharmaceuticals. The study also includes an examination of whether pharmaceutical use is

responsive to differential health needs across the population. The results show that there is a greater number of prescriptions are dispensed in areas where health is generally poorer. The highest use of pharmaceuticals also was found in the lower-income quintiles and among those at greatest socioeconomic risk, traditionally those with the poorest health status.

II.4. Literature on FDA Therapeutic Classification and Quality Measurement

The dual roles of pharmaceutical industry as a manufacturer of health inputs and producer of health services has led to extreme scrutiny by patients and by both legislative and executive branches of federal government (Comanor and Schweitzer 1994). Moreover, the demand for pharmaceutical products is both patient-driven and generated from the decision of others, such as physicians and insurers. This makes it clear that pharmaceutical industry is unique in many ways and the peculiar nature of industry creates particular dilemma in public policy.

The United States has a widely respected but stringent review process overseen by Federal Drug Administration (FDA). The FDA sets out guidelines for basic research and animal testing that must be met before human tests begin. Once humans' tests are allowed, they take place in progressively larger phases to observe dangerous side effects before the product has been distributed to the market. Once FDA approved the new drugs, they label them based on their quality and therapeutic advances. In late 1975 the Federal Drug Administration (FDA) formed a 3-tier rating system for prioritizing review of New Drug Applications (NDA). If the drug provided a significant gain over existing therapy, FDA classified that drug with an A rating, if the drug brought a modest gain then that drug was given a B rating and if drug provided little or no gain over existing therapy, then it was given C rating. In 1992 the FDA switched its rating system into two categories: P (priority) and S (standard). A priority drug would provide a

significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease.

The quality of the drugs is important and has significant impacts on morbidity and mortality. People using newer, or later vintage drugs will be in better health, and will therefore be less likely to be admitted to hospitals and nursing homes, by examining the effect of pharmaceutical innovation on the utilization of hospital and long-term care by elderly Americans during 1997-2003 (Lichtenberg, 2006). That implies that the states that have larger increases in drug vintage will have smaller increases in the number of hospital discharges per elderly individual.

Majority of the new drugs have therapeutic advances over the existing drugs. Pharmaceutical firms set prices for new drugs that provide important therapeutic advances couple of times higher than the existing drugs that are used for the similar therapeutic conditions. If the new drugs provide little improvements or replicate the existing drugs, then they are priced relatively at the range of existing drugs prescribed for the similar therapeutic conditions. In addition, the number of branded drugs has negative impact on launch prices of new drugs that suggest the pressure of competition in that therapeutic field. The empirical findings suggest that both the introductory price and subsequent price increases are lower when there are more branded substitutes in the market (Lu and Comaner, 1998). The pricing regime for new drugs may also depend upon whether the drug is generic or branded. Wiggins and Manes (2004) focused on one segment of the pharmaceutical industry, anti-infective, and they discovered a significant drop in the prices of branded drugs following the entry of generic drugs.

The Food and Drug Administration has accelerated the approval of therapeutically novel drugs so that patients have faster access to innovative drug therapies. Little research, however,

has examined the variation in risks among therapeutically novel and less novel drugs. Olson (2004) examined the variation in risks among therapeutically novel and less novel drugs. This paper uses post-marketing drug safety surveillance data from the FDA to examine the adverse drug reactions associated with novel and less novel drugs. She examined the impact of a drug's FDA novelty rating on its number of adverse drug reactions controlling for differences in drug utilization, the conditions being treated, disease characteristics, patient characteristics, drug review times, and year-specific effects. The results show that drugs deemed novel by the FDA are associated with a greater number of serious drug reactions, including those that result in hospitalization and death, than less novel drugs. These results suggest that novel drugs pose greater risk of serious adverse drug reactions for patients relative to less novel drugs.

The approval of new drugs by FDA involves a balancing of two conflicting objectives: assuring the population access to the latest therapeutic agents available while protecting patients from the risk of dangerous products (Schweitzer, 1997). 1962 regulation by FDA has decreased the number of new chemical entities (NCE) and increase the real level of R&D expenditures. Unlike 1938 amendments, which was basically asking for safety, the new 1962 regulation bring a lot of burden on pharmaceutical firms. Many small firms either stop or seize their R&D expenditures, because it is too costly. On the other hand, big firms have enjoyed this new regulation. Big firms have the motivation to decrease the dissatisfaction of physicians by increasing safety and effectiveness of the new drugs. Clinical testing, especially for serious diseases such as heart diseases, will be crucial for the drugs and it will increase its market power once the clinical tests have been performed successfully. Increasing market size and technological innovations coupled with physician satisfaction and clinical testing for safety and efficacy motivate big pharmaceutical firms to perform FDA regulation. Once they have

completed the sequence, they will entertain a monopoly power on that drug and the sales of that new drug will also increase due to its effectiveness and safety. Hence, big firms profit will increase with a cost of having small number of NCEs and less number of small firms remaining. Thomas (1990) has focused on productivity effects of FDA regulation and finds out that for larger US firms, any declines in NCE introduction rate after 1962 were more than offset by increases in the sales of each NCE. Many small firms have seizes R&D activities hence unlike big firms they have suffered from FDA regulations.

The FDA is recognized as one of the world's most important sources of customer protection information regarding safety and efficacy of new drugs. This highly stringent regulation strictly increased the cost of developing new drugs (Wiggins, 1987 and DiMasi et al., 2003). However, the FDA offered pharmaceutical firms to exercise a monopoly power through patent protection of newer drugs. Caves, Whinston and Hurwitz (1991) investigated the patterns of competition surrounding patent expiration and subsequent generic entry in pharmaceutical markets. The paper discusses the structure of the market and deeply analyzes the demand and supply side influences of the market. Then, decision variables of innovators, which are basically price and sales-promotion outlays have been examined. A descriptive analysis of their data set reveals that generics that enter a given drug market do not enter immediately after the patent expiration date, but rather flow into market over time. One of the main reasons for this delay is the approval time to enter the market. Another interesting fact gathered from data is the change in rate of entry in the last three years that coincides with the Waxman-Hatch Act. Data shows that there is an increase in the number of entrants after patent expiration for first eight years and then there is a cumulative decline starts. They have found that the innovator's price decline with the number of generic entrants, but the rate of decline is smaller than generic drug prices.

Therefore they have concluded that price is an important decision variable for the innovators. Besides price, the second important decision variable is the level of sales-promotion outlays. Though innovators' promotional patterns are complex, however, both anticipated and actual entrance of generic drugs reduce the amount of promotional activities of branded drugs. They have also found that the branded drug price reduction is larger, the generic price discount is smaller and the market share of branded drugs decreases more in hospital than in the pharmacy segment of the market. This paper also points out the importance of product differentiation in this market. Branded producer does accumulate loyalty-inducing goodwill during the period of patent protection, which forces generic producers to have product differentiation. The advantage of branded drugs over generic drugs is mainly coming from the doctor's habitual use of it, which have been established through branded producers' informative and persuasive sales promotion activities. Finally, they have found that there is very little evidence of active attempt by branded producers to prevent entry of generic drugs into the market.

Safety, efficacy and acceptability of pharmaceuticals usually generate consumption externality. Strong consumption externalities may lead a specific drug, which is not necessarily the most safest or efficacious to dominate the market. One way of its diffusion is through word-of-mouth. As more people use the product, word-of-mouth advertising increases and hence increases the product sales. Consumption externality may positively affect the share of a specific brand and hence may have indirect effects on research and development expenditures of pharmaceutical firms (Berndt, Pindyck and Azoulay, 2003). If the product diffusion rate is positively related to the number of its users, then it would be rational for the firm to bring that product into market and taste the advantage of being first-mover. That requires that pharmaceutical firm put significant budget shares in R&D. However, when the consumption

externality occurs at the therapeutic class level, they can create second-mover advantage that is the later entrants free-ride on the information and awareness generated by the innovator firms and put more quality, such decreasing the side effects or dosage, into that generic drugs and than market the product. If the effect of latter is higher than first-mover, then entrant enjoys much higher profit and market share than the innovators. For example, Zantac came to the market much later than Tagamet but it has achieved a much higher sales and market shares in a few years.

Giaccotto, Santerre, and Vernon (2005) also studied the drug prices and research and development investment behavior in the pharmaceutical industry. This paper argues theoretically and shows empirically that pharmaceutical research and development spending increases with real drug prices, after holding constant other determinants of research and development. They find that a 10 percent increase in the growth of real drug prices is associated with nearly a 6 percent increase in the growth of research and development intensity. Their results also suggest that a drug price control regime would have resulted in 330 - 365 fewer new drugs, representing over one-third of all actual new drug launches brought to the global market during 1980 to 2001.

CHAPTER III

THE IMPACTS OF BREAK-THROUGH DRUG CLASSES ON TOTAL HEALTH EXPENDITURES

This chapter contributes to the growing literature regarding the impact of new drugs on medical costs. Using age as a measure of drug quality, Lichtenberg (2001a, 2001b and 2002) concludes that newer drugs cost more, but their use reduces nondrug expenditures by more than the increase in drug costs. Duggan (2005) finds in contrast that newer antipsychotics do not result in substantial cost savings. Our analysis contributes to this literature by examining six different groups of breakthrough drugs, Selective Serotonin Reuptake Inhibitors, Statins, Ace Inhibitors, H2 Antagonists, Proton Pump Inhibitors, Calcium Channel Blockers, and Fluoroquinolones. All drug classes except Fluoroquinolones provide substantial cost savings on overall health care expenditures.

III.1. Introduction

The impact of new drugs and drug classes on overall healthcare expenditures is an important medical and economic question. Pharmaceutical firms spend billions of dollars developing new therapies, which are often sold at a substantial premium over older therapies. The use of these newer and more expensive drugs, however, is controversial. Health plans, Medicare, and Medicaid often restrict the use of newer therapies due to cost considerations. These policies may reduce pharmaceutical costs, but run the risk of excluding valuable therapies that can lower overall healthcare spending, reduce morbidity, lost schooling and work, and hospital stays. Others argue that newer therapies cost more and there are few differences between their therapeutic effects as compared to older, cheaper therapies.

In an important paper, Lichtenberg (2001a) shows that people taking newer drugs pay more, but experience even larger nondrug cost savings and experience fewer lost work-days than people using older drugs. His results indicate that newer drugs reduce overall medical costs and improve health. Lichtenberg (2002) updates the original study by incorporating new observations from the 1997 and 1998 MEPS datasets and by analyzing the sample for the entire population and for just the Medicare population. The new results parallel his previous findings, but the effect of drug age on medical expenditures is found to be even higher, showing that newer drugs decrease nondrug expenditures by about seven times more than the increase in drug expenditures. Lichtenberg (2002) also found that the mean age of drugs used by Medicare enrollees with private prescription insurance is about 9 percent lower than the mean age of drugs used by Medicare enrollees without either private or public prescription insurance.

Duggan (2005) has criticized the argument that the "replacement of older drugs by newer drugs may lower health care spending by reducing the demand for hospitalizations and other health care services." Duggan investigates antipsychotic drugs and shows that newer antipsychotic drugs increase prescription drug expenditures by 610 percent but do not reduce spending on other types of medical care services.

These results call into question certain of Lichtenberg's conclusions. Most important, Duggan shows that, at least for antipsychotics, the use of new drugs does not appear to be linked to reduced health care expenditures. This conclusion raises questions about Lichtenberg's methodology. In particular, Lichtenberg assumes that all newer drugs of a similar age represent comparable improvements compared to older drugs of a similar age. That is, drug improvement is linear in time and the rate of improvement is the same across all classes. This assumption is strong and could potentially lead to biased estimation of the cost impact of drug innovation.

More generally, the Duggan results raise the question of whether newer drugs generally reduce nondrug expenditures, as found by Lichtenberg, or whether such reductions occur in only certain therapeutic classes.

This chapter addresses these issues by using an improved set of methodologies. The most important methodological change regards the identification of drug innovation. In contrast to Lichtenberg's assumption that the pace of innovation is constant across time and therapeutic classes, the available evidence indicates that drug innovation often consists of significant breakthroughs. When a breakthrough occurs, varied firms introduce similar new therapies that replace numerous pre-existing therapies. These new drugs are often comparable to each other even though they may be introduced years apart. Further, these waves do not hit all classes at the same time. A wave of major innovation in one class may occur during a period when innovation is relatively slow in another.

Our approach to measuring innovation builds on these facts by examining the cost savings associated with major groups of new drugs. More specifically, between the late 1970s and early to mid-1990s, there were several widely noted breakthroughs in pharmaceutical research that led to substantial new classes of drugs. These breakthroughs included the Selective Serotonin Reuptake Inhibitors, Statins, Ace Inhibitors, H2 Antagonists, Proton Pump Inhibitors, Calcium Channel Blockers, and Fluoroquinolones.[1] These classes of drugs are important because each class represents a novel approach to therapy or a unique mode of action. Further, if newer drugs have a significant impact on medical expenditures, as suggested by Lichtenberg and

[1] Table 1 presents further details about each new drug class.

challenged by Duggan (2005), then the effects ought to show up strongly for these important new classes of drugs.[2]

These new classes of drugs seemingly focus on new therapeutic methods and provide better treatment. A couple of examples illustrate this phenomenon. An important milestone for the pharmaceutical industry was the introduction of Tagamet. It was the first H2 Antagonist and was specifically designed to control acid secretion. These histamine antagonists are prescribed to treat active duodenal ulcers, benign gastric ulcers, gastro esophageal reflux disease, and the prophylaxis of stress induced ulcers. Other important H2 Antagonists include Zantac, Pepcid and Axid, all of which were introduced during the 1980s. These products offered new modes of action but cost more than previously existing therapies (see below). Our goal is to measure the impact of the use of these drugs on drug and nondrug medical expenditures.

There were similar substantial pharmaceutical breatkthroughs in several other areas. For instance, Selective Serotonin Reuptake Inhibitors (SSRIs) work as antidepressants by blocking the central nervous system's uptake of serotonin. SSRIs offer a novel mode of action and are the treatment of choice for many indications, including depression, panic disorder, obsessive-compulsive disorder, and post-traumatic stress disorders. Their use is aided by their good side-effect profile, efficacy, tolerability, safety in overdose, and patient compliance.

Statins similarly provide a novel approach to therapy and mode of action. The statins treat heart disease by lowering cholesterol. More specifically, they control the production of cholesterol by inhibiting an enzyme, HMG- CoA reductase. They also reduce cholesterol by increasing the liver's ability to remove cholesterol from the blood. Statins are especially helpful

[2] From now on, we will call drugs belonging to break-through therapeutic classes "important drugs" and drugs belonging to other therapeutic classes as "other drugs."

for patients who have had inadequate response to dietary restrictions of saturated fat and cholesterol.

The other innovations listed above exhibit similar changes in therapeutic method and modes of action. These drugs treat conditions in novel ways but improved treatment is associated with increased pharmaceutical costs. This chapter attempts to determine whether these drugs impact other medical expenditures, and if so whether there is a net cost saving from their use.

We depart methodologically from Lichtenberg by examining whether an entire group of breakthrough drugs reduces costs compared to older, pre-existing therapies. Our analysis of these drug groupings offers several improvements over prior work. First, we treat all drugs with a similar pharmacology as the same rather than simply assigning their therapeutic value based on year of introduction. This measure offers substantial improvement over drug age because we can separately estimate the cost impact of each group of important drugs compared to previously existing therapies. Second, our approach recognizes that innovations emerge in waves and that drugs within a particular group are therapeutically similar to each other.

Third, we separately estimate the effects of each of these groups of drugs on drug and nondrug expenditures. Licthenberg's approach implicitly assumes that therapeutic improvements and cost impacts are linear in time and the same across classes. Duggan's analysis raises issues about whether Lichtenberg's analysis applies to all therapeutic areas. Our approach relaxes Lichtenberg's assumption and specifically addresses group-by-group whether innovative classes of drugs lower nondrug medical expenditures.

Finally, we offer an improved way of measuring cost impact. As discussed below, the MEPs data is organized by medical event so that data for a particular medical event records the

contemporaneous drug and nondrug expenditures associated with that event. Lichtenberg uses this event level data and effectively analyzes the contemporaneous cost impact of drug use. While it may be true that usage of a superior drug will reduce contemporaneous medical expenditures, for many drugs, such as those used for chronic conditions, medical cost savings will be distributed over time. For example, cholesterol reducing drugs (Statins) would not likely reduce current expenditures, but instead would lower medical expenditures over time.

These facts raise numerous measurement issues, particularly because some patients (and their doctors) switch drugs regularly, going back and forth between newer and older drugs. Our analysis addresses this issue by separating patients into groups based upon the regularity of their use of particular drugs. We then measure drug and nondrug expenditures for patients over the entire period of treatment. This method permits us to analyze the cost impact of important new drugs over time.

The remainder of the chapter is as follows. Section 2 presents the model, and Section 3 presents an overview of the data. Section 4 displays the results, and Section 5 concludes.

III.2. Model

The analysis relies on a variant of Lichtenberg's (2001a) model where we use a substantially improved measure of new technologies and tighten the definition of drug use. We focus attention on the Selective Serotonin Reuptake Inhibitors, Statins, Ace Inhibitors, H2 Antagonists, Proton Pump Inhibitors, Calcium Channel Blockers, and Fluoroquinolones. These drugs are widely used, have large sales, and are commonly thought to provide substantial therapeutic benefits.

As noted above the MEPS data is organized so that individual records correspond to individual medical events. In contrast, the therapeutic benefit of many drugs will be spread over

time. Since some patients switch drugs regularly, we assigned patients to groups based upon the consistency of their use of breakthrough drugs. We grouped patients into three categories. The baseline category consists of patients who frequently switch back and forth between important drugs and other drugs over time. The second category consists of patients who regularly used the important new groups of drugs. This group includes patients who used the important drugs all the time or patients who switch between important drugs and other drugs only once throughout their treatment history for a particular ICD-9 code. The third category consists of patients who never used the breakthrough drug class.

Our analysis measures the differences in drug and nondrug expenditures across these three patient groups, enabling us to identify the long run cost impact of the use of these groups of important drugs. We control for the same sets of factors used by Lichtenberg and Duggan, incorporating for example the duration of the patient's condition, demographic variables and the patient's diagnosis, or ICD-9 codes.[3]

More formally, our model is a variant of Lichtenberg's:

$$Y^{c}_{ij} = \Phi X_j + \Psi Z_{ij} + \Pi M_i + \xi_{ij}$$

where Y^{c}_{ij} is the category (c) of either prescription drug expenditures (c=DE) or total non-drug expenditure (c=NDE) associated with the j^{th} prescription consumed by person i. The X_j variables measure usage of important drugs. X_1 takes a value of 1 if the patient regularly used important drugs, and a value of zero otherwise. X_2 takes a value of one for patients who never use important drugs and is zero otherwise. The omitted category consists of patients who switch multiple times between important drugs and other drugs. Z_{ij} includes dummy variables for

[3] The ICD-9 codes are described at Medical Condition Files located at the web site: http://www.meps.ahrq.gov/

conditions described as ICD-9-CM 3-digit diagnosis for which person i used prescription j and also includes condition durations. M_i includes patient i's income level and demographic variables for sex, race, insurance status, education, and age. ξ_{ij} is the disturbance term. Φ, Ψ and Π are the set of coefficients to be estimated.

III.3. Data

We use the Medical Expenditure Panel Survey (MEPS) data sets from 1996 to 2001. MEPS is cosponsored by the Agency for Health Care Research and Quality and the National Center for Health Statistics. MEPS is a nationally representative survey of health care use, expenditures, sources of payments, insurance coverage, and demographic characteristics for the U.S. civilian noninstitutionalized population. MEPS consists of three components, including the Household Component (HC), the Medical Provider Component (MPC), and the Insurance Component (IC). These surveys jointly generate exceptionally rich datasets that provide national estimates of the level and distribution of health care use and expenditures.

Our data set consists of the first five panels of MEPS from 1996 to 2001. First, we created our data set for each panel separately by merging the HC files, MPC files, and IC files. Then, we calculated the medical expenditures associated with each condition by event type using the Condition-Event Link File.[4] Finally, we used the Medical Care Index (1982-1984=0) to express all the dollar values in terms of year 2001.[5]

We sorted the MEPS data by patient and condition. We then sorted each patient's records into chronological order so that the drug treatment history for each patient/condition could be assessed. Individual patient treatment histories vary substantially. For some patients, physicians frequently change drugs, while for others there are initial changes followed by

[4] For further information about the MEPS, see the web site: http://www.meps.ahrq.gov/
[5] For the description of Medical Care Index, see the web site: http://www.bls.gov/cpi/cpifact4.htm

stability, and for still others there is little change. These differences lead to our three categories of drug use: one category is the control group, which consists of patients who frequently switch drugs over time; a second category that consists of patients who exclusively use important drugs or switch drugs *only once*; and a third category that consists of patients who never use the important drugs.

The next step was to identify the set of diagnostic codes where particular groups of breakthrough drugs were regularly used. This issue is important because the MEPS data include prescriptions that do not appear to match well with the associated ICD-9 (diagnostic) codes. For example, Statins will be prescribed "for" ulcers, and H2 Antagonists will be prescribed "for" depression. The apparent reason is that patients present with multiple indications (diagnoses) and all codes are not recorded.

This data problem creates issues for cost measurement associated with a medical condition. In particular, when a drug is "used" for an unrelated condition "other medical expenses" will be mismeasured, and these medical expenses cannot be compared to the expenses of conditions for which the drug is normally used. Accordingly, we sought to identify medical conditions for which groups of breakthrough drugs were regularly used. To address this issue, we sought to identify ICD-9 codes where the groups of breakthrough drugs were regularly used. Since the definition of "regularly" is subjective, we carried out our analysis using several alternatives. More specifically, we used all codes where the breakthrough drugs were prescribed for at least four percent of all encounters, at least five percent, and at least six percent. These procedures resulted in three separate data sets for each breakthrough drug group. The exception consisted of the H2 Antagonists and the Proton Pump Inhibitors. Since these drugs are used to treat largely overlapping groups of conditions, their data sets were combined.

Table 1 displays the molecule name, trade name and FDA approval years for each break-through drug classes. Table 2 presents a list of the ICD-9 codes where the SSRIs were used at least four, five, and six percent of the time. The Appendix Table A.3 contains similar lists of ICD-9 codes for the remaining classes of breakthrough drugs. Analysis of these various groupings indicates that the central results are not sensitive to the use of the four, five, or six percent cutoff.

Similar to ICD-9 codes, the beginning year of a patient's condition (duration) and the health insurance coverage for each patient are also used. We include four overlapping health insurance indicators in our analysis because patients at times have more than one type of coverage. The Medicare variable takes a value of one if the patient has Medicare, and otherwise is zero. We include similar Medicaid and Private Insurance variables, and Uninsured identifies patients who do not have insurance.

The MEPS data set also provides detailed demographic characteristics of each patient including age, sex, race, educational attainment, and income. Age represents patient age at the end of the interview year. MEPS data also includes self-reported race, broken down into American Indian, Aleut/Eskimo, Asian, Black, White, and Other Races. MEPS also provides total patient income.

III.4. Empirical Analysis

The empirical analysis focuses on these different groups of important new drugs, beginning with the SSRIs. All of the data presented reflect event level outcomes, which mean average expenditures are per event and the regression coefficients reflect impact per event.

Table 1

New Drug Classes

Molecule Name	Trade Name	App. Year
Selective Serotonin Reuptake Inhibitors		
Fluoxetine Hydrochloride	Prozac	1987
Sertraline Hydrochloride	Zoloft	1991
Paroxetine Hydrochloride	Paxil	1992
Fluvoxamine Maleate	Luvox	1994
Citalopram Hydrobromide	Celexa	1998
Rabeprazole Sodium	Aciphex	1999
Pantoprazole	Protonix	2000
Statins		
Lovastatin	Mevacor	1989
Simvastatin	Zocor	1991
Pravastatin	Pravachol	1991
Fluvastatin	Lescol	1993
Atorvastatin	Lipitor	1996
Cerivastatin Sodium	Baycol	1997
ACE Inhibitors		
Captopril	Capoten	1981
Enalapril Maleate	Vasotec	1985
Lisinopril	Prinivil	1987
	Zestril	1987
Benazepril Hydrochloride	Lotensin	1991
Fosinopril Sodium	Monopril	1991
Quinapril Hydrochloride	Accupril	1991
Ramipril	Altace	1991
Moexipril Hydrochloride	Univasc	1995
Trandolapril	Mavik	1996
H2 Receptor Antagonists		
Cimetidine	Tagamet	1977
Ranitidine	Zantac	1983
Famotidine	Pepcid	1986
Nizatidine	Axid	1988
Proton Pump Inhibitors		
Omeprazole	Prilosec	1989
Lansoprazole	Prevacid	1995
Rabeprazole Sodium	Aciphex	1999
Pantoprazole	Protonix	2000
Calcium Channel Blockers		
Verapamil Hydrochloride	Calan	1981
	Isoption	1981
	Verelan	1981
Nifedipine	Adalat	1981
	Procardia	1981
Diltiazem Hydrochloride	Cardizem	1982
	Tiamate	1982
	Dilacor	1982
	Tiazac	1982
Nicardipine Hydrochloride	Cardene	1988
Nimodipine	Nimotop	1988
Isradipine	DynaCirc	1990
Bepridil Hydrochloride	Vascor	1990
Felodipine	Plendil	1991
Amlodipine Maleate	Norvasc	1992
Nisoldipine	Sular	1995
Fluoroquinolones		
Norfloxacin	Noroxin	1986
Ciprofloxacin	Cipro	1987
Ofloxacin	Floxin	1990
Enoxacin	Penetrex	1991
Lomefloxacin Hydrochloride	Maxaquin	1992
Sparfloxacin	Zagam	1996
Levofloxacin	Levaquin	1996
Gerafloxacin	Raxar	1997
Travofloxacin Mesylate	Trovan	1997
Gatifloxacin	Tequin	1999
Moxifloxacin	Avelox	1999

Note: Trade names are used for identification purposes only and do not imply product endorsement. For more detailed information about each drug class, please check the following sources: 1) Drug Facts and Comparisons 2005, by Facts and Comparisons. 2) Goodman and Gilman's The Pharmacological basis of therapeutic, 10th Edition by McGraw-Hill Companies. 3) Physicians' Desk Reference 2005, by Medical Economics.

Table 2

Selective Serotonin Reuptake Inhibitors[6]
ICD-9 Codes for 4, 5 and 6 Percent Samples

Description of ICD-9 Codes	ICD-9 Codes		
	Four Percent Sample	Five Percent Sample	Six Percent Sample
Viral hepatitis	70	70	70
Malignant neoplasm colon	153	153	153
Schizophrenic disorders	295	295	
Affective psychoses	296	296	296
Neurotic disorders	300	300	300
Personality disorders	301	301	301
Alcohol dependence syndrome	303	303	303
Drug dependence	304	304	304
Special symptom nec	307	307	307
Acute reaction to stress	308	308	308
Adjustment reaction	309	309	309
Conduct disturbance nec	312	311	311
Mental retardation nos	319	312	312
Cerebral degeneration	331		
Extrapyramidal dis nec	333		
Migraine	346	333	333
Cataplexy and narcolepsy	347		
Other brain conditions	348	347	347
Atherosclerosis	440	348	
Noninflamm dis vagina	623	440	
Female genital symptoms	625	623	623
Nutrit/metab/devel symptoms	783	625	625
Oth ill-defined morbidity/mortality	799		
Other brain injury	854	799	799
HX of disease nec	V12	854	854
Mental/behavioral prob	V40	V12	V12
Other psychosocial circumstances	V62	V40	V40
Other reason for consult	V65	V62	V62

[6] For further details regarding ICD-9 codes, see http://www.meps.ahrq.gov, http://icd9cm.chrisendres.com and http://www.cdc.gov/nchs/data/icd9/icdguide.pdf.

III.4.1. Selective Serotonin Reuptake Inhibitors (SSRIs)

The SSRIs[7] include such well-known drugs as Paxil, Prozac, and Zoloft. As noted in Table 1, the first SSRI was Fluoxetine, which was introduced in 1987. During the next 15 years, additional SSRIs were introduced including Sertraline in 1991, Paroxetine in 1992, Fluvoxamine in 1994, Citalopram in 1998, Rabeprazole in 1999, and Pantoprazole in 2000.

These drugs created substantial changes in the pharmacological treatment of numerous diseases. SSRIs have been prescribed for a wide range of conditions, including schizophrenic disorders, neurotic disorders, personality disorders, and depressive disorders. Table 3 presents summary statistics. These data reveal that SSRIs are prescribed for chronic conditions. The reported treatment length is at least five years for 36.8 percent of the conditions. Health care expenditures vary with income, insurance status, sex, race, and age. The data indicate that patients' mean age is about 44.5 years and average per capita income is $17,386. SSRIs, when compared to other drugs used for the same conditions, are typically associated with higher drug expenditures ($81.40 versus $53.30) but lower non-drug expenditures ($306.20 versus $455.40). Table 3 also reveals that on average SSRIs account for 20.1 percent of prescriptions in the categories where they are regularly used.

[7] SSRIs are generally prescribed for the treatment of depressive disorders, obsessive compulsive disorders, social anxiety, and panic attack disorders. Depression usually occurs as a result of the lack of stimulation of the recipient neuron at a synapse. To stimulate the recipient cell, SSRIs inhibit the reuptake of serotonin and increase the chance for serotonin to be recognized by the receptors. The increase in serotonin level by the recipient cell is believed to act as a stimulant, counteracting depression and increasing the motivation. (For detailed information about SSRIs see 2005 Lippincott's Nursing Drug Guide).

Table 3

Summary Statistics for Five Percent Sample
Various Break-Through Drug Categories

		Selective Serotonin Reuptake Inhibitors	Statins	ACE Inhibitors	H2 Antagonists Proton Inhibitors	Calcium Channel Blockers	Fluoroquinolones
Year of First Introduction		1987	1989	1981	1977	1981	1986
Demographics:							
Mean Age		44.5	57.6	59.5	45.2	58.6	43.0
Mean Education Years		11.3	11.5	11.1	9.8	11.1	10.5
Mean Income		$17,386	$22,883	$20,218	$18,468	$20,752	$18,525
Percentage of Male Patients		32.5	47.8	43.2	41.3	43.2	28.7
Percentage of White Patients		86.9	85.4	77.7	84.2	79.4	87.6
Percentage of Medicare Enrollees		23.9	42.1	44.9	28.1	45.4	25.6
Percentage of Medicaid Enrollees		23.8	14.0	16.3	19.6	15.7	13.9
Percentage of Private Insurance Enrollees		56.0	64.5	58.0	60.2	58.9	65.1
Percentage of Patients with No Insurance Coverage		12.2	7.6	9.2	10.8	8.9	12.1
Average Healthcare Expenditures ($):							
Important Drugs:	Drug Expenditures	$81.4	$85.1	$44.5	$95.2	$57.7	$63.2
	Nondrug Expenditures	306.2	714.6	833.7	696.6	662.5	832.7
Other Drugs:	Drug Expenditures	53.3	42.4	43.6	41.3	41.6	29.5
	Nondrug Expenditures	455.4	1,979.4	943.8	1688.1	1236.3	418.9
Percentage of Reported Condition Durations:							
Less than 1 year		17.7%	40.7%	19.1%	37.41%	22.5%	57.8%
1 year		12.1	11.0	10.8	20.28	11.0	6.4
2 years		7.2	8.9	7.4	6.71	7.0	9.4
3 years		7.9	6.4	6.6	4.16	6.0	3.4
4 years		4.4	4.7	4.7	5.51	4.4	5.7
5 years		4.6	3.4	4.8	2.62	4.6	5.5
More than 5 years		46.2	24.9	46.6	23.28	44.5	11.8
Percentage of Important Drugs Prescriptions		20.1%	15.4%	8.4%	17.7%	10.1%	10.0%
Number of Patients in Sample		3,098	2,111	7,846	6,773	6,976	2,746

Table 4

Selective Serotonin Reuptake Inhibitors
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	18.302	-370.987	18.191	-402.159	18.468	-399.022
	(1.415)‡	(51.070)‡	(1.459)‡	(55.279)‡	(1.406)‡	(57.478)‡
Other Drugs	-15.291	-56.219	-15.080	-82.180	-13.358	-132.975
	(1.057)‡	(54.639)	(1.149)‡	(63.085)	(1.074)‡	(66.870)†
Income	0.000	-0.000	0.000	-0.001	0.000	-0.004
	(0.000)*	(0.001)	(0.000)*	(0.001)	(0.000)‡	(0.001)‡
Male	-2.127	45.261	-1.608	39.995	-1.199	40.891
	(1.037)†	(49.213)	(1.115)	(55.195)	(1.129)	(60.839)
Private Insurance	9.289	241.241	10.857	320.718	5.200	447.344
	(1.626)‡	(67.305)‡	(1.765)‡	(79.803)‡	(1.908)‡	(93.084)‡
Medicare	7.999	-13.422	9.260	32.144	0.048	79.966
	(1.632)‡	(51.394)	(1.767)‡	(58.288)	(1.682)	(58.480)
Medicaid	9.206	14.940	11.612	66.257	5.003	145.025
	(1.736)‡	(53.088)	(1.877)‡	(61.027)	(1.995)†	(73.700)†
Uninsured	-5.096	94.051	-6.182	51.443	0.526	-109.634
	(2.064)†	(86.773)	(2.244)‡	(97.827)	(2.314)	(111.148)
Eskimo/Aleut	-24.230	-956.797	-34.307	-1,116.302	-33.238	-1,113.981
	(10.062)†	(592.872)	(10.135)‡	(657.417)*	(10.101)‡	(624.080)*
Asian	-7.696	-413.666	-20.515	-532.736	-21.094	-486.633
	(6.428)	(582.748)	(6.482)‡	(658.770)	(6.219)‡	(621.746)
Black	-18.888	-279.511	-23.323	-331.141	-18.881	-196.583
	(4.720)‡	(608.760)	(5.123)‡	(691.931)	(4.878)‡	(663.194)
White	-12.784	-445.391	-18.024	-542.843	-17.629	-441.127
	(4.533)‡	(589.610)	(4.891)‡	(666.137)	(4.615)‡	(632.513)
Other Race	-42.888	-651.814				
	(6.089)‡	(595.498)				
ICD-9 Codes[8]						
70	184.779	261.513	183.733	289.796	183.191	365.659
	(23.628)‡	(261.486)	(23.511)‡	(263.415)	(23.513)‡	(262.952)
153	12.147	2,152.089	9.459	2,216.539	8.233	2,237.423
	(8.989)	(688.120)‡	(8.839)	(686.774)‡	(8.732)	(692.387)‡
295	30.979	-133.954	29.412	-152.989		
	(2.818)‡	(46.618)‡	(2.825)‡	(48.549)‡		
296	-3.476	-90.471	-3.816	-95.326	-4.040	-99.093
	(1.401)†	(51.508)*	(1.410)‡	(52.701)*	(1.402)‡	(53.416)*
300	-0.819	-221.430	-0.945	-211.921	-0.877	-201.956
	(1.249)	(33.910)‡	(1.255)	(35.033)‡	(1.240)	(35.912)‡

[8] Appendix-3 provides the definition of each ICD-9 codes.

Table 4 (Continued)

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes (continued)						
301	-10.597	-221.112	-7.953	-196.020	-9.647	-163.828
	(6.077)*	(124.510)*	(6.012)	(134.682)	(5.923)	(138.878)
303	12.494	2,602.227	11.263	2,625.870	7.147	2,586.622
	(4.587)‡	(588.033)‡	(4.581)†	(579.788)‡	(4.682)	(571.512)‡
304	-24.209	3,112.247	-23.641	3,168.727	-26.224	3,166.701
	(5.393)‡	(861.060)‡	(5.500)‡	(848.387)‡	(5.604)‡	(838.639)‡
307	2.395	415.744	4.209	418.033	2.886	363.254
	(7.109)	(258.601)	(7.124)	(263.158)	(7.105)	(264.744)
308	-5.396	-374.366	-4.840	-372.262	-8.109	-299.219
	(2.382)†	(47.449)‡	(2.392)†	(51.758)‡	(2.368)‡	(50.870)‡
309	21.340	658.414	22.093	698.305	19.374	734.590
	(4.858)‡	(215.070)‡	(4.812)‡	(215.182)‡	(4.849)‡	(220.587)‡
312	8.459	215.016	9.866	238.000	8.382	243.572
	(6.319)	(267.861)	(6.466)	(270.971)	(6.666)	(271.292)
319	9.465	-307.631				
	(6.258)	(117.273)‡				
331	11.628	-87.003				
	(2.885)‡	(106.840)				
333	-7.504	-285.405	-6.073	-298.409	-10.008	-328.517
	(5.313)	(95.649)‡	(5.327)	(104.921)‡	(5.331)*	(117.568)‡
346	-12.708	-272.020				
	(1.535)‡	(54.915)‡				
347	-9.755	-376.424	-9.908	-427.510	-9.532	-388.920
	(7.190)	(147.468)†	(7.205)	(152.007)‡	(6.907)	(150.681)‡
348	-10.644	339.809	-9.334	389.565		
	(3.877)‡	(152.298)†	(3.930)†	(154.731)†		
440	-13.533	2,570.371	-13.511	2,579.299		
	(2.727)‡	(575.012)‡	(2.782)‡	(578.483)‡		
623	-25.248	-155.280	-25.042	-135.511	-27.246	-96.597
	(2.907)‡	(118.626)	(2.886)‡	(126.473)	(2.831)‡	(133.396)
625	-22.640	-35.186	-22.078	-51.368	-24.041	2.455
	(2.803)‡	(167.224)	(2.801)‡	(171.591)	(2.771)‡	(172.901)
783	0.225	-316.884				
	(5.548)	(69.373)‡				
799	-5.427	-37.321	-5.574	-10.192	-9.118	-63.608
	(1.808)‡	(82.544)	(1.841)‡	(85.506)	(1.794)‡	(84.884)
854	-4.775	2,443.100	-5.143	2,465.954	-5.887	2,565.358
	(3.440)	(1,051.633)†	(3.441)	(1,054.990)†	(3.458)*	(1,056.552)†

Table 4 (Continued)

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes (continued)						
V12	-0.162	-229.366	0.379	-305.110	-3.895	-412.469
	(4.744)	(181.261)	(4.779)	(193.585)	(4.569)	(197.951)†
V40	2.370	622.120	2.838	605.554	4.573	637.635
	(3.543)	(484.535)	(3.604)	(492.361)	(3.405)	(496.500)
V62	-23.177	911.312	-22.541	889.230	-24.175	824.103
	(3.622)‡	(458.003)†	(3.720)‡	(468.354)*	(3.666)‡	(470.962)*
V65	6.181	-282.708	6.209	-264.296	3.216	-236.755
	(4.443)	(59.059)‡	(4.427)	(64.377)‡	(4.428)	(68.915)‡
Constant	47.147	160.359	40.888	163.158	53.780	287.496
	(15.297)‡	(977.019)	(16.066)†	(861.747)	(20.145)‡	(920.635)
Observations	28626	28626	24734	24734	22034	22034
R-squared	0.10	0.05	0.11	0.05	0.11	0.05

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

Table 4 presents regression results measuring the impact of SSRIs on drug and nondrug expenditures. Inspection of the results shows that the control variables are generally significant and plausible.[9] The results show that income is associated with a small but positive effect on total drug expenditures and has an insignificant negative effect on total non-drug expenditures. Patients enrolled with insurance have higher total drug expenditures than uninsured patients. The results also show that, separately controlling for breakthrough drugs, patients enrolled in private insurance have significantly higher total non-drug expenditures than all other patients, except those on Medicaid.

The empirical results indicate that SSRIs cost more than other drugs, controlling for diagnosis, insurance, and demographics, but reduce nondrug expenditure by substantially more.

[9] We will present the results for all the samples, but discuss them only for the 5 percent sample.

The omitted category of drug use consists of patients who sporadically use breakthrough drugs. Focusing on the five percent sample, the estimated results from Table 4 show that the patients regularly using SSRIs incur higher total drug expenditures of $18.19 compared to the patients sporadically using SSRIs. In contrast, patients who never use SSRIs experience savings in total drug expenditures of $15.08 compared to those who sporadically use SSRIs and save $33.27 compared to those who regularly use SSRIs.

The results also show that SSRIs significantly decrease total non-drug expenditures. Estimated results from Table 4 show that patients who regularly use SSRIs experience decreased total non-drug expenditures of $402.16 compared to patients who sporadically use SSRIs, controlling therapeutic conditions. These savings are about 20 times the amount of the measured increase in drug expenditures. Patients who regularly use SSRIs also experience considerable savings compared to patients who never use SSRIs. [10] Our results indicate that SSRIs result in large decreases in total health expenditures for the patients who use them.

III.4.2. Statins

In contrast to the widely used SSRIs, Statins[11] are normally prescribed for a relatively narrow range of conditions, including myocardial infarction and other types of heart disease. Lovastatin (Mevacor) was the first Statin introduced, receiving marketing approval in 1989. As

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[10] We also used a t-test to determine whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. This test will determine whether there are cost savings for those who regularly use important drugs as compared to those who never use them. The statistics in the drug expenditure equation and nondrug expenditure equation are respectively 24.02 and 5.59 indicating that the coefficients on important drugs and other drugs are significantly different from each other in both equations.

[11] Statins are prescribed for the treatment of cholesterol reduction. They control the rate of cholesterol production in the body by inhibiting an enzyme, HMG- CoA reductase. They decrease the cholesterol level by slowing down the production of cholesterol and by increasing the liver's ability to remove the cholesterol from the blood.

noted in Table 1, other Statins were introduced over time, including Zocor (1991), Pravachol (1991), and Lescol (1993). Table 1 contains a complete list.

Statins are designed to reduce cholesterol. They control the rate of cholesterol production in the body by inhibiting an enzyme, HMG- CoA reductase. They also exert vasculoprotective actions that include improvement of endothelial function, antioxidant properties, stabilization of atherosclerotic plaques, regulation of progenitor cells, inhibition of inflammatory responses, and immunomodulatory actions. Stabilization of atherosclerosis will treat and prevent chest pain, heart attacks, and strokes.

Table 3 presents summary statistics for the Statins. The data reveals that on average Statins account for 15.4 percent of prescriptions in the categories where they are regularly used. They are generally prescribed for conditions associated with higher cholesterol levels, and they are associated with a moderate treatment period, though this may in part reflect the newness of these drugs. Twenty-nine percent of patients have a condition treatment period of more than five years. Ninety-two percent of patients are insured and forty-eight percent of patients are male. Patients' mean age is fifty-eight and average per capita income is $22,883. Statins, when compared at sample means to other drugs used for the same conditions, are typically associated with higher drug expenditures ($85.10 versus $42.40) but lower non-drug expenditures ($714.60 versus $1,979.40).

Table 5 presents the regression results regarding the impact of Statins on drug and nondrug medical expenditures. Focusing attention on the five percent sample, the results for the control variables show that income, insurance status, sex, race, and age all affect health care expenditures. The estimated coefficients of these control variables are generally significant and

Table 5

Statins
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	33.566	-675.310	37.329	-593.904	33.343	-425.716
	(2.299)‡	(115.157)‡	(2.371)‡	(162.861)‡	(2.440)‡	(61.138)‡
Other Drugs	-14.862	97.062	-11.042	37.262	-13.520	-331.760
	(1.296)‡	(103.130)	(1.414)‡	(146.277)	(1.664)‡	(65.689)‡
Income	0.000	-0.014	0.000	-0.020	0.000	-0.006
	(0.000)†	(0.002)‡	(0.000)	(0.003)‡	(0.000)†	(0.001)‡
Male	1.980	-266.732	4.681	319.302	0.302	285.951
	(0.976)†	(95.474)‡	(1.087)‡	(121.303)‡	(1.298)	(62.938)‡
Private Insurance	1.384	913.680	-3.903	875.618	-0.608	409.109
	(1.211)	(128.087)‡	(1.567)†	(188.926)‡	(1.863)	(120.343)‡
Medicare	4.889	-1,010.376	-3.442	-910.944	3.608	-279.853
	(3.881)	(170.129)‡	(2.010)*	(210.876)‡	(2.286)	(81.386)‡
Medicaid	-1.619	458.304	-3.641	-246.518	-3.175	490.083
	(1.229)	(153.790)‡	(1.777)†	(219.652)	(2.226)	(120.829)‡
Uninsured	4.576	101.936	10.975	918.284	7.534	-239.994
	(2.309)†	(201.666)	(2.520)‡	(229.114)‡	(3.024)†	(124.308)*
Asian	21.485	3,581.875	24.150	3,052.642	17.984	403.923
	(4.726)‡	(980.508)‡	(6.150)‡	(618.390)‡	(7.089)†	(227.139)*
Black	5.818	3,504.101	13.476	1,914.108	6.675	528.761
	(3.361)*	(994.345)‡	(4.452)‡	(532.174)‡	(5.494)	(222.461)†
White	5.469	3,607.750	9.092	2,208.411	3.984	254.031
	(3.270)*	(996.503)‡	(4.292)†	(516.616)‡	(5.130)	(211.143)
Constant	97.006	789.981	69.863	-1,398.071	60.643	-213.717
	(33.015)‡	(2,723.786)	(36.199)*	(1,580.055)	(36.008)*	(1,441.041)
ICD-9 Coefficients Reported in the Appendix.						
Observations	20337	20337	11589	11589	7028	7028
R-squared	0.06	0.18	0.12	0.26	0.14	0.25

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD-9 Codes, Condition Duration, Age and Education Year are suppressed and available upon request.

plausible. These variables moderately affect drug expenditures and have larger effects on nondrug expenditures. Male patients experience increased total non-drug expenditures of

$319.3. Privately insured patients experience higher non-drug expenditures, while Medicare and Medicaid enrollees experience lower total non-drug expenditures. Increased income is associated with reduced nondrug expenditures, perhaps because of greater attention to health care by the wealthy.

Statins are associated with increased drug expenditures but even larger reductions in nondrug expenditures. Patients who regularly use Statins experience increased total drug expenditures of $37.33 over patients sporadically using Statins, and an increase of $48.07 in drug expenditures compared to patients who did not use Statins. These higher drug expenditures, however, are more than offset by reduced non-drug expenditures. Patients regularly using Statins experience reduced non-drug expenditures of $593.90 compared to other patients, noting that there are insignificant differences in this impact between the other two groups of patients. Hence Statins generate nondrug savings on the order of twelve times their incremental costs. This large decrease in nondrug expenditures indicates that Statins provide a novel and effective mode of action for the treatment of high-level cholesterol diseases and save on other medical costs.[12]

III.4.3. Ace Inhibitors

ACE Inhibitors were first introduced in 1981 when Capoten (Captopril) was marketed. This introduction was followed by the marketing of numerous other ACE Inhibitors over the next 15 years, including Vasotec, Prinivil, Zestril, Lotensin, Accupril, and others.

ACE inhibitors are usually prescribed for the treatment of hypertension and congestive heart failure. These drugs are also used for metabolic diseases and other diseases of the

[12] As above, we used a t-test to determine whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. The t-test statistics in the drug expenditure equation and nondrug expenditure equation are respectively 21.23 and 4.61 indicating that the coefficients on important drugs and other drugs are significantly different from each other in both equations. These statistics suggest that there is significant cost savings for those who regularly use important drugs as compared to those who never use them.

circulatory system. Following a heart attack, the heart muscle may weaken. ACE Inhibitors help slow weakening of the heart. They also help prevent future heart attacks by blocking an enzyme that causes blood vessels to tighten. As a result, blood pressure decreases and the supply of blood and oxygen to the heart increases.[13] Hypertension, myocardial infarction, heart failure, and diabetes mellitus are the most frequently observed conditions where Ace Inhibitors are used. They are generally associated with longer treatment periods; forty-seven percent of patients have treatment periods of more than five years.

Table 3 presents summary statistics. The data reveal that on average Ace Inhibitors account for 8.4 percent of prescriptions in the categories where they are regularly used. Ace Inhibitors are generally prescribed for elderly people; the patients' mean age is fifty-nine and the average per capita income is about $20,218. Forty-three percent of the patients are male and ninety percent of patients have health insurance. Ace Inhibitors, when compared to other drugs used for the same conditions, are associated with slightly lower nondrug expenditures ($833.70 versus $943.80). The drug expenditures for Ace Inhibitors and other drugs are very close to each other ($44.50 versus $43.60).

Table 6 presents the regression results analyzing the impact of the use of ACE Inhibitors on drug and nondrug medical expenditures. The results for the control variables show only a small (if any) impact of income, gender, and insurance coverage on drug expenditures. The race related variables have a significant impact on both drug and nondrug expenditures, with much larger effects on nondrug expenditures. Gender and insurance coverage have significant effects, both statistically and economically, on nondrug medical expenditures in these samples, controlling for drug use.

[13] http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202044.htm and Table 1 provides further information regarding Ace Inhibitors.

Table 6

Ace Inhibitors
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	-2.281	-507.487	-1.435	-592.599	-1.479	-626.421
	(1.023)†	(54.630)‡	(1.277)	(57.402)‡	(1.277)	(59.679)‡
Other Drugs	1.536	-154.202	0.707	-208.558	0.819	-236.283
	(0.455)‡	(46.208)‡	(0.464)	(49.691)‡	(0.490)*	(53.741)‡
Income	0.000	-0.003	0.000	-0.003	0.000	-0.003
	(0.000)‡	(0.001)†	(0.000)‡	(0.001)†	(0.000)‡	(0.001)†
Male	-0.166	175.895	0.103	207.024	0.252	245.925
	(0.414)	(55.035)‡	(0.422)	(60.200)‡	(0.447)	(64.904)‡
Private Insurance	4.317	437.844	3.650	426.267	3.336	403.292
	(0.557)‡	(53.291)‡	(0.565)‡	(56.275)‡	(0.600)‡	(61.457)‡
Medicare	3.322	155.355	2.977	109.198	1.893	119.930
	(1.176)‡	(71.415)†	(1.208)†	(75.722)	(1.242)	(79.018)
Medicaid	1.696	265.221	0.717	212.535	-0.118	210.317
	(0.658)‡	(54.765)‡	(0.607)	(56.627)‡	(0.623)	(61.509)‡
Uninsured	2.268	-63.769	2.779	-55.191	3.459	-43.463
	(0.936)†	(72.097)	(0.954)‡	(76.648)	(1.001)‡	(82.225)
Eskimo/Aleut	27.410	-509.407	31.245	-300.531	32.896	-209.656
	(9.575)‡	(187.674)‡	(9.962)‡	(180.711)*	(10.001)‡	(266.979)
Asian	9.332	645.375	7.934	724.499	10.115	838.000
	(1.974)‡	(143.093)‡	(1.956)‡	(154.317)‡	(2.008)‡	(249.454)‡
Black	3.608	639.396	2.805	686.494	4.776	830.818
	(1.620)†	(115.123)‡	(1.669)*	(121.849)‡	(1.714)‡	(234.470)‡
White	6.821	768.987	6.437	827.827	8.750	960.700
	(1.567)‡	(112.243)‡	(1.630)‡	(119.982)‡	(1.666)‡	(232.861)‡
Other Race	-22.049	150.827	-21.813	97.717	-19.332	157.625
	(4.716)‡	(234.783)	(4.742)‡	(248.632)	(4.809)‡	(336.669)
Constant	81.181	10,831.975	85.689	10,971.423	99.334	8,898.153
	(19.284)‡	(4,577.772)†	(19.722)‡	(4,647.565)†	(54.280)*	(4,550.750)*
ICD-9 Coefficients Reported in the Appendix.						
Observations	84350	84350	77796	77796	71101	71101
R-squared	0.02	0.09	0.02	0.09	0.02	0.09

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD-9 Codes, Condition Duration, Age and Education Year are suppressed and available upon request.

The results show that ACE Inhibitors substantially reduce nondrug expenditures but have little effect on drug expenditures. The coefficients in the drug expenditure equation in Table 6 are small ($1.43) and insignificant. In contrast, patients who regularly use ACE Inhibitors experience sharply lower nondrug expenditures. These patients who regularly use ACE Inhibitors save approximately $592.60 per encounter compared to patients who sporadically use ACE Inhibitors. Regular users of ACE Inhibitors also spend $384.04 less than patients who never use ACE Inhibitors (where $384.04 = $592.60-208.56). The results indicate that ACE Inhibitors are drugs that cost little (if any) more than previously existing therapies but produce large nondrug cost savings. These newer drugs provide an important contribution to medical cost containment.[14]

III.4.4. H2 Receptor Antagonists & Proton Pump Inhibitors (H2s and PPIs)

We group together our analysis of the H2 Antagonists and PPIs[15]. We use this grouping because the focus of our analysis is to determine the impact of classes of breakthrough drugs on drug and nondrug expenditures as compared to older therapies. The hypothesis to be investigated in this section is whether the use of H2 Antagonists and PPIs has affected medical expenditures compared to older therapies.

H2 Antagonists made their first appearance in 1977 with the introduction of cimetidine (Tagamet). This introduction was followed by several other H2 Antagonists in the mid-1980s,

[14] We also used a t-test to determine whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. The statistics in the drug expenditure equation and nondrug expenditure equation are respectively 1.72 and 7.90 indicating that the coefficients on important drugs and other drugs are significantly different from each other in both equations.

[15] Histamine (H2) antagonists are prescribed to treat active duodenal ulcer, benign gastric ulcer, erosive gastro esophageal reflux disease, and prophylaxis of stress induced ulcers. Proton pump inhibitors are usually prescribed for the same treatments offered by H2 antagonists. They work by suppressing the gastric acid secretion through specific inhibition of the hydrogen-potassium ATPase anzyme system at the secretory surface of gastric parietal cells. They are used for short-term treatment of active duodenal ulcer and benign gastric ulcer, severe erosive esophagitis and long-term treatment of pathologic hypersecretory conditions.

including ranitidine (Zantac), famotidine (Pepcid), and mizatidine (Axid). The first Proton Pump Inhibitor, Prilosec, was introduced in 1989. Other PPIs were introduced over the following decade, including Prevacid, Aciphex, and Protonix.

The H2s and PPIs are prescribed for a broad range of conditions including, for example, nutritional and metabolic diseases, as well as digestive and genitourinary system diseases. The most frequently observed conditions are diseases of the esophagus, gastric ulcers, stomach function disorders, and abdominal hernia.

Summary Statistics are presented in Table 3. These statistics show that H2s and PPIs are generally prescribed for conditions requiring short or medium treatment periods. Only twenty-three percent of patients report conditions existing for more than five years, while thirty-seven percent report conditions lasting less than one year. Eighty-nine percent of patients are insured and forty-one percent of patients are male. The patients' average age is forty-five years and per capita income averages $18,468. H2s and PPIs, when compared at sample means to other drugs used for the same conditions, are typically associated with higher drug expenditures ($85.20 versus $41.30) but significantly lower nondrug expenditures ($696.60 versus $1688.10).

Table 7 presents the regression results regarding the impact of the H2s and PPIs on drug and nondrug expenditures. The estimation results show that health care expenditures are influenced by the control variables, including income, gender, insurance status, race, and education. These variables have significant effects on nondrug expenditures but modest effects on drug expenditures. Male patients experience higher nondrug expenditures of $1,215.93. Patients with private health insurance incur higher total nondrug expenditures compared to other

Table 7

H2 Antagonists and Proton Pump Inhibitors
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	40.640	-1,284.852	40.099	-1,580.870	38.696	-414.079
	(1.745)‡	(123.597)‡	(1.894)‡	(156.447)‡	(1.869)‡	(72.331)‡
Other Drugs	-16.699	-817.692	-21.859	-1,149.979	-24.656	123.094
	(1.018)‡	(120.395)‡	(1.286)‡	(157.406)‡	(1.244)‡	(78.342)
Income	-0.000	-0.013	-0.000	-0.008	-0.000	-0.002
	(0.000)*	(0.002)‡	(0.000)‡	(0.002)‡	(0.000)	(0.002)
Male	2.735	935.846	2.814	1,215.929	1.672	500.476
	(0.819)‡	(90.001)‡	(1.130)†	(108.365)‡	(1.133)	(66.813)‡
Private Insurance	2.846	592.724	4.067	323.102	2.636	528.169
	(1.088)‡	(100.963)‡	(1.473)‡	(122.155)‡	(1.541)*	(118.506)‡
Medicare	0.347	-548.015	1.967	-203.995	3.639	30.660
	(1.990)	(118.023)‡	(3.022)	(140.666)	(3.095)	(109.415)
Medicaid	5.510	-124.458	5.623	-80.889	4.412	167.632
	(1.303)‡	(101.326)	(1.695)‡	(130.810)	(1.562)‡	(125.468)
Uninsured	1.979	131.018	1.979	-20.917	7.600	-294.655
	(1.702)	(141.637)	(2.305)	(202.781)	(2.076)‡	(139.154)†
Eskimo/Aleut	0.604	1,586.621	9.606	2,171.633	6.696	1,617.314
	(5.308)	(654.683)†	(7.874)	(1,281.585)*	(7.675)	(1,323.499)
Asian	4.071	-455.990	10.701	-1,429.762	6.946	-325.968
	(3.452)	(316.553)	(4.410)†	(429.190)‡	(4.312)	(306.640)
Black	2.375	354.935	6.420	-217.027	6.880	195.928
	(2.518)	(212.639)*	(2.941)†	(279.325)	(3.308)†	(300.384)
White	5.656	705.013	9.003	375.578	6.365	85.596
	(2.342)†	(190.673)‡	(2.650)‡	(239.838)	(2.964)†	(285.134)
Other Race	-29.655	-568.567	-39.331	-3,044.615	-26.067	577.065
	(10.013)‡	(820.180)	(12.634)‡	(1,377.925)†	(9.876)‡	(503.403)
Constant	25.777	29,324.505	5.951	36,581.191	26.474	5,861.404
	(7.985)‡	(4,185.424)‡	(22.433)	(5,133.497)‡	(26.020)	(1,832.678)‡
ICD-9 Coefficients Reported in the Appendix.						
Observations	29899	29899	19415	19415	15538	15538
R-squared	0.13	0.17	0.15	0.25	0.16	0.24

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD-9 Codes, Condition Duration, Age and Education Year are suppressed and available upon request.

groups. Increased income decreases both total drug and nondrug expenditures. Asian and black patients have lower and white patients have higher total nondrug expenditures when compared to the American Indian patients.

The results in Table 7 strongly support the proposition that H2s and PPIs are associated with higher drug costs but substantially lower nondrug medical expenditures. The estimated results from Table 7 show that patients regularly using H2s or PPIs have greater drug expenditures of $40.09 but lower total non-drug expenditures of $1,581 compared to patients sporadically using these products. In contrast, patients who never used H2s or PPIs incur $61.96 in lower average costs than those regularly using these products (where $61.96 = $40.10 – ($21.86)). These patients, however, incur higher nondrug costs of $430.89. These differences are highly statistically significant. Hence the results indicate that H2 Antagonists and Proton Pump Inhibitors substantially reduce healthcare costs.[16]

III.4.5. Calcium Channel-Blockers (CCBs)

The first CCBs[17], Verapamil (Calan and Isoption) and Nifedipine (Adalat and Procardia) were introduced in 1981. During the next 15 years, additional CCBs were introduced including Diltiazem (Cardizem) in 1982, Nicardipine (Cardene), and Nimodipine (Nimotop) in 1988.

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[16] To determine the cost savings for those who regularly use important drugs as compared to those who never use them, we test whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. The t-test statistics in the drug expenditure equation and nondrug expenditure equation are respectively 36.25 and 4.39 indicating that the coefficients on important drugs and other drugs are significantly different from each other in both equations.

[17] CCBs are antihypertensive and antianginal. They are prescribed for the treatment of angina due to coronary artery spasm, chronic stable angina, hypertension, and arrhythmias. They inhibit the movement of calcium ions across the membranes of cardiac and arterial muscle cell to slowdown the velocity of transmission of cardiac impulse, depression of myocardial contractility, and dilation of coronary arteries. As a result, they relax blood vessels and increase the supply of blood and oxygen to the heart while reducing its workload. (Futher details about CCBs are available at http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202107.html and Lippincott's Nursing Drug Guide, 2005).

Other CCBs are shown in Table 1. CCBs are antihypertensives and are generally prescribed for the treatment of hypertension, chronic stable angina, arrhythmias, and heart valve disorders.

The summary statistics in Table 3 show that CCBs are generally prescribed for chronic conditions with a treatment length of at least five years reported by forty-four percent of patients. Ninety percent of patients are insured and thirty-two percent are male. Patients' average age is forty-three years and per capita income is $20,752. CCBs, when compared at sample means to other drugs used for the same conditions, are typically associated with higher drug expenditures ($57.70 versus $41.60) but lower nondrug expenditures ($662.50 versus $1236.30).

Table 8 presents the regression results measuring the impact of Calcium Channel Blockers on drug and nondrug expenditures. The results for the control variables show that the demographic and insurance variables have some effect on drug expenditures, though these effects are generally small. The control variables generally impact nondrug medical expenditures, and most of these effects are large and significant. Insured patients have significantly higher nondrug expenditures than uninsured patients. Male patients experience higher nondrug expenditures of $135.72, and various population groups experience substantial differences in nondrug expenditures.

The empirical results in Table 8 show that CCBs cost somewhat more than other drugs but lead to significant reductions in nondrug expenditures. Patients regularly using CCBs experience increased total drug expenditures of $7.92, but decreased total non-drug expenditures of $223.49 compared to patients sporadically using CCBs. Comparing patients regularly using CCBs with patients who never use CCBs, the group never using CCBs on average saves $14.32 (=$(7.92-(-$6.40)) in drug expenditures but experience an increase of $70.89

Table 8

Calcium Channel Blockers
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	8.648	-216.385	7.920	-223.494	8.305	-208.329
	(1.093)‡	(72.518)‡	(1.112)‡	(71.687)‡	(1.104)‡	(72.084)‡
Other Drugs	-6.265	-102.320	-6.403	-152.597	-5.807	-148.028
	(0.527)‡	(55.981)*	(0.560)‡	(55.764)‡	(0.529)‡	(56.325)‡
Income	0.000	-0.002	0.000	-0.001	0.000	0.000
	(0.000)‡	(0.001)	(0.000)†	(0.001)	(0.000)‡	(0.001)
Male	1.125	223.543	1.611	135.722	1.001	141.825
	(0.478)†	(61.291)‡	(0.514)‡	(66.674)†	(0.500)†	(68.723)†
Private Insurance	3.685	483.047	3.780	472.624	4.181	398.923
	(0.644)‡	(69.179)‡	(0.696)‡	(75.980)‡	(0.692)‡	(76.273)‡
Medicare	7.315	190.570	8.482	265.338	7.581	108.566
	(1.601)‡	(93.772)†	(1.781)‡	(103.680)†	(1.715)‡	(102.307)
Medicaid	2.237	357.487	2.043	394.039	0.161	308.418
	(0.749)‡	(67.261)‡	(0.811)†	(72.639)‡	(0.704)	(72.963)‡
Uninsured	-0.167	-62.885	0.700	-90.948	0.101	-45.111
	(1.171)	(103.623)	(1.167)	(111.173)	(1.178)	(112.450)
Eskimo/Aleut	10.948	-4,242.223	12.597	-4,020.026	12.230	-4,248.219
	(6.837)	(2,573.193)*	(7.631)*	(2,603.127)	(7.697)	(2,596.222)
Asian	5.332	508.904	6.032	541.090	7.197	604.386
	(2.512)†	(162.372)‡	(2.820)†	(204.674)‡	(2.898)†	(214.187)‡
Black	3.796	816.618	5.382	792.308	3.160	677.732
	(2.152)*	(146.488)‡	(2.509)†	(189.577)‡	(2.568)	(200.381)‡
White	5.973	971.412	6.976	1,009.730	6.060	927.350
	(2.131)‡	(147.666)‡	(2.486)‡	(194.320)‡	(2.568)†	(205.193)‡
Other Race	-18.232	1,200.091	-5.667	1,551.894	-6.092	1,353.715
	(9.890)*	(1,041.881)	(7.688)	(811.965)*	(9.017)	(841.461)
Constant	75.547	8,073.432	85.452	9,913.010	95.472	9,662.076
	(18.073)‡	(3,461.455)†	(24.165)‡	(4,295.244)†	(27.333)‡	(4,406.881)†
ICD-9 Coefficients Reported in the Appendix.						
Observations	63900	63900	57695	57695	55086	55086
R-squared	0.03	0.12	0.03	0.13	0.03	0.13

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD-9 Codes, Condition Duration, Age and Education Year are suppressed and available upon request.

(=$(223.49-152.60)) in nondrug expenditures. Both the savings in drug costs and the increase in nondrug costs are measured at the medical event level and are highly significant.[18]

III.4.6. Fluoroquinolones

The first Fluoroquinolone, Norfloxacin, was introduced in 1986. During the next decade, there were many Fluoroquinolones introduced, such as Enoxacin in 1991, Levofloxacin in 1996 and Moxifloxacin in 1999. Table 1 provides the entire list of Fluoroquinolones with year of introduction.

Fluoroquinolones[19] are prescribed for a narrow range of conditions, for example, infectious and parasitic diseases of the genitourinary system. Cystitis, a bladder infection, and urinary tract disorders are the two most frequently observed conditions for which Fluoroquinolones are used, and they comprise more than half of our observations.

The summary statistics in Table 3 show that Fluoroquinolones are generally prescribed for conditions requiring short treatment length and moderate cost. Fifty-seven percent of the reported conditions have a treatment period of less than one year. Eighty-eight percent of patients are insured and twenty-nine percent of the patients are male. Patients' average age is forty-three and per capita income is $18,525. Unlike breakthrough drug classes described above, Fluoroquinolones are associated with both higher drug expenditures ($63.20 versus $29.50) and higher nondrug expenditures ($832.70 versus $418.90).

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[18] We also used a t-test to determine whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. The statistics in the drug expenditure equation is highly significant, 13.55 indicating that the coefficients on important drugs and other drugs are significantly different from each other. The statistics in the nondrug expenditure equation is not significant, 1.09.

[19] Fluoroquinolones are prescribed for the treatment of infections caused by susceptible gram negative bacteria, like E. coli. They work by killing bacteria or preventing their growth. Further details regarding Fluoroquinolones are available at See http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202656.html.

Table 9

Fluoroquinolones
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Independent Variables:						
Important Drugs	30.519	-427.470	31.455	-294.685	31.658	141.713
	(2.432)‡	(181.856)†	(2.584)‡	(190.719)	(2.613)‡	(182.199)
Other Drugs	-9.953	-539.017	-9.342	-436.255	-11.766	7.138
	(1.476)‡	(126.280)‡	(1.631)‡	(132.013)‡	(1.682)‡	(85.983)
Income	-0.000	-0.003	-0.000	-0.004	-0.000	-0.002
	(0.000)†	(0.002)	(0.000)*	(0.001)‡	(0.000)	(0.001)*
Male	2.775	360.170	3.924	406.386	3.795	371.022
	(1.194)†	(85.898)‡	(1.411)‡	(98.173)‡	(1.436)‡	(99.681)‡
Private Insurance	1.859	-87.183	3.212	23.643	-1.131	-125.241
	(1.681)	(90.823)	(1.876)*	(94.109)	(1.710)	(101.563)
Medicare	9.449	54.299	7.315	-219.994	4.445	-203.882
	(2.465)‡	(121.359)	(2.610)‡	(119.939)*	(2.683)*	(122.716)*
Medicaid	3.600	-240.935	5.792	-158.528	0.360	-182.731
	(1.967)*	(94.072)†	(2.170)‡	(89.009)*	(1.925)	(97.901)*
Uninsured	-3.096	490.554	-3.916	456.987	-0.299	454.147
	(1.975)	(107.074)‡	(2.193)*	(114.219)‡	(2.168)	(111.499)‡
Eskimo/Aleut	-3.774	71.462	-2.835	-369.146	-4.465	-290.416
	(5.506)	(247.170)	(5.522)	(328.606)	(5.824)	(237.966)
Asian	13.201	-79.771	14.489	-313.024	-3.310	528.181
	(5.226)†	(344.039)	(5.570)‡	(382.705)	(5.359)	(406.173)
Black	-1.629	339.234	-2.778	-32.177	0.258	182.722
	(3.911)	(182.530)*	(4.105)	(163.494)	(4.088)	(157.907)
White	1.754	167.028	0.943	10.928	1.267	-78.845
	(3.633)	(153.144)	(3.797)	(146.989)	(3.858)	(138.472)
Constant	44.699	-565.807	70.917	205.912	69.372	362.030
	(13.649)‡	(768.047)	(18.516)‡	(529.104)	(18.711)‡	(447.487)
ICD-9 Coefficients Reported in the Appendix.						
Observations	7337	7337	6317	6317	5053	5053
R-squared	0.19	0.17	0.21	0.17	0.19	0.12

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD-9 Codes, Condition Duration, Age and Education Year are suppressed and available upon request.

The regression results for Fluoroquinolones are presented in Table 9. These results show that the control variables are generally small in the drug expenditures equation. With the exception of the race variables, the demographic and insurance variables are generally large and

significant in the nondrug expenditures equation. Male patients experience increased total nondrug expenditures of $406.39. Income has a small, negative impact on total nondrug expenditures. Uninsured patients face higher total nondrug expenditures of $456.99.

In contrast to the results for the other breakthrough classes of drugs, the results for the Fluoroquinolones do not support the hypothesis of cost savings for nondrug medical expenditure. The results show that Fluoroquinolones are more expensive than other drugs - - the coefficients indicate that patients who regularly use Fluoroquinolones on average pay $31.46 more than patients who sporadically use them and pay $40.90 more than patients who never use them.

There is some weak evidence that there are cost savings from the use of Fluoroquinolones compared to some but not all groups. Specifically, the point estimate indicates a cost savings of $295 for patients regularly using Fluoroquinolones as compared to patients who sporadically use them. This difference, however, is not statistically significant. Nondrug expenditures, moreover, are lowest for the group that never uses Fluoroquinolones.

It is important to note the differences between Fluoroquinolones and other drugs under study. Fluoroquinolones are expensive antibiotics, and it may be that for this category expensive, leading edge drugs are used for more severe cases, which may also entail other complementary and expensive treatments. Still, regardless of the reason, the evidence does not point toward nondrug cost savings for this class of drugs.[20]

III.5. Conclusion

This chapter investigated impact of new drugs and drug classes on overall healthcare expenditures. The chapter provides a more flexible approach than the existing literature by

[20] We also used a t-test to determine whether the coefficients for the impact of important drugs on drug and nondrug expenditures are different from the coefficients on other drugs. The statistics in the drug expenditure equation is highly significant, 16.41 indicating that the coefficients on important drugs and other drugs are significantly different from each other. The statistics in the nondrug expenditure equation is not significant, 0.71

separately estimating the cost impact of important new groups of breakthrough drugs. The chapter also improves on the previously existing methodology by capturing the long term effects of using drugs rather than just focusing on contemporaneous medical expenditures associated with a single medical event.

Our analysis used a variant of Lichtenberg's (2001a) model where we have substantially improved the measure of new technologies and tightened the definition of drug use. We measure improvements in drug technology by determining whether patients regularly used drugs belonging to selected groups of breakthrough drugs. Our measure captures the fact that innovations emerge in waves and that drugs within a particular group are more similar therapeutically to each other than to other existing drugs. We then separately estimate for each group the impact of the group on drug and nondrug medical expenditures. This method improves on the previously existing literature because it allows for differences in the pace of innovation across therapeutic classes, differences in the cost impact, and measures long run effects. To measure long run effects, we created three groups of patients: those regularly using the breakthrough drugs, those sporadically using them, and those who never used them. We then identified conditions for which the drugs were regularly used.

The results confirm that with the exception of ACE Inhibitors breakthrough drugs are associated with higher drug expenditures. The results also show, however, that these breakthrough drug groups, with the exception of the Fluoroquinolones, are associated with very substantial reductions in nondrug expenditures. These reduced nondrug expenditures are typically many times larger than the increase in drug expenditures. Hence, the use of these groups of breakthrough drugs substantially reduce overall medical expenditures and have contributed to medical cost containment.

CHAPTER IV

NOVEL DRUGS AND HEALTH CARE EXPENDITURES

Prescription drug expenditures constitute an important account for each individual in the United States. The quality and effectiveness of drugs take place an important role in total health care expenditure. There is a conflict among researchers about the benefits and costs of newer and better drugs. Some researchers argue that newer and better drugs reduce hospital stays and provide significant cost savings. Another group of researchers argue that newer and better drugs are more expensive than older therapies and do not provide significant cost savings. In this chapter, we offered a new methodology by incorporating both the quality and the age of the drugs to capture their effects on total health care expenditures. We analyzed the impacts of the quality and the age of the drugs on the following therapeutic classes: Musculoskeletal system and connective tissue diseases, skin and subcutaneous tissue diseases, neoplasm, mental disorders, diseases of nervous system and sense organs, circulatory system diseases, respiratory system diseases, digestive system diseases, genitourinary system diseases.

IV.1. Introduction

The impact of newer and better drugs on overall healthcare expenditures is an important medical and economic question. Pharmaceutical firms spend billions of dollars developing new therapies, which are usually sold at a substantial premium over older therapies. Health plan and Medicare/Medicaid often restrict the use of newer therapies pointing to associated cost savings. These policies may lead to prescription cost savings, but run the risk of excluding therapies that lower total healthcare spending.

There are few studies discussing the impacts of drugs on total health care expenditures. The most influential of these studies (Lichtenberg, 2001a and 2002) shows that the replacement of older drugs by newer drugs reduce total medical expenditures. Duggan (2005), on the other hand, argued that the replacement of older drugs by newer, more expensive drugs may not decrease total medical expenditures by analyzing health care expenditures for antipsychotic drugs.

This chapter addresses this issue by extending the study of Lichtenberg (2001 and 2002). He measured the therapeutic advances of a drug by the number of years that drug had been on the market. This measurement is valuable but limited because it implicitly treats all drugs of comparable age as the same quality. Our approach is to look at both the quality and the age of the drugs to measure their impacts on pharmaceutical spending and total healthcare expenditures. We have used the FDA Drug Evaluation as our quality indicator.

In late 1975 the FDA formed a 3-tier rating system for prioritizing review of New Drug Applications (NDA). If the drug provided a significant gain over existing therapy, FDA classified that drug with an A rating, if the drug brought a modest gain then that drug was given a B rating and if the drug provided little or no gain over existing therapy, then it was given a C rating. In 1992 the FDA switched its rating system into 2 categories: P (priority) and S (standard). A priority drug would provide a significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease. We grouped those approved NDAs that had received an A or B rating with those NDAs that had received P rating to form a "priority-rated" category for our analysis. Similarly, we grouped NDAs that had been assigned a C rating by the FDA with NDAs that had been assigned an S rating to form a "standard-rated" category.

The impact of the quality and the age of the drugs may differ across conditions. For example, drugs prescribed for infectious diseases may totally have different impacts on health care expenditures than the drugs prescribed for mental disorders. While infectious diseases are cured with one or two purchase of prescriptions, however, mental disorders generally require long-term treatment. We analyzed the impacts of the quality and the age of the drugs on each therapeutic class separately based on their clinical modification of the 9th edition of International Classes of Diseases prepared by United States and adopted in 1979 (ICD-9-CM)[21]. ICD-9-CM categorizes diseases and injuries broadly into 18 categories. Availability of the data from Medical Expenditure Panel Survey (MEPS) allowed us to create unique data sets for only nine of them, namely; musculoskeletal system and connective tissue diseases, skin and subcutaneous tissue diseases, neoplasm, mental disorders, diseases of nervous system and sense organs, circulatory system diseases, respiratory system diseases, digestive system diseases, genitourinary system diseases.

Newer drugs generally make patients' life more comfortable by providing better and reliable treatment. Better and reliable treatment comes with a higher cost. This chapter studies if better and newer drugs are worth to pay higher prices. This chapter examines the change in total drug and nondrug expenditures when patients are on priority drugs and/or standard drugs. In this study, we offered a better methodology by incorporating the quality and the ages of the drugs to capture the effects of better and newer drugs on pharmaceutical spending and total healthcare expenditures. Our results confirm the empirical findings of Lichtenberg (2001a, 2002), Olson (2004) and Lu & Comanor (1998) by displaying that for some of the therapeutic categories, newer priority drugs are better and for some therapeutic categories newer standard drugs are

[21] For further information about ICD-9-CM codes, see the web site: http://www.cdc.gov/nchs/data/icd9/icdguide.pdf

better. Our results also support the empirical findings of Duggan (2005) by showing that newer drugs do not decrease total non-drug expenditures for mental disorders and diseases of the nervous system and sense organs.

The remaining of the chapter is as follows: Section-2 displays the model and its theoretical background. Section-3 provides details about the data set. The results are presented and discussed in section-4. The final section concludes.

IV.2. Model

The model we use is a variant of the model used by Lichtenberg (2001a and 2002). He estimated the effect of drug age on expenditures across the patients by using the random variations in prescribing behaviors of physicians and by controlling for many important attributes of the individuals, conditions, and prescriptions that influence outcomes and non-drug expenditures and that may be correlated with drug age.

The most important distinction between our approach and Lichtenberg's is that we incorporate the effects of both drug's age and quality on expenditures within patients. This measure offers a substantial improvement over drug age because multiple drugs introduced in a given year do not necessarily represent the same level of quality over existing therapies.

The second improvement we offer is to measure the impacts of drugs on total health care expenditures by determining whether drugs prescribed for a selected group of therapeutic classes. The random variations in prescribing behaviors of physicians and in patients' consumptions of drugs help us to analyze the effect of novel drugs on total drug and non-drug expenditures.

The third substantial improvement is that we measure the impact of drug usage on expenditures within patients. Lichtenberg measures drug input by examining differences in drug

and non-drug expenditures across patients while controlling for demographic variables such as sex, age, education and the like. Our specification tests favor the model with individual patient effects.

Our analysis incorporates each of these methodological improvements in measuring the effects of newer and better drugs on healthcare outcomes. We control the effects of the conditions by incorporating the condition duration and their ICD-9 codes. We also controlled both individuals' observed and unobserved characteristics by introducing an individual fixed effects variable. The model is as follows:

$$Y^{c}_{ij} = \alpha_i + \beta_1 (PRIORITY\_DRUG_{ij}) + \beta_2 \ln(AGE\_PRIORITY\_DRUG_{ij})$$
$$+ \beta_3 \ln(AGE\_STANDARD\_DRUG_{ij}) + \lambda_1 GENERIC_{ij}$$
$$+ \lambda_2 BEFORE\_1970_{ij} + \sum_c \theta_c CONDITION_{ijc} + \sum_d \delta_d CON\_DUR_{ijd} + \xi_j$$

where:

Y^{c}_{ij} is the category (c) of either prescription drug expenditures (c=DE) or total non-drug expenditure (c=NDE) associated with the j^{th} prescription consumed by person i.

$\alpha_i = 1$ for the i^{th} person, zero otherwise.

$PRIORITY\_DRUG_{ij} = 1$ if prescribed drug j consumed by person i is rated as priority drugs by FDA, otherwise zero.

$AGE\_PRIORITY\_DRUG_{ij}$ = the age of the priority drug j used by person i.

$AGE\_STANDARD\_DRUG_{ij}$ = the age of the standard drug j used by person i.

$GENERIC_{ij} = 1$ if the prescribed drug used by person i is generic, otherwise zero.

$BEFORE\_1970_{ij}$ = 1 if the prescribed drug consumed by person i was first approved by FDA before 1970, otherwise zero. Since FDA started classifying drugs after 1970, we assumed that all the drugs approved before 1970 were standard drugs and have controlled this effect by introducing a year dummy variable, BEFORE_1970.

$CONDITION_{ijc}$ = 1 if prescription drug j consumed by person i is prescribed for condition c, otherwise zero.

CON_DUR_{ijd} = 1 if the condition for which prescription drug j consumed by person i began d years ago, otherwise zero.

ξ_j is the disturbance term.

Estimates of parameters of β's are of interest here. Hereafter, the superscripts and subscripts are suppressed for notational conveniences.

IV.3. Data

We used Medical Expenditure Panel Survey (MEPS) data sets from 1996 to 2001. MEPS, which is cosponsored by the Agency for Health Care Research and Quality and the National Center for Health Statistics is a nationally representative survey of health care use, expenditures, sources of payments, insurance coverage and demographic characteristics for the U.S. civilian noninstitutionalized population. MEPS consist of three surveys: Household Component (HC), Medical Provider Component (MPC) and Insurance Component (IC). HC is the core survey and it establishes the basis for the MPC and part of the IC. These surveys jointly generate exceptionally rich datasets that provide national estimates of the level and distribution of health care use and expenditures, support health services research, and can be used to evaluate health care policy implications.

Our data set consists of the first five panels of MEPS from 1996 to 2001. First, we created our data set for each panel separately by merging the HC files, MPC files and IC files. Then, we calculated the expenditures associated with each condition, by event type using Condition-Event Link File.[22] And finally, we have used medical care index (1982-1984=0) and expressed all the dollar values in terms of year 2001.

Following the ICD-9-CM categorization of diseases and injuries and using ICD-9 codes within each category, we generate unique data sets for only 9 therapeutic classes, which are musculoskeletal system and connective tissue diseases, skin and subcutaneous tissue diseases, neoplasm, mental disorders, diseases of nervous system and sense organs, circulatory system diseases, respiratory system diseases, digestive system diseases, genitourinary system diseases.

The MEPS Prescribed Medicine Event file contains information about the amount paid for the each prescription, by source of payment but does not include information about the year in which the active ingredient was first approved by FDA. We have created a dataset by collecting information for some drugs from the Orange Book, Physician's Desk Reference 2003, Drug Facts and Comparisons 2003 and from a data set that was graciously provided to us by Frank L. Lichtenberg. Using National Drug Code, we merge this data file into Prescribed Medicine Event file so that we have information about the year in which the active ingredient was first approved by FDA. Finally, we have used the data set that was graciously provided to us by Joseph A. DiMasi to incorporate the quality of drugs into our data set.

IV.4. Empirical Results

The empirical analysis focuses on these different groups of important therapeutic categories, beginning with the Musculoskeletal System and Connective Tissue Diseases. All of

[22] For further information about the MEPS, see the web site: http://www.meps.ahrq.gov/

the data presented reflect event level outcomes, which mean average expenditures are per event and the regression coefficients reflect impact per event.

IV.4.1. Musculoskeletal System and Connective Tissue Diseases

Diseases of musculoskeletal system and connective tissue[23] include some of the well-known diseases such as arhtropathies, dorsopathies, osteopathies and rheumatism. Rheumatoid arthritis is a chronic disease of the joints, marked by inflammatory changes in the synovial membranes and articular structures, widespread fibrinoid degeneration of the collagen fibers in mesenchymal tissues, and by atrophy and rarefaction of bony structures.

Musculoskeletal system and connective tissue diseases are usually associated with longer treatment period and higher health care expenditures. Table 10 presents the descriptive statistics. These data reveal that 45.85 percent of conditions have more than five years of treatment period. Data also reveals that priority drugs occupy 14.63 percent of the prescriptions and generic drugs occupy 50.52 percent of prescriptions. Patients who use priority drugs experience higher drug expenditures but lover nondrug expenditures when compared to standard drugs. Data show that priority drugs when compared to standard drugs used for same condition, are typically associated with higher drug expenditures ($65.94 versus $34.59), but lower nondrug expenditures ($436.23 and $509.66).

Table 11 presents the regression results measuring the impact of priority and standard drugs on total drug and nondrug expenditures. The inspection of the results shows that control variables are generally significant and plausible. The estimated results also indicate that generic drugs have significant impact on health care expenditures. They decrease total drug and non-drug expenditures respectively by $18.96 and $90.99.

[23] Includes the diseases defined by ICD-9-CM codes from 710 to 739

Table 10

Summary Statistics for Various Therapeutic Classes of Diseases

ICD9 CODES		710-739	680-709	140-239	290-319	320-389	390-459	460-519	520-579	580-629
Average Healthcare Expenditures ($):										
Priority Drugs:	Drug Expenditures	$65.94	$85.07	$78.40	$85.56	$43.13	$64.87	$32.63	$78.17	$62.92
	Nondrug Expenditures	436.23	256.65	5170.38	302.79	287.40	1290.25	470.97	926.34	790.97
Standard Drugs:	Drug Expenditures	$34.59	$36.85	$47.43	$50.84	$32.01	$38.03	$32.47	$39.13	$30.11
	Nondrug Expenditures	509.66	248.81	4294.46	331.54	333.76	1319.08	510.54	953.57	601.25
Percentage of Reported Condition Durations:										
Less than one year		24.2	34.38	47.07	18.25	25.9	22.80	28.43	49.87	47.24
1 year		9.65	18.47	20.14	12.06	10.82	11.05	8.46	15.17	13.73
2 years		6.73	6.39	8.35	7.89	6.66	7.22	5.71	6.86	4.63
3 years		4.3	4.55	7.4	8.05	6.86	6.54	5.4	2.7	4.1
4 years		5.79	3.27	3.86	4.21	2.55	4.66	3.63	3.17	6.24
5 years		3.48	5.26	1.16	4.78	6.66	4.58	4.05	0.88	3.83
More than 5 years		45.85	27.70	12.01	44.75	40.56	43.14	44.32	21.35	20.23
Percentage of Priority Drugs		14.63%	14.12%	13.14%	21.14%	27.84%	18.37%	26.83%	22.37%	13.72%
Percentage of Generic Drugs		50.52%	44.43%	42.03%	35.95%	47.77%	37.49%	46.45%	40.98%	42.14%
Number of Patients in Sample		6276	3816	1352	3151	9124	6760	16073	3810	4405

Note: Definitions of ICD9 Codes are as follow = [710-739] : Musculoskeletal system and connective tissue diseases; [680-709]: Skin and subcutaneous tissue diseases; [140-239]: Neoplasm; [290-319]: Mental disorders; [320-389]: Nervous system and sense organs diseases; [390-459]: Circularity system diseases; [460-519]: Respiratory system diseases; [520-579]: Digestive system diseases; [580-629]: Genitourinary system diseases.

Table 11

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Musculoskeletal System and Connective Tissue

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	16.424	(6.66)‡	-337.147	(2.44)†
Log Age of Priority Drugs	-12.055	(14.68)‡	227.319	(4.94)‡
Log Age of Standard Drugs	-8.061	(12.29)‡	84.543	(2.30)†
Generic	-18.975	(30.22)‡	-90.997	(2.59)‡
Year Before 1970	-16.902	(16.19)‡	-11.702	(0.20)
ICD-9-CODS				
711	-13.571	(0.27)	304.135	(0.11)
712	22.686	(1.31)	93.035	(0.10)
714	-13.971	(3.89)‡	-315.899	(1.57)
715	-16.103	(4.24)‡	-34.520	(0.16)
716	-8.617	(2.79)‡	155.336	(0.90)
717	-15.637	(1.63)	615.398	(1.15)
718	-6.477	(0.63)	961.754	(1.66)*
719	-13.751	(4.03)‡	550.102	(2.88)‡
720	-21.423	(2.26)†	87.133	(0.16)
721	-12.249	(2.69)‡	-206.889	(0.81)
722	-17.235	(5.24)‡	170.694	(0.93)
723	-17.518	(3.86)‡	582.962	(2.29)†
724	-9.982	(3.12)‡	474.428	(2.65)‡
725	2.408	(0.26)	-521.164	(1.02)
726	-11.838	(2.94)‡	136.271	(0.60)
727	-13.571	(3.16)‡	304.135	(1.26)
728	-5.496	(1.26)	845.520	(3.46)‡
729	-13.651	(4.45)‡	31.213	(0.18)
730	-1.110	(0.06)	2,445.384	(2.50)†
731	12.850	(0.74)	4,099.924	(4.20)‡
732	0.000	(.)	0.000	(.)
733	-16.245	(4.78)‡	-597.511	(3.14)‡
734	34.179	(1.54)	16.327	(0.01)
735	-15.422	(1.24)	-339.751	(0.49)
736	20.565	(1.31)	3,973.369	(4.53)‡
737	-12.706	(1.60)	-139.932	(0.31)
738	-7.737	(0.38)	1,294.704	(1.15)
Constant	98.342	(11.97)‡	-89.429	(0.19)
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Control For Condition Duration	Yes		Yes	
Observations	32405		32405	
R-squared	0.54		0.61	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration are suppressed.

The empirical results show that priority drugs cost more than standard drugs. The estimated results from Table 11 show that priority drugs are on average $16 more expensive than standard drugs when both are one year old. Estimated results also reveal that replacement of fifteen years old priority (standard) drugs with five years old priority (standard) drug increases total drug expenditures respectively by $12.06 ($8.06).

The empirical results also show that priority drugs reduce nondrug expenditures by substantially more than the increase in drug expenditures. The estimated results from Table 2 indicate that one-year old priority drugs reduce total nondrug expenditures by $337.15 compared to one-year old standard drugs prescribed for the same conditions. The results support the empirical findings of Lichtenberg (2001a and 2002) by showing that a unit decrease in the log age of priority and standard drugs will decrease total non-drug expenditures respectively by $227.32 and $84.54. It is straight forward to show that 10.6 years old or younger priority drugs are associated with lower non-drug expenditures when compared to standard drugs prescribed for the same condition.

Our empirical findings suggest that policymakers of any insurance or health care agency should allow patients to have access to the younger priority drugs prescribed for musculoskeletal system and connective tissue diseases, because they provide significant cost benefits over any standard drugs or older priority drugs.

IV.4.2. Skin and Subcutaneous Tissue Diseases

Seborrheic, atopic dermatitis and eczema are some of the well-know skin and subcutaneous disease[24]. Seborrheic dermatitis is a chronic inflammatory disease of the skin characterized by moderate erythema, dry, moist, or greasy scaling, and yellow crusted patches on

[24] Includes the diseases defined by ICD-9-CM codes from 680 to 709.

various areas, especially the scalp.[25] It generally appears first as small patches of and then progressing to involve the entire scalp with exfoliation of excessive amounts of dry scales.

Diseases of skin and subcutaneous tissue are usually associated with shorter treatment period; one or two prescriptions usually cure the condition. Descriptive statistics presented in Table 10 show that 34.38 percent of the conditions has less than one year treatment period. Inspections of the data also show that priority drugs and generic drugs occupy respectively 14.12 and 44.43 percent of the prescriptions and 71.55. Priority drugs are usually cost more than standard drugs. Priority drugs when compared to standard drugs used for same condition, are associated with higher drug expenditures ($85.07 and $36.85), but slightly lower nondrug expenditures ($248.81 and $256.65).

Table 12 presents the empirical results regarding the impact of priority and standard drugs on total drug and nondrug expenditures. The results for control variables show that generic drugs decrease both drug and nondrug expenditures ($20.62 and $70.20) when compared to branded drugs prescribed for the same condition. The results also show that the dummy the coefficient on "Year Before 1970" is only significant for drug expenditures regression and imply that drugs approved before 1970 decrease drug expenditures.

The results also show that priority drugs are associated with increased drug expenditures but even larger reductions in nondrug expenditures when compared to standard drugs. The estimated results from Table 12 show that one-year old priority drugs are on average $126.48 more expensive than one-year old standard drugs prescribed for the same condition. Similarly, the replacements of fifteen years old priority (standard) drugs with five years old priority (standard) drugs increase total drug expenditures by $38.43 ($3.00).

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[25] http://www.icd9data.com/2006/Volume1/680-709/690-698/690/default.htm provides more details.

Table 12

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Skin and Subcutaneous Tissue

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	126.476	(10.69)‡	-562.303	(3.97)‡
Log Age of Priority Drugs	-38.425	(9.74)‡	228.435	(4.84)‡
Log Age of Standard Drugs	-3.001	(1.53)	38.903	(1.66)*
Generic	-20.616	(9.91)‡	-70.199	(2.82)‡
Year Before 1970	-20.979	(7.17)‡	-9.468	(0.27)
Constant	230.165	(2.62)‡	-273.850	(0.26)
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	9915		9915	
R-squared	0.70		0.87	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

Even though priority drugs are associated with higher drug expenditures, however, they are associated with even larger reductions in nondrug expenditures when compared to standard drugs. The estimated results in Table 12 indicate that one-year old priority drugs reduce total nondrug expenditures by $562.30 when compared to one-year old standard drugs prescribed for the same conditions. The results also suggest that both younger priority and standard drugs decrease nondrug expenditures when compared to older drugs. A unit decrease in the log age of priority and standard drugs decrease total non-drug expenditures respectively by $228.44 and $38.90 indicating that younger priority drugs are superior over younger standard drugs regarding cost-benefit analysis. It is straightforward to show those 19.46 years old or younger priority

drugs decrease nondrug expenditures more than standard drugs of any age prescribed for the same conditions. Our empirical findings suggest that policymakers of any insurance or health care agency should allow patients to have access to the younger priority drugs prescribed for skin and subcutaneous tissue diseases, because they provide crucial cost savings over any standard drugs or older priority drugs.

IV.4.3. Neoplasm

Neoplasm[26] includes a wide range of conditions, for example, malignant neoplasm of lip, oral cavity, digestive organs, respiratory organs, genitourinary organs and hematopoietic tissue. Malignant neoplasm of esophagus is a well-known disease of malignant growth of cells in the esophagus. This is a common cancer in the in France, Switzerland with highest mortality rates seen in China, Singapore, and Puerto Rico.[27] Excessive consumption of ethanol and cigarette increases the risk for development of this cancer, acting in a synergistic fashion.

The drugs prescribed for neoplasm are usually more expensive than other drugs, may be because of higher research and development cost involved. The average total drug and nondrug expenditures vary across conditions for each treatment method. Inspections of the summary statistics presented in Table 10 show that patients using priority drugs experience higher drug and nondrug expenditures. Priority drugs when compared to standard drugs used for same condition, are associated with higher drug expenditures ($78.40 and $47.43), and higher nondrug expenditures ($5170.38 and $4294.46). Priority (generic) drugs occupy only 13.14 (42.03) percent of the prescriptions. Data also reveals that 47.07 conditions have reported less than one year treatment period and 13.14 (42.03) percent of the prescribed prescriptions belong to priority (generic) drugs.

[26] Includes the diseases defined by ICD-9-CM codes from 140 to 239.
[27] http://www.icd9data.com/2006/Volume1/140-239/150-159/150/default.htm provides further details.

Table 13 presents the regression results regarding the impact of priority and standard drugs on drug and nondrug expenditures associated with neoplasm. Contrary to the previous therapeutic categories, the estimated results show those younger standards are more expensive than priority drugs. Estimated results from Table 13 show that priority drugs are on average $22.85 cheaper than standard drugs when both are one-year old and prescribed for the same conditions. The results also indicate that both younger standard and priority drugs increase total drug expenditures and the results are highly significant. A unit decrease in log of drug age increase total drug expenditures by $ 38.54 and $31.67 respectively for standard and priority drugs.

Table 13

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Neoplasm

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	-22.854	(1.06)	762.067	(0.30)
Log Age of Priority Drugs	-31.673	(4.24)‡	1,699.351	(1.92)*
Log Age of Standard Drugs	-38.537	(9.39)‡	2,128.864	(4.39)‡
Generic	-30.602	(8.70)‡	-14.937	(0.04)
Year Before 1970	-10.072	(1.66)*	-2,443.631	(3.42)‡
Constant	275.148	(2.34)†	30,787.730	(2.21)†
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	6594		6594	
R-squared	0.45		0.89	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

The empirical results in Table 13 show that standard drugs lead to significant reduction in total health care expenditures. One-year old standard drugs reduce total drug expenditures by $762.08 when compared to one-year old priority drugs prescribed for the same condition. Estimated results reveal that replacement of older drugs with younger drugs significantly decrease total nondrug expenditures. For example, the replacement of fifteen years old priority (standard) drugs with five years old priority (standard) drug significantly decrease total nondrug expenditures by $1699.35 ($2128.86). These results imply that prescribing younger standard drugs for neoplasm diseases over priority drugs of any age and older standard drugs significantly decrease total health care expenditures.

IV.4.4. Mental Disorders

Organic psychotic conditions, neurotic and personal disorders and mental retardations are common disease of mental disorders[28]. A well-know mental disorder is Schizophrenia, which is a severe emotional disorder of psychotic depth characteristically marked by a retreat from reality with delusion formation, hallucinations, emotional disharmony, and regressive behavior.[29]

Table 10 presents summary statistics for mental disorders. The data reveals that 21.14 (35.955) percent of prescriptions is chosen from priority (generic) drugs. Priority drugs when compared to standard drugs are associated with higher drug expenditures ($85.55 and $50.54), but slightly lower nondrug expenditures ($302.79 and $331.54). The mental disorder diseases are generally chronic and require long-term drug treatment. Inspection of the data reveals that the treatment duration for 44.75 percent of conditions is more than five years.

Table 14 presents the regression results regarding the impact of priority and standard drugs on drug and nondrug expenditures associated with mental disorders. The estimated results

[28] Includes the diseases defined by ICD-9-CM codes from 290 to 319.
[29] http://www.icd9data.com/2006/Volume1/290-319/295-299/295/default.htm provides further details.

from Table 14 show that both younger priority and standard drugs increase drug expenditures. One-year old priority drugs increase drug expenditures by $47.84 when compared to one-year old standard drugs prescribed for the same condition. Similarly, a unit decrease in log of drug age increase total drug expenditures by $ 38.06 and $28.07 respectively for priority and standard drugs.

Table 14

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Mental Disorders

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	47.834	(9.24)‡	-13.605	(0.09)
Log Age of Priority Drugs	-38.062	(19.23)‡	-92.870	(1.57)
Log Age of Standard Drugs	-28.065	(31.42)‡	-85.743	(3.20)‡
Generic	-30.119	(26.16)‡	97.619	(2.83)‡
Year Before 1970	8.084	(5.15)‡	31.536	(0.67)
Constant	83.813	(1.11)	1,054.906	(0.47)
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	26799		26799	
R-squared	0.52		0.61	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

The empirical results from Table 14 show neither priority drugs no standard drugs provides cost saving on total nondrug expenditures. The results are only statistically significant for the standard drugs. The estimated results show that younger standard drugs increase total

nondrug expenditures. A unit decrease in the log of the age of standard drugs increase total non-drug expenditures by $85.74.

The empirical results presented in Table 14 support a Duggan (2005) finding, which is despite newer drugs increase prescription drug expenditures; however, they do no reduce spending on other types of medical care services for antipsychotic diseases. Our results suggest that older standard drugs for the mental disorders provides more saving when compared to younger standard drugs or both younger and older priority drugs.

IV.4.5. Diseases of Nervous System and Sense Organs

Inflammatory, hereditary and degenerative disease of the nervous system and disorders of eye and adnexa and peripheral nervous system are the common diseases of this category[30]. One of the well-know disease of this category is Parkinson's disease, which is a progressive disorder of the nervous system marked by muscle tremors, muscle rigidity, decreased mobility, stooped posture, slow voluntary movements, and a mask-like facial expression.[31]

The condition duration and treatment mode for nervous system and sense organs diseases are very close to mental disorders. Summary statistics presented in Table 10 show that 40.65 percent of the reported conditions have more than five years of treatment period. Data reveal that priority (generic) drugs occupy 27.84 (47.77) percent of the total dispensed prescriptions. The average total drug and nondrug expenditures vary across conditions for each treatment method. Data shows that patients using priority drugs experience higher drug expenditures. Priority drugs when compared to standard drugs used for same condition, are associated with higher drug expenditures ($43.13 and $32.01), but lower nondrug expenditures ($287.40 and $333.76).

[30] Includes the diseases defined by ICD-9-CM codes from 320 to 389.
[31] http://www.icd9data.com/2006/Volume1/320-389/330-337/332/default.htm provides further details.

Table 15 presents the regression results regarding the impact of priority and standard drugs on total drug and nondrug expenditures associated with nervous system and sense organs diseases. The empirical results presented in Table 15 show that the priority drugs are generally more expensive and increase total drug expenditures. Estimated results show that one-year old priority drugs when compared to standard drugs of same age increase drug expenditures by $15.02. Similarly, a unit decrease in the log of drug age increases total drug expenditures by $12.83 and $10.53 for priority and standard drugs respectively; suggesting that younger drugs are expensive and increase total drug expenditures. The results are statistically significant and support the existing studies.

Table 15

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Nervous System And Sense Organs

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	15.019	(3.10)‡	356.857	(2.60)‡
Log Age of Priority Drugs	-12.821	(8.47)‡	-112.175	(2.62)‡
Log Age of Standard Drugs	-10.529	(8.33)‡	6.624	(0.18)
Generic	-23.834	(19.11)‡	-87.127	(2.47)†
Year Before 1970	-8.899	(4.36)‡	118.644	(2.05)†
Constant	23.897	(0.30)	-3,439.784	(1.51)
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	28113		28113	
R-squared	0.59		0.79	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

The empirical results presented in Table 15 show that priority drugs increase total nondrug expenditures too. Estimated results from Table 15 indicate that one-year old priority drugs when compared to standard drugs of same age increase total drug expenditures by $356.86. The replacement of 15 year-old priority drug with a 5.5 year old priority drug increases total nondrug expenditures by $112.18. These empirical results support both Duggan (2005) and Olson (2004) empirical findings, which are respectively; younger drugs do not reduce total health care expenditures and novel drugs increase total health care expenditures.

IV.4.6. Circulatory System Diseases

Most frequently observed diseases of circularity system[32] are ischemic hearth diseases, cerebrovascular diseases and acute and chronic rheumatic diseases. One of the well-known diseases of circularity system is angina pectoris, which is the symptom of paroxysmal pain consequent to myocardial ischemia usually of distinctive character, location and radiation; provoked by a transient stressful situation during which the oxygen requirements of the myocardium exceed that supplied amount coronary circulation.[33]

Circularity system diseases are widespread among the elder people and associated with long term treatment periods. Inspection of summary statistics presented in Table 10 show that the 43.19 percent of reported conditions have at least five years of treatment history. Data show that priority (generic) drugs occupy 18.37 (37.49) percent of total dispensed prescriptions. Descriptive statistics reveal that average total drug and nondrug expenditures vary across conditions for each treatment methods. Patients who use priority drugs face higher drug expenditures. The average total drug expenditures per priority and standard drug prescription are respectively $64.87 and $38.03. On the other hand, patients on priority drugs experience slightly

[32] Includes the diseases defined by ICD-9-CM codes from 390 to 459.
[33] http://www.icd9data.com/2006/Volume1/390-459/410-414/413/default.htm provides further details.

lower non-drug related health care expenditures. The average total non-drug expenditures per prescription on priority and standard drugs are respectively $1290.25 and $1319.08.

The empirical results presented in Table 16 show that priority drugs are very expensive drugs. The estimated results in Table 16 show that one-year old priority drugs increase drug expenditures by $42.66 when compared to one-year old standard drugs prescribed for the same conditions. The results also show that both younger priority and standard drugs are expensive and increase total drug expenditures. A unit decrease in the log of the ages of the priority and the standard drugs increase total drug expenditures respectively by $23.20 and $10.14. The results are highly statistically significant and plausible.

Table 16

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Circulatory System

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	42.658	(18.58)‡	-357.827	(1.77)*
Log Age of Priority Drugs	-23.200	(31.00)‡	101.688	(1.55)
Log Age of Standard Drugs	-10.144	(17.93)‡	-78.876	(1.59)
Generic	-21.681	(45.09)‡	61.736	(1.46)
Year Before 1970	-17.600	(19.68)‡	205.074	(2.61)‡
Constant	124.134	(4.71)‡	5,710.454	(2.47)†
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	57239		57239	
R-squared	0.53		0.78	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

The empirical results presented in Table 16 also show that priority drugs decrease total nondrug expenditures substantially more when compared standard drugs. The estimated results displayed in Table 16 imply that one-year old priority drugs when compared to standard drugs of same age decrease total nondrug expenditures by $357.83 more. It is straightforward to show that any priority drugs younger than 34 years (=exp (357.83 / 101.68)) decrease total nondrug expenditures. Contrary to the empirical findings of Lichtenberg 2001a and 2002, replacements of older standard drugs with younger ones do not decrease total health care expenditures. Our empirical findings suggest that policymakers of any insurance or health care agency should allow patients to have access to the priority drugs. They may lead to higher prescription cost, but decrease the risk of higher nondrug expenditures when compared to standard drugs.

IV.4.7. Respiratory System Diseases

Acute respiratory infections, chronic obstructive pulmonary diseases and pneumoconioses are some of the common respiratory diseases[34]. Asthma is one of the well-known and widespread respiratory system diseases. It is a form of bronchial disorder associated with airway obstruction, marked by recurrent attacks of paroxysmal dyspnea, with wheezing due to spasmodic contraction of the bronchi.[35]

Respiratory system diseases are usually associated with moderate term treatment and observable across all ages. Analysis of the descriptive statistics presented in Table 10 show that 44.32 of conditions have history of more than five years. Data also reveals that priority (generic) drugs occupy 26.83 (46.45) percent of the prescriptions and priority drugs are associated with drug but slightly lower nondrug expenditures when compared to standard drugs. The average

[34] Includes the diseases defined by ICD-9-CM codes from 460 to 519.
[35] http://www.icd9data.com/2006/Volume1/460-519/490-496/493/default.htm provides further details.

drug and nondrug expenditures per priority (standard) drug prescription are respectively $32.63 and $470.97 ($32.46 and $510.54).

The empirical results presented in Table 17 shows that priority drugs costs more than standard drugs but lead to significant reductions in nondrug expenditures. Patients using one-year old drugs over one-year old standard drugs experience increased total drug expenditures by $41.89, but decreased total nondrug expenditures of $310.57. The estimated results also show that younger priority drugs increase total drug expenditures but decrease total nondrug expenditures by substantially more. The replacement of a 15 year-old priority drug with a 5.5 year-old priority drug increases drug expenditures by $ 23.98, but decreases total nondrug expenditures by $142.79. The results are highly statistically significant and plausible.

Table 17

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Respiratory System

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	41.885	(16.24)‡	-310.571	(1.95)*
Log Age of Priority Drugs	-23.984	(27.64)‡	142.789	(2.67)‡
Log Age of Standard Drugs	-4.891	(8.99)‡	17.297	(0.52)
Generic	-18.195	(32.83)‡	-93.375	(2.73)‡
Year Before 1970	-21.200	(23.10)‡	62.710	(1.11)
Constant	82.543	(4.37)‡	-397.830	(0.34)
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	57232		57232	
R-squared	0.54		0.86	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

The estimated coefficients on standard drugs are not large in magnitude for drug expenditures regression and not significant for nondrug expenditures regression. It is easy to show that 9.5 years old or younger priority drugs - which includes 29.46 percent of the priority drugs in our sample- decrease total health care expenditures when compared to standard drugs prescribed for the same condition. Contrary to the empirical findings of Lichtenberg 2001a and 2002, our empirical results show that there is no cost benefit through prescription of younger standard drugs. The empirical findings suggest that having access to the priority drugs decrease the total healthcare expenditures.

IV.4.8. Digestive System Diseases

The most common diseases of digestive systems[36] are oral cavity, esophagus, gastric and peptic ulcers, appendicitis and other diseases of intestines and peritoneum. The defects in the mucosa barrier cause peptic ulcer, which occurs in the regions of the gastrointestinal tract which come into contact with gastric liquid containing pepsin and gastric acid.[37]

Digestive system diseases are widespread among the elder people and associated with moderate term treatment periods. Table 10 displays the descriptive statistic. Inspection of the data shows that only 21.35 percent of reported condition duration is associated with more than five years of treatment period. Data also show that while priority drugs occupy only 22.37 percent of the dispensed prescriptions; generic drugs, however, occupy majority of the drugs, 40.38 percent of total prescriptions. Data reveals that priority drugs are more expensive than standard drugs. The average drug and non-drug expenditures per priority (standard) drug prescription are respectively $78.17 and $924.34 ($39.13 and $953.57).

[36] Includes the diseases defined by ICD-9-CM codes from 520 to 579.
[37] http://www.icd9data.com/2006/Volume1/520-579/530-537/533/default.htm provides further details.

Table 18 presents the regression results regarding the impact of both priority and standard drugs on total drug and nondrug expenditures associated with diseases of digestive systems. The empirical results presented in Table 18 show that the priority drugs are very expensive and increase total drug expenditures. Estimated results show that one-year old priority drugs when compared to standard drugs of same age dispensed for the same conditions increase total drug expenditures by $50.21. Similarly, a unit decrease in the log of drug age increases total drug expenditures by $31.92 for priority drugs and by $17.22 for standard drugs suggesting that younger priority drugs are much more expensive than standard drugs of same ages. The results are statistically significant and plausible.

Table 18

Analysis of Impacts of Quality and Age Of Drugs on Total Health Care Expenditures Associated with Diseases of Digestive System

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	50.208	(7.57)‡	89.133	(0.27)
Log Age of Priority Drugs	-31.917	(13.29)‡	42.770	(0.35)
Log Age of Standard Drugs	-17.217	(12.74)‡	121.752	(1.79)*
Generic	-22.534	(16.72)‡	-132.774	(1.96)†
Year Before 1970	-10.973	(4.75)‡	-55.238	(0.48)
Constant	127.581	(2.61)‡	8,576.797	(3.49)‡
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	13279		13279	
R-squared	0.66		0.77	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

Empirical results presented in Table 18 show, however, that priority drugs do not decrease total nondrug expenditures and coefficients on priority drugs are not statistically significant. Estimated results in Table 18 indicate that younger standard drugs significantly decrease the total nondrug expenditures. The replacement of a 15 year-old standard drug with a 5.5 year-old standard drug decreases total non-drug expenditures by $121.75 and the results are highly statistically significant. These results support the findings of Lichtenberg 2001a and 2002 by displaying that newer drugs are more expensive than older drugs. Our results also reveal that despite priority drugs provide a significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease, they, however, may not decrease total health care expenditures.

IV.4.9. Genitourinary System Diseases

Nephritis, nephrotic syndrome, diseases of male genital organs and inflammatory disease of female pelvic organs are the most common diseases of genitourinary system[38]. One of the well-know disease of this category is solitary cyst of breast, which appear as a single large cyst in one breast, multifocal, or bilateral in fibrocystic breast disease. It occurs as a result of a fluid-filled closed cavity or sac that is lined by an epithelium and found in the breast.[39]

Genitourinary system diseases are usually observed among the elder patients and associated with shorter treatment period. Inspection of the summary statistics presented in Table 10 reveals that only 20.23 percent of the conditions have more than five years treatment period. Analysis of the data also show priority drugs occupy only 13.72 percent of total dispensed prescriptions and they are generally sold at a substantial premium over standard drugs. The

[38] Includes the diseases defined by ICD-9-CM codes from 580 to 629.
[39] http://www.icd9data.com/2006/Volume1/580-629/610-611/610/default.htm includes futher details.

average total drug and non-drug expenditures per priority (standard) drug prescription are respectively $62.92 and $790.97 ($30.11 and $601.25).

Table 19 presents the regression results regarding the impact of both priority and standard drugs on total drug and nondrug expenditures associated with diseases of genitourinary systems. The estimated results presented in Table 19 shows that both younger priority and standard drugs increase total drug expenditure about the same scale. A unit decrease in log age of the drugs increases total drug expenditures by $12.15 and $13.72 respectively for the priority and standard drugs.

Table 19

Analysis of Impacts of Quality and Age of Drugs on Total Health Care Expenditures Associated with Diseases of Genitourinary System

Dependent Variable	Total Drug Expenditures		Total Non-Drug Expenditures	
	Coefficient	t-value	Coefficient	t-value
Priority Drugs	4.393	(0.46)	165.260	(0.55)
Log Age of Priority Drugs	-12.147	(3.60)‡	109.631	(1.02)
Log Age of Standard Drugs	-13.721	(7.22)‡	179.912	(2.98)‡
Generic	-19.111	(11.26)‡	-67.267	(1.25)
Year Before 1970	-12.961	(4.31)‡	-181.572	(1.90)*
Constant	281.146	(3.22)‡	-28,489.932	(10.29)‡
Control for Separate "ICD9 Codes" Dummy Variables	Yes		Yes	
Control for Separate "Condition Duration" Dummy Variables	Yes		Yes	
Observations	12273		12273	
R-squared	0.52		0.79	

Absolute value of t statistics in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for ICD9 Codes and Condition Duration are suppressed and available upon request.

Similar to digestive system diseases, priority drugs do not provide cost savings and coefficients on priority drugs are not statistically significant. However, younger standard drugs significantly decrease the total non-drug expenditures. Estimated results in Table 19 indicate that the replacement of a 15 year-old standard drug with a 5.5 year-old standard drug decreases total non-drug expenditures by $179.91. These results support the empirical findings of Lichtenberg (2001a and 2002) by displaying those newer drugs are more expensive than older drugs. Our results also suggest policymakers or physicians that prescribing younger standard drugs over novel drugs provides significant cost benefits despite novel drugs have therapeutic advances over standard drugs.

IV.6. Conclusion

Contrary to literature and FDA evaluations, newer and better drugs do not always reduce health care expenditure. The nature of therapeutic conditions coupled with their duration yield us to conclude that newer priority drugs decrease overall health care expenditures for diseases of skin and subcutaneous tissue, musculoskeletal system and connective tissue, circulatory system and respiratory system. The empirical findings presented in this chapter show that newer standard drugs decrease overall health care expenditures for diseases of digestive system, genitourinary system and neoplasm. Newer drugs do not decrease total health care expenditures for mental disorders and diseases of the nervous system and sense organs.

CHAPTER V

CONCLUSION

This dissertation explores two important aspects of new pharmaceuticals and health care expenditures: The impact of breakthrough drug classes on total health care expenditures and the correlation between FDA Drug Classification and health care expenditures. Empirical evidence presented in this dissertation shows that drugs belonging to new drug classes provide significant advances in treatment of conditions compared to other drugs. The dissertation provides a more flexible approach than the existing literature by separately estimating the cost impact of important new groups of breakthrough drugs. The dissertation also improves on the previously existing methodology by capturing the long term effects of using drugs rather than just focusing on contemporaneous medical expenditures associated with a single medical event. Our unique approach in measuring innovation allowed us to analyze the cost savings associated with major groups of new drug classes, which are Selective Serotonin Reuptake Inhibitors, Statins, Ace Inhibitors, H2 Antagonists, Proton Pump Inhibitors, Calcium Channel Blockers, and Fluoroquinolones.

The results presented in this dissertation confirm that with the exception of ACE Inhibitors breakthrough drugs are associated with higher drug expenditures. The results also show, however, that these breakthrough drug groups, with the exception of the Fluoroquinolones, are associated with very substantial reductions in nondrug expenditures. These reduced nondrug expenditures are typically many times larger than the increase in drug expenditures. Hence, the use of these groups of breakthrough drugs substantially reduce overall medical expenditures and have contributed to medical cost containment.

This dissertation also explores the relations between FDA Therapeutic Drug Classification and total health care expenditures. This dissertation incorporates both the quality and the age of the drugs to capture their impacts on total health care expenditures. The availability of the data allowed us to examine the following therapeutic classes: Musculoskeletal system and connective tissue diseases, skin and subcutaneous tissue diseases, neoplasm, mental disorders, diseases of nervous system and sense organs, circulatory system diseases, respiratory system diseases, digestive system diseases, genitourinary system diseases.

The empirical results suggest that newer priority drugs significantly reduce total health care expenditures for diseases of the circulatory system, diseases of the respiratory system, diseases of the skin and subcutaneous tissue, and diseases of the musculoskeletal system and connective tissue; newer standard drugs, however, provide cost savings for neoplasm, diseases from digestive and genitourinary systems. Both newer priority and standard drugs do not provide any cost savings for mental disorders and diseases of the nervous system and sense organs.

Contrary to literature and FDA evaluations, newer and better drugs do not always reduce health care expenditure. The nature of therapeutic conditions coupled with their duration yield us to conclude that newer priority drugs decrease overall health care expenditures for diseases of skin and subcutaneous tissue, musculoskeletal system and connective tissue, circulatory system and respiratory system. The empirical findings presented in this chapter show that newer standard drugs decrease overall health care expenditures for diseases of digestive system, genitourinary system and neoplasm. Newer drugs do not decrease total health care expenditures for mental disorders and diseases of the nervous system and sense organs.

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APPENDIX A

Table A.1

A Hypothetical Example to Demonstrate the Methodology of Chronological Orderings of the Patients

Patient Identifier	Purchase Round	ICD-9 Codes	Drug Name
09155028	2	311	XANAX
09155028	2	311	PROZAC
09155028	2	311	PROZAC
09155028	2	311	XANAX
09155028	2	311	XANAX
09155028	3	311	CLOMIPHENE
09155028	3	311	PROZAC
09155028	3	311	BUSPAR
09155028	5	311	PROZAC
09809019	1	311	ZOLOFT
09809019	1	311	ZOLOFT
09809019	1	311	ZOLOFT
09809019	2	311	MEDROXYPROGESTERONE
09809019	2	311	MEDROXYPROGESTERONE
01726016	3	311	ALPRAZOLAM
01726016	4	311	PAXIL
01726016	4	311	PAXIL
72986019	1	311	PAXIL
72986019	2	311	PAXIL
72986019	2	311	PAXIL
01751012	1	311	EFFEXOR
01751012	1	311	EFFEXOR
01751012	2	311	EFFEXOR
01751012	2	311	EFFEXOR

We develop three categories of drug use. The first category consists of the patients who frequently switch drugs over time. The second category consists of patients who use important drugs all the time or switch drugs *only once*. The third category consists of patients who never use important drugs. To clarify the categorization of patients, we chose five patients diagnosed with the same condition of Depressive Disorders (ICD-9 Code 311). The patient with personal identification number 09155028 is placed in category 1 due to frequent switches between important drugs and other drugs over time. The patients with personal identification number 09809019 and 01726016 switched between important drugs and other drugs *only once*; while the patient with personal identification number 72986019 always used important drugs. All three of these patients are grouped as category 2 patients. The last patient with personal identification number 01751012 has been placed under category 3, since that patient never used important drugs.

Table A.2

Summary Statistics for 4, 5 and 6 Percent Samples
Various Break-Through Drug Categories

		Selective Serotonin Reuptake Inhibitors			Statins			ACE Inhibitors		
		4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample
Year of First Introduction		1987	1987	1987	1989	1989	1989	1981	1981	1981
Demographics:										
Mean Age		43.8	44.5	44.3	59.4	57.6	58.3	58.3	59.5	59.3
Mean Education Year		11.3	11.3	11.3	11.0	11.5	11.7	11.2	11.1	11.2
Mean Income($)		$17,629	$17,386	$17,487	$20,512	$22,883	$24,301	$20,809	$20,218	$20,277
Percentage of Male Patients		31.0	32.5	31.3	46.1	47.8	46.9	43.9	43.2	43.0
Percentage of White Patients		86.4	86.9	87.1	83.0	85.4	86.2	79.2	77.7	77.7
Percentage of Medicare enrollees		22.3	23.9	23.0	48.6	42.1	41.9	43.9	44.9	45.6
Percentage of Medicaid enrollees		22.3	23.8	23.2	17.2	14.0	13.0	15.8	16.3	16.3
Percentage of Private Insurance Enrollees		58.1	56.0	56.7	58.3	64.5	66.4	59.1	58.0	57.5
Percentage of Patients with No Insurance Coverage		12.0	12.2	12.4	7.7	7.6	7.2	9.0	9.2	9.3
Average Healthcare Expenditures ($):										
Important	Drug Expenditures	$81.6	$81.4	$81.3	$86.1	$85.1	$83.4	$44.5	$44.5	$44.6
Drugs:	Nondrug Expenditures	298.7	306.2	313.1	81.9	714.6	225.8	802.3	833.7	837.5
Other	Drug Expenditures	51.8	53.3	50.3	40.7	42.4	42.9	44.9	43.6	43.6
Drugs:	Nondrug Expenditures	413.9	455.4	442.9	123.2	1,979.4	450.6	900.7	943.8	965.0
Number of Patients in Sample		3,701	3,098	2,978	3,033	2,111	1,483	8,401	7,846	7,147

		H2 Antagonists Proton Inhibitors			Calcium Channel Blockers			Fluoroquinolones		
		4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample
Year of First Introduction		1977	1977	1977	1981	1981	1981	1986	1986	1986
Demographics:										
Mean Age		45.2	45.2	45.2	57.8	58.6	59.1	43.0	43.0	41.2
Mean Education Year		9.8	9.8	9.8	11.0	11.1	11.1	10.6	10.5	10.5
Mean Income($)		18,468	18,468	18,468	20,479	20,752	20,658	19,204	18,525	18,090
Percentage of Male Patients		41.3	41.3	41.3	43.0	43.2	42.4	30.9	28.7	21.6
Percentage of White Patients		84.2	84.2	84.2	79.8	79.4	79.1	87.4	87.6	88.0
Percentage of Medicare enrollees		28.1	28.1	28.1	44.6	45.4	46.1	24.7	25.6	22.5
Percentage of Medicaid enrollees		19.6	19.6	19.6	16.1	15.7	15.8	13.9	13.9	14.3
Percentage of Private Insurance Enrollees		60.2	60.2	60.2	58.7	58.9	58.5	65.1	65.1	65.1
Percentage of Patients with No Insurance Coverage		10.8	10.8	10.8	9.1	8.9	8.8	12.3	12.1	12.5
Average Healthcare Expenditures ($):										
Important	Drug Expenditures	94.5	95.2	95.3	57.9	57.7	57.8	64.0	63.2	62.9
Drugs:	Nondrug Expenditures	767.9	696.6	535.8	682.2	662.5	625.1	878.1	832.7	440.7
Other	Drug Expenditures	40.5	41.3	36.6	41.7	41.6	41.1	28.9	29.5	24.2
Drugs:	Nondrug Expenditures	1,635.2	1,688.1	1,189.9	1,256.7	1,236.3	1,160.2	527.2	418.9	372.6
Number of Patients in Sample		6,773	6,773	6,773	7,616	6,976	6,581	3,098	2,746	2,442

Table A.3

Icd-9 Codes for 4, 5 and 6 Percent Samples
Various Break-Through Drug Categories

Selective Serotonin Reuptake Inhibitors			Statins			ACE Inhibitors			H2 Antagonists & Proton Inhibitors			Calcium Channel Blockers			Fluoroquinolones		
ICD-9 Codes			ICD-9 Codes			ICD-9 Codes			ICD-9 Codes			ICD-9 Codes			ICD-9 Codes		
4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample
070	070	070	272	272	272	185			5	5	5	38	38	38	5	5	5
153	153	153	276			250	250	250	41	41	41	276	276	276	136	136	
295	295		410	410		251	251	251	42	42		289	289		185	185	
296	296	296	411			272			78	78	78	294	294	294	380	380	380
300	300	300	412	412	412	276	276	276	151	151	151	298	298	298	562	562	562
301	301	301	414	414		298	298	298	185			401	401	401	590	590	590
303	303	303	429			309	309	309	198	198	198	402	402	402	592	595	595
304	304	304	431	431	431	401	401	401	199	199	199	410	410	410	595		
307	307	307	433	433	433	410	410	410	202	202		413	413	413	597	597	597
308	308	308	442	442	442	411	411		203	203	203	414	414	414	599	599	599
309	309	309	444	444		412	412	412	208	208	208	424	424	424	601	601	601
312	311	311	447	447	447	414	414	414	211	211	211	426	426	426	602	602	
319	312	312	781			416	416	416	269	269	269	427	427	427	608	608	608
331			V12	V12		424	424	424	306	306		428			614		
333			V42	V42	V42	426	426	426	309			429	429	429	682		
346	333	333	V47	V47		427	427		356	356	356	435	435	435	730	730	730
347			V70	V70		428	428	428	411			436	436	436			
348	347	347	V72	V72	V72	429	429	429	414			438	438	438			
440	348		V77	V77	V77	435	435	435	441	441	441	440	440	440			
623	440		V82	V82	V82	436	436	436	442	442	442	441	441	441			
625	623	623				438	438		444			442	442				
783	625	625				444	444	444	454	454	454	443	443	443			
799						454	454	454	458	458	458	444	444				
854	799	799				459	459	459	459			447					
V12	854	854				514	514		507	507	507	454	454	454			
V40	V12	V12				524	524	524	530	530	530	458					
V62	V40	V40				560	560	560	531	531	531	459					
V65	V62	V62				586	593		532	532	532	514					
						593	737	737	533	533	533	531					
						737	753	753	535	535	535	578	578				
						753	790	790	536	536	536	586	586				
						790	791	791	537	537	537	593	593	593			
						791	796	796	553	553	553	600	600				
						796	797		555	555	555	710					

Table A.3 (Continued)

Selective Serotonin Reuptake Inhibitors			Statins			ACE Inhibitors			H2 Antagonists Proton Inhibitors			Calcium Channel Blockers			Fluoroquinolones		
4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample	4 % Sample	5 % Sample	6 % Sample
						797			558	558	558	747	747	747			
						V42	V42		562	562	562	781					
						V47	V47	V42	564	564	564	785	785	785			
						V72	V72	V47	569	569	569	790					
									573	573	573	796	796	796			
									574	574	574	V12	V12	V12			
									575	575	575	V42	V42	V42			
									577	577	577	V45	V45	V45			
									578	578	578	V49	V49	V49			
									593	593		V70	V70				
									682			V72	V72	V72			
									707	707	707						
									714								
									786								
									787	787	787						
									789	789	789						
									805								
									850	850	850						
									V42	V42	V42						
									V43	V43	V43						
									V45	V45	V45						
									V47	V47	V47						
									V53								
									V56	V56	V56						
									V76	V76	V76						

Table A.4

Statins
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes						
272	2.433	-1,444.461				
	(1.382)*	(95.918)‡				
276	4.785	915.993				
	(4.801)	(254.307)‡				
410	1.523	3,948.794	-3.797	5,434.941		
	(1.490)	(260.673)‡	(1.515)†	(250.913)‡		
411	7.300	3,843.937				
	(4.079)*	(908.470)‡				
412	-13.294	1,762.808	-22.058	2,876.183	-18.103	3,152.949
	(2.696)‡	(462.017)‡	(2.794)‡	(447.092)‡	(2.921)‡	(422.964)‡
414	4.305	1,344.644	2.580	3,006.599		
	(2.323)*	(282.466)‡	(2.091)	(291.819)‡		
431	14.053	-83.489	14.160	1,382.708	11.748	3,014.434
	(4.817)‡	(732.855)	(4.986)‡	(771.441)*	(5.210)†	(692.535)‡
433	3.837	-865.618	2.341	987.089	-1.929	1,715.007
	(4.351)	(494.345)*	(4.403)	(479.522)†	(4.820)	(523.397)‡
442	9.420	2,559.216	3.873	4,155.006	0.340	4,080.339
	(4.394)†	(658.535)‡	(4.512)	(655.310)‡	(4.630)	(689.584)‡
444	-0.487	4,934.336	-3.646	6,490.118		
	(2.650)	(484.454)‡	(2.662)	(483.388)‡		
447	-0.828	343.809	-0.715	1,589.236	-1.208	2,023.731
	(4.114)	(518.611)	(4.027)	(526.471)‡	(4.086)	(506.360)‡
781	9.410	-961.621				
	(3.319)‡	(146.075)‡				
V12	2.730	-1,468.157	1.239	641.522		
	(4.305)	(266.502)‡	(4.531)	(316.327)†		
V42	28.535	750.809	23.098	3,528.432	17.581	2,549.848
	(10.508)‡	(819.784)	(9.392)†	(852.429)‡	(8.565)†	(814.743)‡
V47	11.275	-536.123	7.062	1,088.361		
	(3.556)‡	(224.256)†	(3.549)†	(242.192)‡		
V70	14.731	-1,280.012	12.684	516.573		
	(4.314)‡	(156.770)‡	(4.216)‡	(131.091)‡		
V72	6.968	-1,181.810	2.897	406.131	2.309	97.296
	(1.619)‡	(90.038)‡	(1.504)*	(89.818)‡	(1.573)	(45.202)†
V77	-12.081	-2,663.447	-12.909	-1,328.058	-14.578	-852.047
	(3.222)‡	(337.413)‡	(3.216)‡	(274.970)‡	(3.402)‡	(186.672)‡
V82	14.373	-1,849.683	38.277	-21.206	37.090	-329.401
	(14.317)	(257.947)‡	(10.574)‡	(347.057)	(12.214)‡	(299.635)

Table A.4 (Continued)

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Control for Separate "Condition Duration" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Age" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Education Year" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

Table A.5

Ace Inhibitors
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes						
185	25.790	951.632				
	(4.540)‡	(252.589)‡				
250	3.443	198.017	3.353	187.633	3.306	186.887
	(0.542)‡	(44.585)‡	(0.541)‡	(44.314)‡	(0.540)‡	(43.998)‡
251	16.391	8,202.254	15.713	8,204.968	15.053	8,232.455
	(6.066)‡	(1,130.246)‡	(6.050)‡	(1,119.883)‡	(6.068)†	(1,109.630)‡
272	13.717	-318.998				
	(0.857)‡	(21.546)‡				
276	-0.166	1,815.568	-0.161	1,847.772	-0.376	1,748.621
	(4.225)	(215.188)‡	(4.224)	(215.439)‡	(4.272)	(232.967)‡
298	15.523	494.846	15.215	490.144	16.319	481.623
	(6.039)†	(185.858)‡	(6.061)†	(186.950)‡	(6.149)‡	(188.544)†
309	31.770	855.861	31.773	841.121	30.521	814.193
	(4.801)‡	(220.431)‡	(4.825)‡	(223.265)‡	(4.881)‡	(222.920)‡
410	0.406	4,636.714	0.016	4,535.529	0.354	4,502.939
	(1.015)	(216.299)‡	(1.016)	(216.811)‡	(1.020)	(217.790)‡
411	5.778	5,221.913	4.317	5,138.958		
	(3.894)	(828.573)‡	(3.894)	(826.903)‡		
412	-11.607	3,267.074	-12.976	3,152.717	-12.558	3,133.044
	(2.019)‡	(516.397)‡	(2.030)‡	(513.522)‡	(2.028)‡	(510.030)‡
414	4.191	1,936.045	4.213	1,915.882	4.374	1,897.560
	(1.702)†	(214.397)‡	(1.707)†	(213.943)‡	(1.711)†	(214.272)‡
416	3.419	8,715.757	3.401	8,609.717	2.633	8,711.369
	(4.959)	(776.843)‡	(4.933)	(771.362)‡	(4.965)	(784.835)‡
424	-5.685	6,886.781	-5.505	6,853.279	-5.636	6,812.689
	(1.923)‡	(678.107)‡	(1.926)‡	(676.139)‡	(1.934)‡	(675.049)‡
426	-4.294	822.439	-4.424	781.500	-4.478	756.695
	(4.227)	(316.783)‡	(4.210)	(315.863)†	(4.200)	(315.737)†
427	-4.889	507.499	-4.883	488.488		
	(0.943)‡	(61.582)‡	(0.942)‡	(62.192)‡		
428	-6.835	1,795.962	-7.083	1,734.839	-6.933	1,718.381
	(1.026)‡	(199.841)‡	(1.027)‡	(200.849)‡	(1.035)‡	(202.219)‡
429	-0.131	1,070.634	-0.287	1,043.432	-0.292	1,021.341
	(0.801)	(70.040)‡	(0.803)	(71.135)‡	(0.810)	(67.971)‡
435	4.309	950.522	4.519	843.031	4.832	862.548
	(3.242)	(221.090)‡	(3.219)	(225.316)‡	(3.236)	(224.904)‡

Table A.5 (Continued)

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
436	-3.330	3,892.327	-3.780	3,796.796	-3.254	3,785.669
	(1.007)‡	(340.953)‡	(1.013)‡	(338.290)‡	(1.018)‡	(336.120)‡
438	-7.295	460.375	-7.423	471.494		
	(3.076)†	(122.600)‡	(3.062)†	(126.566)‡		
444	-0.355	4,851.070	-0.716	4,814.663	-0.846	4,814.301
	(2.246)	(352.637)‡	(2.245)	(352.192)‡	(2.248)	(352.276)‡
454	-5.231	2,665.179	-5.461	2,720.715	-5.253	2,757.827
	(5.018)	(511.745)‡	(5.034)	(511.475)‡	(5.044)	(513.302)‡
459	1.481	712.140	1.633	737.492	1.687	708.677
	(1.663)	(125.675)‡	(1.662)	(125.955)‡	(1.664)	(126.330)‡
514	-5.418	1,635.097	-5.539	1,647.832		
	(2.553)†	(395.669)‡	(2.552)†	(395.333)‡		
524	-25.308	458.257	-25.343	487.358	-26.092	566.137
	(2.220)‡	(127.644)‡	(2.207)‡	(134.083)‡	(2.234)‡	(142.827)‡
560	-13.469	4,189.310	-14.045	4,206.740	-14.513	4,219.873
	(4.811)‡	(754.794)‡	(4.844)‡	(754.928)‡	(4.832)‡	(756.570)‡
586	25.053	4,123.555				
	(11.513)†	(571.261)‡				
593	10.310	854.134	10.346	877.126		
	(2.958)‡	(150.945)‡	(2.957)‡	(151.396)‡		
737	-6.641	946.307	-6.308	983.742	-6.411	1,004.662
	(3.541)*	(395.135)†	(3.541)*	(392.999)†	(3.554)*	(387.617)‡
753	6.159	525.066	5.007	481.782	3.182	419.838
	(7.178)	(259.865)†	(7.177)	(263.411)*	(7.410)	(316.019)
790	-0.721	147.619	-1.074	136.709	-1.140	138.567
	(2.132)	(85.605)*	(2.137)	(88.111)	(2.146)	(92.091)
791	21.580	281.464	21.648	308.469	21.259	331.675
	(6.687)‡	(114.198)†	(6.627)‡	(124.005)†	(6.682)‡	(133.206)†
796	-3.013	-51.881	-2.816	-35.563	-2.942	-51.945
	(1.093)‡	(33.466)	(1.098)†	(35.191)	(1.103)‡	(37.468)
797	-3.439	209.719	-3.446	242.852		
	(2.765)	(83.507)†	(2.774)	(85.830)‡		
V42	40.541	1,348.100	42.370	1,301.272	40.184	1,288.414
	(11.086)‡	(536.457)†	(11.107)‡	(539.996)†	(11.065)‡	(552.880)†
V47	4.437	583.706	4.852	629.953	4.631	562.124
	(2.883)	(156.693)‡	(2.886)*	(158.808)‡	(2.914)	(170.744)‡
V72	5.934	-11.920	6.215	19.573		
	(1.093)‡	(29.574)	(1.091)‡	(30.594)		

Table A.5 (Continued)

Dependant Variable	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Control for Separate "Condition Duration" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Age" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Education Year" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

Table A.6

H2 Antagonists And Proton Pump Inhibitors
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes						
-8	7.517	2,686.313	11.364	2,347.299		
	(2.973)†	(278.047)‡	(2.738)‡	(270.339)‡		
041	-3.165	-287.312	0.454	-520.244	-2.583	-495.498
	(3.204)	(161.555)*	(3.010)	(178.578)‡	(3.460)	(153.313)‡
151	-23.952	16,336.309	-24.245	14,626.991	-22.074	17,083.473
	(5.704)‡	(2,300.239)‡	(6.324)‡	(2,263.402)‡	(5.918)‡	(2,310.862)‡
185	21.976	-468.620				
	(4.925)‡	(297.894)				
198	-0.184	-2,189.488	-3.308	-1,857.360	-11.315	-837.352
	(6.734)	(279.899)‡	(8.109)	(296.358)‡	(8.472)	(271.447)‡
199	1.209	-150.298	4.457	-377.528	-0.367	800.904
	(3.698)	(345.852)	(3.839)	(391.050)	(4.104)	(314.568)†
202	2.987	10,889.295	3.928	10,162.932		
	(4.621)	(1,911.983)‡	(4.750)	(1,822.551)‡		
203	19.274	385.082	19.602	-150.411	7.711	259.480
	(11.633)*	(347.255)	(11.909)*	(398.104)	(12.090)	(388.776)
208	-3.062	2,543.580	0.923	2,148.458	-3.618	2,849.324
	(6.652)	(1,096.434)†	(6.985)	(1,146.003)*	(6.927)	(919.533)‡
211	-9.729	253.750	-5.163	289.247	-6.200	314.557
	(4.287)†	(331.647)	(4.059)	(359.780)	(4.302)	(304.163)
269	7.498	-498.100	13.876	-732.277	8.082	-394.480
	(21.698)	(332.514)	(21.746)	(378.558)*	(21.794)	(356.379)
306	-1.225	-469.109	3.353	-289.445		
	(5.137)	(186.031)†	(4.853)	(200.997)		
309	39.987	-443.280				
	(5.600)‡	(260.788)*				
356	19.419	-1,388.877	24.645	-665.792	22.533	-441.974
	(5.765)‡	(427.690)‡	(5.693)‡	(546.733)	(5.882)‡	(234.805)*
41	-0.994	3,045.765				
	(3.684)	(1,243.917)†				
411	5.967	4,052.816				
	(4.564)	(902.160)‡				
414	7.610	1,079.941				
	(2.703)‡	(258.553)‡				
42	109.647	-706.796	109.520	-948.967		
	(9.226)‡	(196.513)‡	(9.325)‡	(219.398)‡		

Table A.6 (Continued)

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
441	-4.038	7,108.807	5.145	7,781.451	3.733	7,541.492
	(4.589)	(1,323.467)‡	(4.745)	(1,235.159)‡	(4.946)	(1,184.048)‡
442	7.537	2,214.191	9.604	2,412.351	2.866	2,451.130
	(4.758)	(636.786)‡	(4.621)†	(641.483)‡	(4.884)	(623.296)‡
444	2.067	3,853.142				
	(3.038)	(423.743)‡				
454	-2.109	1,815.060	2.153	1,822.585	-1.451	1,527.579
	(5.417)	(527.465)‡	(5.380)	(501.356)‡	(5.474)	(473.484)‡
458	-1.241	379.717	5.217	128.683	2.761	-218.848
	(4.010)	(321.950)	(3.964)	(359.979)	(4.104)	(309.015)
459	4.020	-365.098				
	(2.598)	(194.510)*				
5	-2.841	106.379	1.871	66.086	-0.949	-282.998
	(3.848)	(226.700)	(3.651)	(269.032)	(3.949)	(192.651)
507	-8.402	-871.200	-12.633	-469.560	-18.438	299.612
	(8.406)	(489.196)*	(9.362)	(428.966)	(9.549)*	(290.508)
530	11.289	-614.446	12.151	-699.169	8.398	-272.094
	(2.631)‡	(149.753)‡	(2.329)‡	(159.294)‡	(2.712)‡	(116.108)†
531	9.487	-729.962	11.313	-944.702	7.561	-212.517
	(3.067)‡	(170.895)‡	(2.985)‡	(188.108)‡	(3.160)†	(135.406)
532	4.191	-308.990	7.665	-411.692	4.854	-626.031
	(12.269)	(340.303)	(12.266)	(304.206)	(12.095)	(306.935)†
533	6.504	-417.310	6.859	46.387	11.381	362.183
	(5.723)	(333.357)	(6.018)	(343.921)	(5.950)*	(308.808)
535	8.244	-413.282	8.830	-701.585	6.698	-274.801
	(2.937)‡	(199.983)†	(2.731)‡	(237.203)‡	(3.022)†	(130.259)†
536	-3.312	95.296	-1.479	11.896	-4.021	-34.164
	(2.343)	(151.873)	(1.999)	(163.876)	(2.435)*	(127.638)
553	-1.810	149.024			-1.790	409.925
	(2.519)	(160.073)			(2.529)	(134.656)‡
555	13.545	-204.485	13.565	-696.366	12.561	368.407
	(4.296)‡	(269.221)	(4.262)‡	(298.901)†	(4.429)‡	(239.123)
558	3.920	175.831	7.813	483.473	6.334	161.137
	(3.206)	(258.816)	(3.034)†	(279.430)*	(3.265)*	(239.153)
562	-5.957	428.905	-2.423	570.646	-4.585	586.781
	(2.757)†	(220.491)*	(2.438)	(228.744)†	(2.813)	(204.368)‡
564	0.063	-659.008	3.892	-679.127	0.145	-555.683
	(2.918)	(158.594)‡	(2.654)	(171.447)‡	(2.967)	(121.173)‡

Table A.6 (Continued)

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
569	3.124	220.658	7.245	348.957	4.241	129.496
	(4.757)	(199.838)	(4.616)	(217.672)	(4.790)	(187.184)
573	3.438	621.042	5.268	428.588	4.725	128.034
	(4.556)	(218.615)‡	(4.464)	(238.356)*	(4.567)	(192.428)
574	-5.967	2,749.643	-4.017	2,505.964	-6.795	2,493.244
	(3.283)*	(403.566)‡	(3.099)	(426.213)‡	(3.344)†	(373.124)‡
575	-6.012	399.054	-5.189	30.126	-7.281	867.722
	(3.064)†	(287.454)	(2.922)*	(308.001)	(3.093)†	(237.839)‡
577	4.111	778.932	4.362	762.682	0.498	1,395.846
	(5.594)	(372.516)†	(5.235)	(378.297)†	(5.233)	(378.907)‡
578	0.829	849.494	5.391	497.774	0.032	1,196.798
	(4.511)	(473.663)*	(4.384)	(516.056)	(4.594)	(417.082)‡
593	12.599	224.674	17.644	397.415		
	(3.598)‡	(196.978)	(3.439)‡	(213.233)*		
682	0.572	515.369				
	(3.363)	(250.632)†				
707	9.550	-327.883	10.487	-581.170	8.980	-414.477
	(2.786)‡	(173.322)*	(2.609)‡	(185.160)‡	(2.843)‡	(154.797)‡
714	1.297	-759.538				
	(2.392)	(146.927)‡				
78	15.274	-280.367	18.663	-639.791	19.176	-470.166
	(4.650)‡	(198.082)	(4.459)‡	(224.769)‡	(4.557)‡	(178.367)‡
786	-4.506	456.649				
	(2.154)†	(155.435)‡				
787	2.598	-301.472	6.059	-271.991	3.480	-340.565
	(3.483)	(142.952)†	(3.274)*	(154.792)*	(3.708)	(118.370)‡
789	-4.505	89.385	-1.908	145.471	-3.317	136.734
	(2.942)	(184.574)	(2.719)	(207.660)	(3.013)	(141.386)
805	-0.447	2,077.803	4.104	2,221.523		
	(3.401)	(437.198)‡	(3.228)	(438.294)‡		
850	-8.205	594.439	-6.320	156.490	-10.606	263.315
	(3.931)†	(294.499)†	(3.904)	(306.355)	(4.120)†	(274.374)
V42	21.208	721.592	27.494	630.278	29.334	1,902.720
	(10.948)*	(617.977)	(10.744)†	(692.436)	(10.671)‡	(612.281)‡
V43	3.457	2,193.155	4.818	1,826.423	3.584	2,188.753
	(7.465)	(774.880)‡	(7.392)	(767.083)†	(7.452)	(786.687)‡
V45	-5.713	-1,094.420	-1.228	-1,155.014	-0.819	-700.613
	(4.059)	(270.242)‡	(4.058)	(307.339)‡	(4.216)	(226.196)‡

Table A.6 (Continued)

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
V47	5.415	-347.945	9.814	-174.033	6.789	-272.608
	(3.740)	(214.077)	(3.763)‡	(236.742)	(3.932)*	(196.073)
V53	-7.004	-594.790				
	(3.428)†	(261.413)†				
V56	10.678	-1,152.534	5.347	-1,058.595	5.968	160.511
	(8.938)	(362.942)‡	(8.950)	(453.629)†	(9.004)	(177.056)
V76	8.109	-1,145.510	10.204	-1,085.970	9.402	-630.280
	(3.517)†	(211.108)‡	(3.637)‡	(279.333)‡	(3.744)†	(168.868)‡
Control for Separate "Condition Duration" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Age" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Education Year" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

Table A.7

Calcium Channel Blockers
Analysis of Impact on Health Care Expenditures

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Dependant Variable	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes						
276	2.339	1,102.390	2.400	1,066.074	1.777	1,070.293
	(4.208)	(141.651)‡	(4.222)	(149.108)‡	(4.227)	(152.866)‡
289	15.952	1,849.302	16.428	1,853.216		
	(4.871)‡	(325.611)‡	(4.872)‡	(323.948)‡		
294	7.432	178.130	8.299	-78.303	8.538	71.331
	(5.861)	(682.524)	(5.907)	(670.438)	(5.868)	(672.603)
298	17.034	229.405	16.264	187.199	15.769	255.752
	(6.153)‡	(216.163)	(6.192)‡	(208.962)	(6.171)†	(208.410)
38	5.495	7,702.429	6.295	7,679.520	6.520	7,700.774
	(5.087)	(2,461.496)‡	(5.116)	(2,434.669)‡	(5.157)	(2,430.594)‡
402	-20.328	3,652.028	-19.649	3,608.922	-20.724	3,559.597
	(3.441)‡	(1,592.599)†	(3.495)‡	(1,585.852)†	(3.524)‡	(1,593.218)†
410	-0.152	5,057.474	-0.273	5,048.425	-0.186	5,049.964
	(0.978)	(221.134)‡	(0.991)	(224.236)‡	(0.986)	(225.235)‡
413	-0.710	756.357	-0.264	765.016	-0.628	849.414
	(1.318)	(156.931)‡	(1.321)	(159.460)‡	(1.322)	(158.807)‡
414	4.574	1,718.740	4.351	1,705.285	4.335	1,733.536
	(1.773)‡	(213.487)‡	(1.776)†	(213.780)‡	(1.778)†	(213.731)‡
424	-2.627	6,730.146	-2.917	6,698.257	-3.609	6,702.187
	(1.986)	(672.068)‡	(1.995)	(668.783)‡	(1.990)*	(668.938)‡
426	-3.002	636.718	-2.980	656.189	-4.408	598.782
	(4.277)	(326.929)*	(4.287)	(327.021)†	(4.282)	(325.703)*
427	-4.012	196.338	-3.783	219.835	-4.031	249.868
	(0.944)‡	(61.112)‡	(0.942)‡	(63.057)‡	(0.944)‡	(63.367)‡
428	-6.125	1,721.690				
	(1.033)‡	(213.120)‡				
429	-0.462	1,110.507	-0.467	1,131.302	-0.364	1,155.097
	(0.812)	(70.331)‡	(0.821)	(70.390)‡	(0.823)	(70.254)‡
435	6.389	676.607	7.167	614.973	6.566	553.476
	(3.226)†	(238.845)‡	(3.253)†	(244.773)†	(3.240)†	(246.237)†
436	-3.769	4,500.751	-3.790	4,460.302	-3.185	4,535.726
	(1.004)‡	(347.089)‡	(1.025)‡	(333.116)‡	(1.023)‡	(331.049)‡
438	-1.283	4,814.027	-1.892	4,946.280	-1.213	4,978.196
	(3.902)	(704.572)‡	(3.943)	(712.805)‡	(3.941)	(719.842)‡
440	-2.376	2,798.360	-2.857	2,771.044	-3.573	2,848.715
	(2.126)	(475.979)‡	(2.144)	(476.435)‡	(2.136)*	(475.703)‡

Table A.7 (Continued)

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Dependant Variable	Total Drug Expenditures	Total Non-Drug Expenditures
441	-6.055	7,835.129	-5.470	7,661.469	-5.968	7,579.262
	(3.839)	(1,229.745)‡	(3.850)	(1,216.154)‡	(3.834)	(1,209.420)‡
442	7.954	3,417.543	8.268	3,412.409		
	(4.311)*	(673.658)‡	(4.332)*	(675.751)‡		
443	5.461	695.602	3.926	730.938	2.909	761.975
	(5.429)	(213.748)‡	(5.274)	(215.336)‡	(5.157)	(215.097)‡
444	-0.042	5,056.107	-0.091	5,062.133		
	(2.226)	(399.345)‡	(2.226)	(399.643)‡		
447	2.806	1,611.458				
	(4.173)	(384.990)‡				
454	-3.771	2,820.085	-3.698	2,836.105	-3.799	2,812.275
	(4.987)	(516.014)‡	(4.972)	(516.509)‡	(4.959)	(514.134)‡
458	-3.060	818.283				
	(3.418)	(284.105)‡				
459	2.474	615.953				
	(1.689)	(130.042)‡				
514	-3.186	1,556.244				
	(2.452)	(360.118)‡				
531	22.944	409.502				
	(2.049)‡	(86.734)‡				
578	-2.775	1,980.682	-2.612	1,879.249		
	(3.766)	(418.457)‡	(3.767)	(427.547)‡		
586	36.866	5,206.878	36.129	5,268.675		
	(15.056)†	(732.488)‡	(15.092)†	(734.947)‡		
593	11.416	853.705	11.050	744.543	10.723	764.088
	(2.953)‡	(148.876)‡	(2.978)‡	(160.250)‡	(3.003)‡	(166.064)‡
600	8.476	385.873	8.218	451.531		
	(2.755)‡	(168.322)†	(2.761)‡	(170.411)‡		
710	1.106	930.527				
	(3.040)	(159.354)‡				
747	-11.279	4,977.037	-11.816	5,092.546	-12.256	5,109.623
	(3.108)‡	(818.982)‡	(3.159)‡	(783.820)‡	(3.164)‡	(777.013)‡
781	4.829	135.979				
	(2.849)*	(94.721)				
785	-0.633	883.005	-0.467	822.592	-1.318	828.087
	(1.683)	(147.241)‡	(1.696)	(152.344)‡	(1.711)	(155.658)‡
790	1.503	97.566				
	(2.171)	(89.841)				

Table A.7 (Continued)

	4 percent Sample		5 percent Sample		6 percent Sample	
Dependant Variables:	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Dependant Variable	Total Drug Expenditures	Total Non-Drug Expenditures
796	-4.013	-20.152	-4.126	-2.155	-4.162	17.678
	(1.130)‡	(44.017)	(1.134)‡	(45.892)	(1.130)‡	(44.914)
V12	-0.580	-723.363	-0.535	-900.371	-0.543	-834.540
	(4.033)	(358.016)†	(4.067)	(437.961)†	(4.053)	(440.807)*
V42	36.387	2,238.996	36.032	2,277.779	36.278	2,307.721
	(10.940)‡	(528.269)‡	(10.856)‡	(510.605)‡	(10.864)‡	(512.418)‡
V45	-5.528	119.950	-6.075	154.266	-6.140	333.554
	(3.458)	(175.745)	(3.459)*	(178.441)	(3.476)*	(178.289)*
V49	4.450	642.078	3.594	609.349	2.909	695.939
	(3.778)	(119.632)‡	(3.714)	(128.308)‡	(3.701)	(121.558)‡
V70	11.509	55.673	11.757	27.402		
	(3.793)‡	(66.065)	(3.812)‡	(75.979)		
V72	6.663	-30.852	6.749	-16.252	6.882	5.129
	(1.098)‡	(33.850)	(1.100)‡	(36.000)	(1.095)‡	(35.365)
Control for Separate "Condition Duration" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Age" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Education Year" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

Table A.8

Fluoroquinolones
Analysis of Impact on Health Care Expenditures

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
ICD-9 Codes						
005	-2.965	42.490	-3.648	65.008	-6.856	-470.626
	(4.087)	(137.820)	(4.063)	(120.384)	(4.008)*	(137.818)‡
136	4.813	180.422	4.937	159.575		
	(2.833)*	(161.683)	(2.879)*	(157.570)		
185	40.324	1,395.634	40.447	1,658.827		
	(4.769)‡	(324.878)‡	(4.972)‡	(330.058)‡		
380	5.936	-50.564	5.590	-155.284	4.370	-473.155
	(2.544)†	(65.261)	(2.555)†	(67.991)†	(2.615)*	(79.746)‡
5	9.907	390.571	9.651	317.406	3.093	-79.353
	(3.610)‡	(138.145)‡	(3.650)‡	(144.948)†	(3.670)	(158.840)
562	12.045	1,099.323	12.015	1,062.565	10.544	748.592
	(2.322)‡	(195.400)‡	(2.376)‡	(193.057)‡	(2.385)‡	(205.052)‡
590	2.345	501.644	2.598	454.488		
	(1.395)*	(85.815)‡	(1.414)*	(85.642)‡		
592	-2.057	1,188.592				
	(1.604)	(126.254)‡				
597	6.385	213.392	8.486	276.404	8.947	-63.626
	(6.256)	(157.239)	(6.411)	(158.225)*	(5.653)	(173.981)
599	1.733	226.340	1.768	210.758	-0.027	-207.809
	(1.118)	(50.660)‡	(1.127)	(49.408)‡	(1.359)	(90.348)†
601	10.772	-228.136	9.613	-228.908	5.040	-740.576
	(3.315)‡	(119.142)*	(3.419)‡	(126.951)*	(3.387)	(134.098)‡
602	19.278	-368.151	18.624	-287.277		
	(2.391)‡	(110.693)‡	(2.526)‡	(116.964)†		
608	29.562	379.602	28.216	223.782	26.287	-248.165
	(6.928)‡	(164.787)†	(6.874)‡	(171.766)	(6.865)‡	(187.822)
614	6.793	319.453				
	(2.241)‡	(83.949)‡				
682	15.906	1,232.305				
	(2.867)‡	(144.888)‡				
730	3.068	1,730.777	2.947	1,694.970	0.375	1,163.738
	(5.032)	(582.862)‡	(5.003)	(576.723)‡	(4.824)	(565.818)†
Control for Separate "Condition Duration" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Table A.8 (Continued)

Dependant Variables:	4 percent Sample		5 percent Sample		6 percent Sample	
	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures	Total Drug Expenditures	Total Non-Drug Expenditures
Control for Separate "Age" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes
Control for Separate "Education Year" Dummy Variables	Yes	Yes	Yes	Yes	Yes	Yes

Absolute value of robust standard errors in parentheses; * significant at 10%; † significant at 5%; ‡ significant at 1%
Note: The estimated coefficients of dummy variables for Condition Duration, Age and Education Year are suppressed.

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