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Impact of Medicare Part D coverage gap on beneficiaries' adherence to prescription medications

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IMPACT OF MEDICARE PART D COVERAGE GAP ON BENEFICIARIES' ADHERENCE TO PRESCRIPTION MEDICATIONS

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

By

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To my family

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TABLE OF CONTENTS

LIST OF TABLES

ABSTRACT

IMPACT OF MEDICARE PART D COVERAGE GAP ON BENEFICIARIES' ADHERENCE TO PRESCRIPTION MEDICATIONS

By: URVI S DESAI, Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

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Advisor: Norman V Carroll, Professor, Department of Pharmacotherapy and Outcomes Sciences

INTRODUCTION: Medicare Part D provides prescription drug coverage to seniors through a benefit plan with a major deductible inserted in the middle. It is important to study the extent to which this structure affects seniors' adherence to prescription medications. Therefore, this study had the following objectives: (1) To identify characteristics of beneficiaries reaching and not reaching the coverage gap, (2) To study the entry and exit times from the coverage gap, (3) To study the impact of a complete gap in coverage on beneficiaries' adherence to prescription medications, (4) To study the impact of a partial gap in coverage on beneficiaries' adherence to prescription medications

METHODS: This was a retrospective quasi-experimental analysis with matched control groups using a nationally representative sample of Part D enrollees from 2008 Centers for Medicare and Medicaid (CMS) datasets. Adherence to each oral medication taken for one or more of the seven pre-defined therapeutic classes before and after reaching the coverage gap was measured using the Medication Possession Ratio (MPR). Appropriate statistical tests for significance were performed for each analysis

RESULTS: A quarter of our sample (24.42%) reached the coverage gap in 2008. Most of the beneficiaries reaching the coverage gap did so by end of September. Those reaching the coverage gap and losing all coverage experienced significantly greater reductions in adherence (3% more for beta-blockers to 9% more for oral anti-diabetic agents), compared to those not reaching the coverage gap. A considerable proportion of beneficiaries stopped taking medications in both the groups and the proportion of beneficiaries considered adherent also dropped in both the groups during the coverage gap period.

CONCLUSIONS: Medicare Part D beneficiaries face significant barriers to adherence and this is especially highlighted among those reaching the coverage gap. Interventions to improve adherence in this group should target all beneficiaries, especially those with several chronic conditions.

CHAPTER 1:

INTRODUCTION

This chapter presents background information about the concept of health insurance and demand, which is the underlying conceptual framework guiding this study, followed by historical issues surrounding prescription drug coverage for the seniors in the United States and the newly introduced Medicare Part D benefit. The first section of conceptual framework also contains information about the empirical evidence to support the theory that presence (or absence) of insurance affects utilization of healthcare services; especially prescription drugs. The second section details the historical issues surrounding prescription drug coverage for seniors. This section provides an overview of Medicare and its efforts to provide coverage for prescription drugs to beneficiaries prior to implementation of Medicare Part D. It also contains results from pre-Part D studies that explored the need for prescription drug coverage for the Medicare beneficiaries. Next, it contains information about the Medicare Prescription Drug and Modernization Act of 2003 and its provisions for prescription drug coverage, including the structure of Medicare Part D. It also explores the projected impact of this policy change on access to and use of medications using the pre-Part D literature. Finally, the chapter provides a brief overview of the remainder of the document.

Section 1: Conceptual Framework
The Concept of Health Insurance

Healthcare is an area of great uncertainty because illnesses are often difficult to predict and the associated treatments are often very costly. This leaves individuals in constant fear of losing a significant amount of their income in a relatively short period of time. Insurance is an arrangement that allows risk-averse people to reduce the uncertainty associated with these events by making regular contributions (premiums) to an agency that provides them assurance of financial assistance at the time of need. While it is not possible to predict the probability of illness per individual, the average probability of illnesses can be predicted fairly well for a large group of people. This is done based on the law of large numbers, which shows that for a given probability of illness, the distribution of the average rate of illness in a group will collapse around the probability of illness as the group size increases[1]. Thus, insurance reduces the variability of the insureds' income by pooling their risks into a large group.

Most insurance agencies in the healthcare industry require that insured individuals share a percentage of the cost of treatment of an illness. This percentage to be paid by the insured at the time of the event is typically referred to as co-insurance[1]. For example, if the total cost of treatment is $100, then with a 20% co-insurance rate, the insured will pay $20 (out-of-pocket (OOP)) at the time of treatment and the insurer will pay the remaining $80. The purpose of requiring some form of cost sharing at the time of treatment (in addition to the premiums) is to make consumers more aware of the true costs of the treatment and to prevent unnecessary use of healthcare services[1]. This concept can be better explained using the economic theory of price elasticity of demand for goods and services.

The Economic theory of Price Elasticity of Demand

The demand curve for most goods and services is downward sloping, indicating an inverse relationship between price charged and the quantity demanded. Thus, for a given service, as the price of the service increases, the quantity demanded decreases and vice versa. This relationship between price change and quantity demanded is explained economically using the concept of "price elasticity". The price elasticity of demand can be defined as the ratio of percent change in quantity demanded to percent change in price of the service[2]. Thus, if the initial price for a given product is P0, the quantity demanded at this price is Q0 and if the price changes to P1 and the quantity demanded changes to Q1, then

$$price\ elasticity\ of\ demand\ =\ ((Q1 - Q0) \div Q0)/((P1 - P0) \div P0)$$

The sign of the ratio indicates the direction of change in quantity demanded with respect to change in price. It is typically negative because quantity demanded decreases with increase in price or vice versa. The greater the absolute value of the price elasticity of demand, the greater is the effect of change in price on quantity demanded. In absolute terms (ignoring the sign), the farther the ratio is from 1,the greater the elasticity of demand for a product or service and the closer the ratio is to 1, the less the elasticity of demand for a product or service.[2]

As mentioned earlier, the relationship between insurance cost sharing and utilization of healthcare products and services can be explained using this fundamental principle of price elasticity of demand. Economic theory suggests that presence of insurance (versus patients having to pay the full cost themselves) makes the demand for healthcare services less elastic, thereby, increasing the quantity demanded at any given market price.[3] In other words, in the presence of insurance, changes in the market price for a service will not affect the consumer as much as they did when the price was paid out of pocket. This is illustrated in Figure 1 below. In

3

this figure, the graph presents a hypothetical example of the relationship between market price and quantity of a health service demanded for various price levels. It further provides information on the changes that would occur in the presence of different co-insurance rates. According to this figure, for a person with a 100% co-insurance rate (complete self-pay or no insurance), for a market price of $40, quantity demanded is X1; for $20, quantity demanded is X2 and for $10, the quantity demanded is X3. However, if the co-insurance rate drops to 50%, the quantity demanded will correspond to the quantity demanded at 50% of the actual market price. Thus, now, for market price of $40, the quantity demanded will be X2, because now the patient is paying only $20 and so he/she will demand the service as if the price was $20. If the co-insurance rate further decreases to 25%, the quantity demanded for a market price of $40 will be X3.
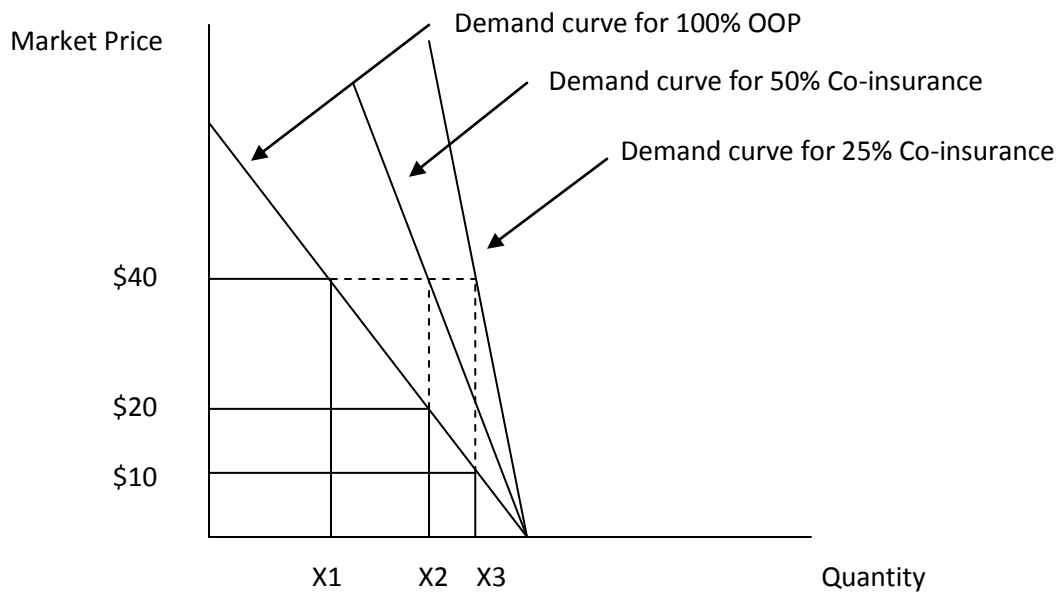
Figure 1: Relationship between co-insurance and demand for healthcare services *Adapted from Figure 9-7: The effect of coinsurance rate on healthcare demand on Pg: 184[3]*

This change in demand for services at any given market price is represented graphically by the outward rotation of the demand curve with decreasing co-insurance rates. Thus,

decreasing co-insurance rates increases the utilization of healthcare services beyond what a patient would normally consume at any given market price. In other words, a decrease in patient cost sharing leads to an increase in utilization of healthcare services. The opposite of this is also true; i.e. an increase in co-insurance rates decreases the utilization of healthcare services. The following section provides the empirical evidence to support this theory, focusing on its relevance to prescription drug utilization.

Empirical Evidence

Empirical evidence suggests that the economic theory of cost sharing and demand for services is true for most healthcare products and services including prescription drugs. The breakthrough study by RAND Corporation in 1985 was among the first to provide evidence in support of the above theory. The study found that the quantity of prescription drugs demanded increased with a decrease in cost sharing.[4] For example, the group with free care filled about 5 prescriptions per month compared to 4 prescriptions used by enrollees of plans with 25% and 50% cost sharing.

Coulson et al. concluded that within a Pennsylvania Health Plan Medicare population, enrollees with some form of coverage for prescription drugs filled and refilled more prescriptions compared to those who did not have any form of coverage for prescription drugs.[5] Upon analyzing the completed surveys, it was observed that enrollees with insurance for both physician visits and prescription drugs filled and refilled approximately 1.87 prescriptions whereas those without supplemental insurance filled and refilled only 0.80 prescriptions in the given two week reference period.

Using data from the RAND Elderly Health Supplement to the 1990 panel study of income dynamics, Lillard et al. concluded that presence of insurance coverage for prescription

5

drugs significantly increased the probability of use of these drugs.[6] Using simulations to estimate the effects of providing insurance to Medicare enrollees without prior drug coverage, the researchers observed that under such a provision, the probability of medication use would increase by 8.8% ($p < 0.01$) in this population. The study further estimated a 12.2% increase among beneficiaries with no private insurance (Medicare only) and 7.5% among beneficiaries with private insurance but with no drug coverage.

A study of the existing data of 7,285 community dwelling Medicare beneficiaries from the Cost and Use files for the 2000 Medicare Current Beneficiary Survey (MCBS) found that enrollees with drug coverage had 4.5 times higher probability of any drug use compared to those with no coverage.[7] A more recent study of Medicare beneficiaries from the MCBS of 1992-2000 estimated that presence of prescription drug coverage increased utilization by 4%-10% depending on the type (i.e. public coverage vs. HMO or employer sponsored coverage) and generosity of coverage compared to lack of coverage altogether.[8]

There is ample literature indicating that the opposite of these findings is also true; i.e. the demand for prescription medications decreases with increased cost sharing. In a 2007 systematic review, Goldman et al.[9] reviewed 132 articles to study the effect of cost sharing on utilization of prescription drugs from 1985 to 2006. The studies reviewed looked at several types of cost sharing strategies employed by insurers including incentive based formulary design, capped benefits and not providing coverage for certain classes of drugs. From this comprehensive review, the authors concluded that irrespective of the strategy used, increases in cost sharing led to decreases in utilization of prescription medications. The authors summarize their findings using the principle of price elasticity of demand by stating that for every 10% increase in cost-sharing prescription drug use decreased by 2%-6% depending on the drug and therapeutic class;

6

i.e. the price elasticity of demand for prescription drugs according to this study ranges from -0.2 to -0.6.

In other words, the result is consistent among the articles reviewed: presence (or absence) of insurance and the generosity of cost-sharing structures affects the demand for prescription drugs. The next section outlines the historical issues surrounding prescription drug coverage for seniors and presents an overview of the basic structure of the recently implemented Medicare Part D prescription drug benefit

Section 2: Prescription Drug Coverage and the seniors
History of Medicare

The need for financial assistance for the seniors was first recognized in the United States with the passage of the Social Security Act (SSA) of 1935. While it was originally intended to include government sponsored health insurance for the seniors eligible for receiving Social Security, health insurance coverage was omitted from the final Act of 1935 due to political concerns[10]. Proponents of compulsory health plans were no more successful for the next two decades. However, immediately after his election in 1964, President Johnson, who was a strong proponent of health insurance for the aged even before his election, signed Medicare and Medicaid into law on June 30, 1965[10, 11]. Through this law, Medicare was established under Title XVIII of the SSA to provide federally administered health insurance to individuals age 65 and older regardless of income or medical history[12]. Under Title XIX of the SSA, Medicaid was established as a federal-state administered program to provide health insurance coverage to certain low-income groups of people who could not otherwise afford health insurance[10]. In 1972, Medicare expanded coverage to citizens under the age of 65 years who were either permanently disabled or suffered from End-Stage Renal Disease (ESRD)[11, 12].

Historically, Medicare provided compulsory hospital insurance (called Part A) to the seniors and disabled that helped pay for inpatient care, skilled nursing facility, and hospice care, with an optional medical insurance program (called Part B) that helped pay for physician services, home health and preventive services including physician administered drugs for beneficiaries who wish to subscribe. However, Medicare did not provide any coverage for outpatient drugs.

With the passage of the Medicare Catastrophic Coverage Act of 1988, Medicare proposed provision of outpatient prescription drug coverage to beneficiaries with a cap on out-of-pocket (OOP) expenses[11]. Through this act, Medicare planned to cover a set percent of catastrophic expenses for outpatient drugs including insulin and immuno-suppressants used after organ transplant surgeries after meeting a certain deductible each year. The proposed timeline of implementation was that Medicare would cover 50% of the costs of such medications after a deductible of $500 in 1990 and $600 in 1991 and 60% of the costs after a deductible of $652 in 1992[13]. In the long term, the deductible value was proposed to be set so that 16.8% of all Medicare beneficiaries would exceed the amount and Medicare paid 80% of the costs in excess of that amount. The program was proposed to be financed through an increase in premium based on a beneficiary's income[13]. The act was repealed in 1989 following increasing political pressure and protests by higher income seniors who were likely to be faced with increased premiums [11, 14]. Since then, Medicare did not provide coverage for outpatient prescription drugs until the passage of the Medicare Prescription Drug Improvement and Modernization Act (MMA) of 2003[11].

The Need for a Medicare Drug Benefit

Studies done before 2003 concluded that most seniors suffered from several chronic conditions, took a number of medications, and paid a significant proportion of their income towards prescription medications. For instance, results from the 1980 National Medical Care Utilization and Expenditure Survey indicated that four out of five seniors used prescription drugs in a given year[15]. It also found that although seniors constituted 10.1% of the national population, they accounted for about 33% of the total spending on prescription drugs. Approximately 68% of this cost was paid out-of-pocket. Mueller et al.[16] used data from the 1987 National Medical Expenditure Survey and found similar results: 12% of the population comprised seniors, who in

9

turn accounted for 34% of total spending on prescription drugs. They also found that 36% of the seniors in their sample had more than three chronic conditions.

Davis et al.[17] used data from 1995 MCBS and found that Medicare beneficiaries paid half of their prescription costs OOP compared to the much lower national average OOP spending by the entire U.S population (34%) and an even lower percent paid by Medicaid enrollees (21%). Crystal et al.[18] also used 1995 MCBS data. They found that beneficiaries spent 19% of their income on healthcare, 50% of which was spent on prescription drugs and dental services. The burden was higher in sicker (28.5% of income) and low income beneficiaries (31.5% of income).

Several studies reported that a lack of insurance for prescription drugs adversely affected medication adherence among seniors. The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) defines medication adherence as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen".[19] Thus, to be adherent to a prescribed regimen, a patient must first purchase the medication and then utilize it as prescribed. A lack of insurance has been found to result in decreased procurement of drugs which in turn resulted in non-adherence among seniors. For example, Davis et al.[17] reported that nearly 35% of Medicare beneficiaries living in the community did not have coverage for prescription drugs. It was further found that beneficiaries without prescription drug coverage used 31% less prescription drugs compared to the national average usage (12.7 vs. 18.5). Steinman et al. concluded that 8% of seniors without insurance reported medication restriction due to cost compared to 3% with partial coverage and 2% with full coverage[20].

A national survey of Medicare beneficiaries aged 65 and older revealed that almost a quarter of seniors did not have prescription drug coverage in 2003 and almost half of low-income seniors lacked coverage in some states[21]. The study also found that cost was cited as the

most common reason for non-adherence (26.3%) as compared to non-adherence due to unfavorable experiences like side effects (24.5%) or perceived need for taking the medications (14.5%). The effect was even more pronounced among beneficiaries with low income and/or multiple chronic conditions and/or no coverage. For example, among beneficiaries with low income and complex chronic conditions, almost 50% of those without coverage for prescription drugs reported some form of cost-related non-adherence compared to 25% of those beneficiaries who had some form of coverage for prescription drugs[21].

A number of studies have concluded that medication non-adherence leads to severe clinical and economic implications. A study by Mojtabai and Olfson used the Health and Retirement Study (HRS) data which is an ongoing longitudinal survey of community dwelling older Americans and concluded that participants with cost related poor adherence were more likely to have been hospitalized compared to their peers (43% vs. 33% respectively)[22].

In a study of hypertensive patients, Psaty et al. observed that patients with less than 80% adherence to their medication (as measured from a computerized pharmacy database) have a 4 fold increase in risk of developing acute cardiac events compared to those with adherence ratio of 80% or higher[23]. Horwitz et al. reported that among patients on beta-blocker therapy, poor adherers (i.e. those who took less than or equal to 75% of the prescribed medication) were 2.6 times more likely to die compared to good adherers (i.e. those who took more than 75% of the prescribed medication) (95% CI (1.2, 5.6)) and that such non-adherence to medications (i.e. taking less than or equal to 75% of the prescribed medication) was independently associated with a higher mortality risk[24].

A study involving epileptic patients[25] found that non-adherence to medications (defined as Medication Possession Ratio, (MPR) less than or equal to 0.80) was associated with

11

significantly higher incidence of hospitalizations [incident rate ratio (IRR) = 1.39, 95% CI = 1.37-1.41], inpatient days (IRR = 1.76, 95% CI = 1.75-1.78), and ED visits (IRR = 1.19, 95% CI = 1.18-1.21). Non-adherence was also associated with cost increases related to serious outcomes, including inpatient ($4,320 additional cost per quarter, 95% CI = $4,077-$4,564) and ED services ($303 additional cost per quarter, 95% CI = $273-$334).

Balkrishnan et al. found that adherence to anti-diabetic medications (defined as MPR ≥ 0.70) was a greater driver of cost reduction than use of other medications in this population. The results indicated that a 10% increase in adherence to anti-diabetic medications resulted in 8.6% reduction in total annual health care costs (including ER visits and hospitalization)[26].

Svarstad et al. studied Medicaid patients suffering from mental illnesses and observed that within the total sample, patients with an irregular use of medications (defined as patients taking oral medications who had one or more quarters without a claim) had significantly higher rates of hospitalization than regular users (42 percent versus 20 percent), more hospital days (16 days versus four days), and higher hospital costs ($3,992 versus $1,048). Irregular medication use was one of the strongest predictors of hospital use and costs even after the analyses controlled for other confounders[27].

From the pre-MMA literature, it is reasonable to conclude that lack of sufficient financial assistance (in other words, "insurance") posed a significant burden to seniors which compelled them to forego medications; this in turn increased their chances of developing adverse clinical outcomes that led to unnecessary increases in the treatment costs . A systematic review of the literature has indicated that non-adherence leads to anywhere from 5-40% of all hospital admissions in the seniors[28]. As noted by Haynes et al., "Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any

improvement in specific medical treatments" [29]. Partly in response to studies like these, the MMA was signed into law on December 8, 2003[14].

Structure of Medicare Part D

Administration

Beginning January 1, 2006, Medicare Part D, a voluntary outpatient prescription drug benefit program, was implemented for all Medicare beneficiaries except for those who are dually eligible for Medicare and Medicaid and certain low-income beneficiaries. These patients are automatically enrolled into a plan if they did not choose one during the open enrollment period beginning in November of every year. Medicare Part D is delivered through private plans, either stand-alone prescription drug plans (PDPs) or Medicare Advantage prescription drug (MA-PD) plans, that contract with Medicare to provide either the "standard benefit" required by the MMA (explained in section: Benefit Structure), or a benefit structure that is "actuarially equivalent" or enhanced.

As of April 2010, approximately 27.6 million beneficiaries were enrolled in Part D, of which two-thirds were enrolled in PDPs[30]. It is important to distinguish between beneficiaries enrolled in PDPs and MA-PDs because of the difference in the benefit structure offered. Most PDPs offer coverage using some modification of this basic structure [31]. In 2010, about 60% of the PDPs required the standard deductible (compared to 11% of MA-PDs), 80% of PDP plans had the "coverage gap" and offered no coverage for drugs during that time (compared to 51% of MA-PDs). The 20% of the plans that did offer gap coverage limited it to generic drugs only. By comparison, 49% of MA-PD plans offered generic with some brand name drug coverage during the gap [30, 32]. Thus, 80% of beneficiaries enrolled in PDPs were solely responsible for the full

13

cost of their medications during the coverage gap while about half of those enrolled in MA-PDs received some assistance. Now in its fifth year of implementation, Medicare Part D is funded by general revenues, beneficiary premiums, and state payments and accounted for 10% of the total Medicare spending in 2009 [12].

Benefit Structure

The prescription drug coverage offered though Medicare Part D includes a small deductible at the front end and a major coverage gap inserted in the middle. The coverage gap, where the beneficiary is responsible for full cost, is also called the "doughnut-hole"; and the limit above which the coverage resumes is called the "catastrophic coverage limit". In 2010, there was an initial deductible of $310, followed by 25% coinsurance until total drug spending reached $2,830. At this point the coverage gap began and continued until total drug spending reached $6,440 [30]. Thus, in addition to monthly premiums, in 2010, an average beneficiary paid $310 + 25% ($2,830 - $310) = $940 in OOP costs before reaching the coverage gap. After this, the beneficiary was responsible for paying 100% of the cost until the total drug spending reached $6,440. In other words, the beneficiary was responsible for the next $3,610 in prescription spending before reaching the catastrophic coverage limit after which Medicare would cover 95% of drug costs. This structure is pictorially represented in Figure 2 below.

Catastrophic Coverage: 5% coinsurance after total spending exceeds $6,440 (Very few beneficiaries reach this phase)

Coverage Gap: No coverage till total spending reaches $6,440

Deductible ($310) + 25% co-insurance up to total spending of $2,830 (Most beneficiaries stay in this phase)
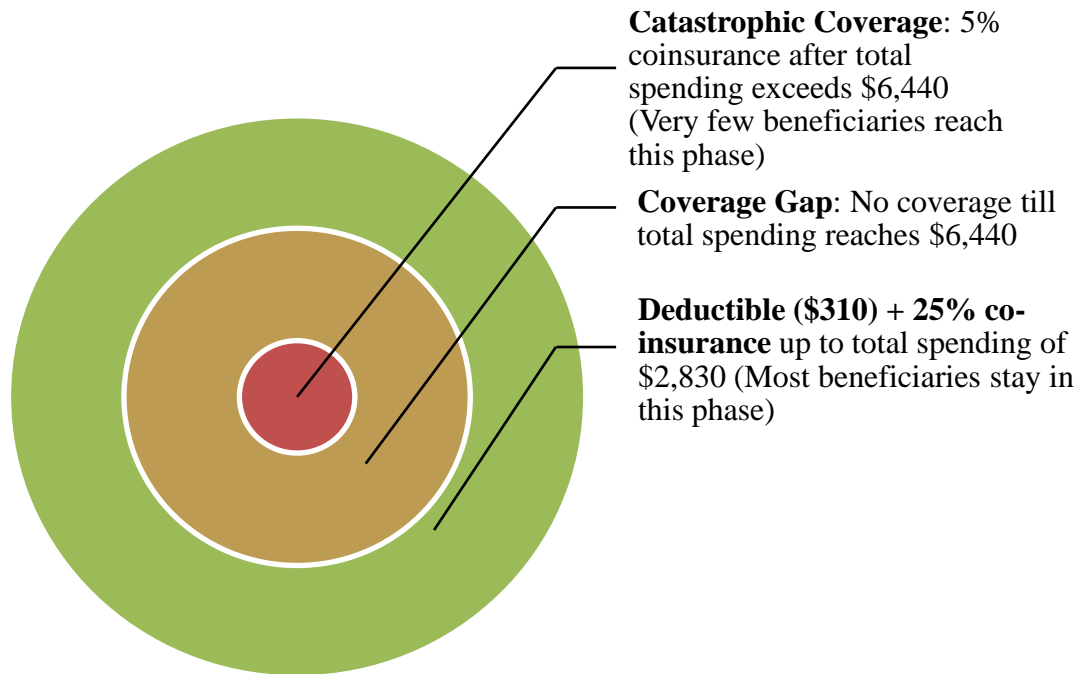
Figure 2: Standard Benefit Structure of Medicare Part D for 2010

Medicare Part D beneficiaries have the choice to enroll in plans that offer coverage through either the Medicare defined standard benefit structure (shown above) or some alteration of the same. There are three different alternatives to the standard benefit design. The "actuarially equivalent" designs are those that have a deductible at the front end followed by Medicare defined limits for beginning of coverage gap and catastrophic coverage limits. They differ from the Medicare defined "standard benefit" only in the fact that these plans are allowed to charge beneficiaries various cost-sharing structures in lieu of the standard 25% co-insurance in the standard benefit. A "basic alternative" is a design where the deductible can be eliminated or reduced and the cost-sharing structures can be altered compared to the Medicare Standard but the limits for the coverage gap and catastrophic coverage are not altered. In contrast, plans offering coverage through an "enhanced alternative" have the freedom of whether or not to charge a deductible as well as whether or not to include a coverage gap. They can change the cost-sharing

structure as well as spending limits to determine the beginning of the coverage gap. The catastrophic limit and cost-sharing, however, stay in place similar to the other designs. In addition, these plans are allowed to offer coverage for some or all drugs for beneficiaries in the coverage gap.

The novel cost-sharing structure employed by Medicare Part D generated interest in trying to estimate the proportion and characteristics of beneficiaries who would reach the coverage gap under the standard Part D benefit structure using historical (pre-MMA) data. Further the research community was interested in estimating the effects of reaching the coverage gap on beneficiaries' medication taking behavior and costs. The following section summarizes the findings of the pre-MMA studies.

Projections pertaining to the coverage gap

Stuart et al. used data from the MCBS for years 1998-2000 and estimated that about 40% of all Part D enrollees will spend some time in the coverage gap each year from 2006-2008 and only 15% of these would have spending high enough to reach the catastrophic coverage level[33].

Tjia and Schwartz studied medication utilization behavior of seniors with diabetes mellitus from the 2001 Medical Expenditure Panel Survey (MEPS) and estimated that the percentage of beneficiaries having expenditures in excess of the initial gap limit of 2006 ranged from 60% for those using traditional hypoglycemic agents to 75% for those on novel agents[34]. Tjia and Schwartz also concluded that having three or more co-morbid conditions as well as clinical indicators of greater illness burden and poorer health status significantly increased the likelihood of falling in the coverage gap[34]. However, they concluded that sociodemographic

16

factors were not significantly associated with the risk of falling in the coverage gap in their sample of diabetic beneficiaries.

Using historical data of patients diagnosed with atrial fibrillation between January 2001 and June 2003, Evans-Molina et al. projected that the percentage of beneficiaries in their sample expected to enter the coverage gap in 2006 ranged from 27% to 46%, of which 3% to 11% would have spending high enough to exit into catastrophic coverage before the end of the year[35].

Patel and Davis analyzed the MCBS data for 1997 through 2001 and estimated that approximately 43% of beneficiaries without ESRD would fall in the coverage gap in 2006 of which about 14% would be able to exit before the end of the year[36]. These numbers were even higher for those with ESRD. The researchers predicted that70% of those with ESRD would reach the coverage gap in 2006 and almost 40% of those would reach the catastrophic phase before the end of the year.

There was much ado about beneficiaries reaching the coverage gap, because there is ample evidence to conclude that experiencing a gap in coverage or having an annual spending limit (cap) for prescription drugs leads to decrease in medication use and increase in OOP spending. The next section highlights the effects of such gaps and/or caps imposed on drug spending among non-Medicare Part D beneficiaries.

Impact of caps and gaps

Research aimed at examining the impact of gaps in coverage or caps on total spending for prescription drugs on non-Medicare Part D (pre or post implementation) seniors' utilization of medications has concluded that beneficiaries with caps or gaps in coverage were more likely to

foreg medications due to cost. Studies outlined in the next few paragraphs also identified cost lowering strategies used by seniors having some form of insurance coverage with capped benefits. These strategies include reducing drug use, reducing use of other necessities, borrowing money to pay for prescriptions, and finding less expensive prescriptions including free samples from their physicians.

Stuart et al. studied a representative sample of Medicare beneficiaries with gaps in their coverage using information from MCBS files for 1998 and 2000 and concluded that such interruptions in drug coverage led to significant reductions in medication use and spending, especially among beneficiaries with many chronic illnesses[37].

A survey of beneficiaries with coverage for prescription drugs capped at $500 or $1,000 annually found that almost 70% of the respondents engaged in one or more of the aforementioned cost-lowering strategies despite having some coverage for their drugs[38]. Another survey of Medicare beneficiaries with capped benefits found that taking less than prescribed amounts and discontinuing prescribed medications were among the top mentioned strategies to cope with prescription costs (23.6% and 16.3% respectively)[39]. Tseng et al.[40] reported that a greater proportion of beneficiaries exceeding the cap imposed on their prescription spending or those who experienced a gap in their coverage used less medication compared to those who had a higher annual cap that they did not exceed (18% vs. 10%, p-value $\leq$ 0.001). The researchers also found that a greater proportion of these beneficiaries reported shopping around for drugs and having difficulty with paying for prescriptions compared to their peers.

Soumerai et al. analyzed responses to questions about cost-related non-adherence (measured as self-reported skipping or taking smaller doses to make the medicine last) as well as

18

cost-cutting strategies (e.g. obtaining free samples, using generic drugs, shopping for best price) added to the MCBS[41]. The researchers found that although only 13% of the elderly and 29% of the non-elderly disabled beneficiaries reported cost-related non-adherence; almost 70% of all Medicare beneficiaries (both elderly and non-elderly disabled) surveyed engaged in some form of cost-cutting strategy to cover prescription drug costs. The most frequently cited strategy was either using generic drugs or requesting samples from physicians (~50% for each), followed by shopping around for best pricing and spending less on other needs.

In a cross-sectional study of 222 homebound older adults aged 60 and older, Sharkey et al. found that 20.3% of the sample population reported using one or more strategies to restrict medication use because of cost (skipping doses or taking less than prescribed) while another 21.2% of the sample reported using strategies to cut OOP expenses (e.g. choose between food and medicine). While shopping around and reducing expenses on other household expenditures is prudent, to stop taking medications or to take less than prescribed or to reduce expenditures on daily necessities including food could adversely affect the health outcomes of these beneficiaries[38].

Conclusion

Medicare Part D is a major expansion to the Medicare program. In addition, the cost-sharing structure used by this prescription benefit is highly unusual. Therefore, there has been a tremendous interest in studying the impact of the program as well as its design before and after its implementation.

19

Overview of the Remaining Document

The remaining chapters of this document present a detailed review of the literature focused on studying the effects of Medicare Part D, the rationale for doing the study, followed by the research objectives and specific aims, methods used to achieve these aims, results and a discussion of the findings. Finally, we present the main conclusions drawn from the study findings and a bibliography of cited literature.

20

CHAPTER 2:

LITERATURE REVIEW

This chapter is divided into two sections. The first section presents results of the literature that studied the overall impact of Medicare Part D program on Medicare beneficiaries. This includes a review of the impact on medication utilization and spending as well as medication adherence. This is followed by a section that presents a review of studies focused on examining the impact of the coverage gap on Medicare Part D enrollees. This includes studying the proportion of beneficiaries reaching the coverage gap and the characteristics of these beneficiaries, the impact on utilization of prescription medications and cost-cutting strategies used by beneficiaries affected by the coverage gap. Finally, the chapter discusses gaps in the existing literature that merit attention in future research.

Section 1: Impact of Medicare Part D
On Overall Medication Use and Spending

Despite its novel structure for cost-sharing, the intention of Medicare Part D was to improve utilization of necessary prescription medications by making them more affordable. Prior to its implementation, Pauly used the economic principles of price elasticity of demand for prescription drugs and healthcare utilization in the presence of insurance presented earlier and estimated that following implementation of Medicare Part D, there would be a 20% increase in utilization of prescription drugs for those who previously lacked coverage and a 6% increase for those who had some form of prior coverage[42].

Several studies done since the implementation of Part D uphold Pauly's estimates. Lichtenberg and Sun used prescription claims data from one of the nation's largest retail pharmacy chains for the period of September 2004-December 2006 to estimate the impact of Medicare Part D on user cost (defined as cost of a day of therapy to the beneficiary) and medication use (defined as days of therapy). They used a difference-in-difference research design to evaluate the impact of Medicare Part D on the elderly compared to the non-elderly. The researchers found that the average user cost for both the groups increased between September 2004 and December 2005. However, the average cost of therapy decreased gradually for the seniors group from January 2006 through June 2006 while the cost for the non-seniors remained unchanged. They attribute this finding to the gradual enrollment in Part D from January 2006-June 2006. Overall, the study estimated that Medicare Part D reduced user cost by 18.4% and increased their use of prescription drugs by 12.8%[43]. These results, however, need to be interpreted with caution because of the lack of information on the characteristics of groups

compared. Additionally, the study used data from a single pharmacy chain and did not account for baseline characteristics like demographics and chronic conditions.

Yin et al.[44] used data from a 5% random sample of drug users from a single pharmacy chain aged 60 – 79 years from September 2004 to April 2007. The researchers compared the utilization pattern of the Part D eligible group (age 66-79 years as of January 1, 2006) to that of the Part D ineligible group (age 60-63 as of January 1, 2006). Using a generalized estimating equation modeling technique and accounting for baseline characteristics by including the similar (except for age) Part D ineligible comparison group, they estimated that the implementation of Medicare Part D reduced beneficiaries' OOP spending by 13% in 2006 compared to that in 2005. The researchers further estimated that implementation of Medicare Part D increased the number of prescriptions used by the eligible seniors by 7%.

Ketcham and Simon used data from the Wolters Kluwer Health's Source Lx database for December 2004 through December 2007 to estimate the change in utilization and OOP costs for beneficiaries enrolled in Part D in 2006. To achieve their goals, the researchers compared the data for beneficiaries aged 66 and older to that of near-elderly (those aged 58-64 years)[45]. Their analysis indicated that the elderly had 8.1% greater increase in utilization in 2006 over their level of use in 2005 compared to the change in utilization for the near-elderly patients. However, the change from 2006 to 2007 was much smaller; with only about 1% increase in utilization in 2007 over 2006. The researchers also found that the number of beneficiaries filling prescriptions in 2006 increased by 4.8% when compared to the number in 2005. Additionally, their results indicate that Part D enrollees' OOP costs declined by 15.9% and 8.3% in 2006 and 2007 respectively, as compared to a 1.39% increase and 2.42% decrease in the OOP of near-elderly patients in 2006 and 2007 respectively. The relative decrease in cost for the elderly compared to

23

the near-elderly was found to be 17.2% in 2006 and 5.8% in 2007.The price elasticity of demand based on utilization from 2005-2007 in this study was -0.44, which is in accordance with the previous literature.

A common limitation of all three studies mentioned above is that they used a near-elderly or non-elderly comparison group. It is well known that elderly have different drug utilization patterns and requirements compared to the non-elderly. In addition, there is a difference in financial characteristics of the two groups and, therefore, comparing the cost and utilization among these two groups may generate spurious results.

A study of nationally representative claims data for beneficiaries with Type 2 Diabetes Mellitus aged 65 years or older from July 1, 2004 through September 30, 2007 concluded that enrollees in PDPs experienced an 11.2% increase in utilization whereas those enrolled in MA-PDs increased their use by 6.2%. The study also concluded that OOP costs per prescription were 35% lower among PDP enrollees and 25% lower in MA-PD enrollees compared to beneficiaries not enrolled in Part D plans, some of who had coverage from other sources while others completely lacked drug coverage[46]

Schneeweiss et al. performed a time-trend analysis of patient level dispensing data of seniors aged 65 years or older as obtained from three large pharmacy chains from January 1, 2005 through December 31, 2006. The researchers reported that among seniors without prior coverage, the use of statins, clopidogrel and proton-pump inhibitors was 11%-37% higher than their expected utilization without implementation of Medicare Part D[47].

A recent study by Joyce et al. used administrative claims data to compare pharmaceutical use and OOP spending of beneficiaries enrolled in the 10 largest Part D plans in 2006 to that of

24

utilization information from 2004 MCBS cost and use data.[48] The researchers found that enrollees of Medicare Part D plans had a 16% decrease in annual OOP costs with a 7% increase in utilization compared to utilization and spending as calculated from the 2004 MCBS data. Joyce et al. also concluded that poorer beneficiaries who are either dually eligible for Medicare and Medicaid or receive Low-Income Subsidies (LIS) benefitted the most from Medicare Part D.

Zhang et al. analyzed data of beneficiaries continuously enrolled in a Medicare Advantage plan between 2004 and 2007 and compared several groups to identify the effect of Part D on OOP costs of the enrollees[49]. Their findings suggest that compared to beneficiaries with stable continuous coverage for prescription drugs, beneficiaries without prior coverage or those who had caps on spending had significant decreases in their OOP spending (13.4%, 95% CI (-17.1%, -9.1%) and 15.9%, 95% CI (-19.1%, -12.8%), respectively) after implementation of Medicare Part D.

In 2006, Safran et al. conducted a follow-up survey[50] of surviving Medicare enrollees surveyed in 2003[21] to estimate the effect of Medicare Part D on their OOP spending and prescription utilization. In addition, they aimed to identify the strata of beneficiaries benefitting the most by the enactment of Part D. Upon completion of the study, the researchers found that except beneficiaries previously enrolled in Medicaid, all Part D enrollees reported a greater utilization of prescription medications compared to 2003 (p-value $\leq$ 0.001). They also found that all Part D enrollees experienced a significant decrease in OOP spending, except those beneficiaries previously reporting employer-sponsored coverage (p-value $\leq$ 0.001). These effects were more pronounced among beneficiaries without prior drug coverage and among those who had capped benefits prior to enrolling in Part D.

A recent systematic review by Polinski et al., appropriately summarizes the findings of these studies by estimating that implementation of Part D was associated with 6-13% increase in utilization of prescription drugs and 13-18% decrease in OOP spending for the enrollees[51].

On Medication Adherence

A study by Madden et al. compared changes in use of self-reported cost-lowering strategies before and after implementation of Medicare Part D (2005 and 2006) and compared it to the changes from 2004 to 2005 from the MCBS[52]. The study design accounted for self-reported covariates including socio-demographic characteristics and health status. In addition, the study design also accounted for interview sequence bias (i.e. when the same questions are asked to the participants at different intervals, their responses are affected by their knowledge of the purpose of the question from previous interview and this creates the interview sequence bias) and year-to-year changes in reporting trend. The adjusted analyses found that the 2006 vs. 2005 odds ratio (OR) for self-reported cost-related non-adherence (CRN), as calculated from responses to questions pertaining to medication strategies like skipping doses, taking less than prescribed, not filling or refilling a prescription due to cost) relative to that for 2005 vs. 2004 was 0.85 (95% CI (0.74, 0.98), and the corresponding OR for spending less on basic needs after implementation of Medicare Part D was 0.59 (95% CI (0.48, 0.72). This indicates that implementation of Medicare Part D decreased the proportion of beneficiaries reporting CRN or spending less on basic needs to cope with prescription costs. The subgroup analyses, however, suggested that beneficiaries in fair to poor health, those with more co-morbidities and those with higher incomes did not experience a significant change in self-reported CRN. This implies that the financial needs of the sickest beneficiaries may not be fully addressed by Medicare Part D; probably because they are more likely to reach the coverage gap.

26

Zivin and colleagues used a similar study design as Madden et al. to examine the impact of Medicare Part D on medication adherence among beneficiaries with and without depressive symptoms[53]. The study reported that after controlling for historical changes (2004-2005) and demographic characteristics, the group with depressive symptoms did not experience a significant decrease in CRN (ratio of ORs = 0.85, 95%CI (0.65, 1.12)) from 2005-2006. By contrast, there was a marginally significant decrease in CRN among beneficiaries without depressive symptoms (ratio of ORs = 0.83, 95%CI (0.70, 0.97)). However, when the two groups were compared with each other, the adjusted analyses indicate that there were no significant decreases in CRNs between the two groups studied (Ratio of ORs = 0.98, 95% CI (0.73, 1.32)). The study findings indicate that Medicare Part D did not improve CRN among beneficiaries with depressive symptoms.

In another investigation, Safran and colleagues found similar results after comparing the survey responses of the same group of Medicare beneficiaries in 2003 and 2006[54]. The study used the same measure of CRN as used by Madden et al. and concluded that self-reported CRN significantly declined for beneficiaries who previously lacked prescription coverage (OR = 0.4, p-value < 0.001), as well as for those who were previously enrolled in Medicare HMO or Medigap/private plans (OR = 0.4 and 0.6, p-value $\leq$ 0.001, and p-value $\leq$ 0.01 respectively). By contrast, however, those who switched from employer sponsored programs in 2003 to a Part D plan in 2006 reported a significantly increased rate of CRN (OR = 1.7, p-value $\leq$ 0.01). Beneficiaries who retained their employer sponsored coverage in 2003 and 2006 reported the lowest overall CRN rate and showed slightly lower rates in 2006 compared to 2003 (OR = 0.7, p-value $\leq$ 0.05).

27

Zhang et al. studied pharmacy and medical claims data for beneficiaries aged 65 years or older who were enrolled continuously from 2003 through 2007 with a large Pennsylvania insurer to identify the impact of Medicare part D on adherence to medications used to treat or prevent hypertension, hyperlipidemia and/or diabetes[55]. The researchers studied adherence behaviors (measured using MPR) among 3 groups with poor insurance coverage prior to implementation of Part D and compared them with a group that had continuous coverage through a retiree health benefit program throughout the study period. Among the three intervention groups, one group did not have drug coverage prior to 2006, one group had a quarterly spending cap of $150 and the third group had a quarterly spending cap of $350. The study results showed that after adjusting for covariates and applying propensity score weighting, the group with no prior coverage (irrespective of the disease condition) experienced the greatest increase in adherence after implementation of Part D (13.4% for patients taking anti- hyperlipidemics 95% CI (10.1, 16.8), 17.9% for anti-diabetic 95% CI (13.7, 22.1) and 13.5% for anti-hypertensive group 95% CI (11.5, 15.5)). In comparison, the group with $350 quarterly cap experienced the lowest increases in adherence for every disease condition (4.4% for patients taking anti-hyperlipidemics 95% CI (3.3, 5.6), 3.6% for anti-diabetic 95% CI (1.8, 5.3) and 2.5% for anti-hypertensive group 95% CI (1.7, 3.2)).

Based on the preceding literature review, it is reasonable to conclude that implementation of Medicare Part D increased the overall utilization of drugs for the beneficiaries by decreasing their OOP costs; however, the impact of the 'coverage gap' still remains to be explored. The next section presents a detailed review of studies that have looked at the impact of this 'coverage gap' incorporated in the Part D benefit since its enactment 4 years ago.

28

Section 2: Recent Literature on Medicare Part D Coverage Gap

Despite speculation of its potentially unfavorable effects on senior patients' adherence and health outcomes, the "coverage gap" was incorporated into Part D. The purpose of the gap was to encourage financial discipline and contain healthcare expenditures [56]. It was believed that in addition to encouraging cautious spending among the beneficiaries, the coverage gap would offset the impact of the availability of insurance coverage for prescription drugs on Medicare's overall costs. Given the brief time that has elapsed since the implementation of Medicare Part D, only a few studies have examined the effects of the coverage gap on beneficiaries' medication use and spending. The following sections describe the findings of this literature in detail.

Proportion of beneficiaries reaching the "gap"

Some studies have estimated the proportion of beneficiaries qualifying for entry and exit from the coverage gap for specific disease conditions. Schmittdiel et al. studied the entry and exit proportions from the coverage gap for beneficiaries enrolled in 2 large MA-PD health plans in California and diagnosed with Type 2 diabetes. The study reported that 26% of the sample entered the coverage gap at some point in 2006 and only 2% exited the gap[57]. In another investigation using claims data for Type 2 Diabetes beneficiaries from Avalere Health's DataFrame database and the Wolters Kluwer's Source Lx database, Karaca and colleagues found that 43% of non-Medicaid beneficiaries enrolled in the PDPs reached the coverage gap in 2006 compared to 33% of those in MA-PD plans[46]. Kim et al. used nationally representative data on patients hospitalized for atrial fibrillation between January, 2005 and December, 2006 and estimated that 58.8% of their cohort entered the coverage gap in 2006 in a mean of just 199 days[58].

Several other studies estimated the proportion of beneficiaries reaching the coverage gap for more diverse samples. Ettner et al. linked pharmacy, outpatient and inpatient claims data to Census data for beneficiaries enrolled in a large MA-PD plan that serves eight states and found that 15.9% of the beneficiaries who did not receive LIS, were not dually eligible for Medicare and Medicaid, and did not have gap coverage in their plan entered the coverage gap in 2006; with only 6.7% of these exiting into the catastrophic coverage zone[59]. Twelve percent of the sample analyzed by Schneeweiss et al. reached the coverage gap in 2006[47]. From a retrospective study of beneficiaries enrolled in a Kaiser Permanente MA-PD plan, Raebel et al. estimated that about 6% of their sample population reached the coverage gap in 2006[60]. Zhang et al. studied data from a large Pennsylvania insurer that offered MA-PD type coverage as well as employer sponsored coverage for Part D beneficiaries in 2006. The researchers estimated that among beneficiaries with employer-sponsored coverage, 40% reached the coverage gap in 2006, whereas 25% of MA-PD enrollees did so by the end of 2006[61].

A study by researchers at Kaiser Family Foundation estimated that in 2007, of those Medicare Part D beneficiaries who were neither dual eligible nor received low income subsidies, 26% reached the coverage gap and that most spent the rest of the year in the gap; only about 4% of those who entered the coverage gap also reached the catastrophic coverage limit[62]. The study also reported that almost half of those who reached the coverage gap in 2007 did so by the end of August. Pedan et al.[63] analyzed pharmacy claims data from 2 large retail pharmacy chains and found that 18.5% of their sample population reached the coverage gap in 2007.

A few studies also reported the characteristics of beneficiaries reaching the coverage gap. Overall, it can be concluded that older beneficiaries suffering from a large number of chronic conditions were more likely to reach the coverage gap. A study by Kaiser Family Foundation

reported that the proportion of beneficiaries reaching the gap increased with age (25% of those aged 65-74 years vs. 33% aged 85 years and older)[62]. Raebel et al. also concluded that beneficiaries reaching the gap were older and had more diseases compared to those who either did not have a gap in coverage or did not reach it[60] while Ettner et al. reported that age was inversely proportional to the likelihood of entering the coverage gap[59]. Zhang et al. estimated the effect of co-morbidities on reaching the coverage gap and found that the likelihood of having spending greater than the threshold for the coverage gap increased with an increase in the number of co-morbidities. For example, among the MA-PD enrollees, 17% of beneficiaries with 'only hypertension' reached the coverage gap whereas 34% with both hypertension and diabetes and 61% with hypertension, diabetes and Congestive Heart Failure (CHF) did so in 2006[61]. Bayliss et al. studied the characteristics of beneficiaries reaching the coverage gap in both 2006 and 2007 using data from a not-for-profit HMO offering many MA-PD plans and found that reaching the gap threshold in both years was a function of existence of chronic co-morbidities and utilization of brand-name drugs. The study, however, found that socio-demographic factors were not significant predictors of reaching the gap[64].

Impact on medication utilization and spending

A report published by the Kaiser Family Foundation in 2008 was among the first studies to present the consequences of the coverage gap in the Medicare Part D structure[62]. This study utilized the IMS Health Longitudinal Prescription Database containing information on 4.5 million Part D enrollees using medications in 2007. The researchers reported that on average, 20% of enrollees reaching the coverage gap in 2007 decreased their medication usage during the gap phase. Of these, 15% stopped taking one or more medications after reaching the coverage gap, while 1% reduced their medication use in some other way. The study further estimated that

31

monthly OOP expenditures nearly doubled during the gap (from $104 to $196), whereas for those who also entered the catastrophic coverage, the monthly OOP spending increased during the gap ($207 to $408) and then decreased after reaching the catastrophic coverage (from $408 to $285). For those who did not enter the coverage gap, overall spending was much lower throughout the year ($26 per month). One of the biggest strengths of this study was that it used the claims data from a nationally representative sample of PDP enrollees using some medication in 2007. However, this is also a limitation, because not including information on beneficiaries not using medications implies that the actual proportion of beneficiaries reaching the coverage gap might be much lower. Another limitation of the study is that the database did not contain information about a beneficiary's phase status or Low-Income Subsidy status; these were computed by the researchers. Therefore, any coding error in these might inflate or deflate their estimates. An additional limitation of the study is that there is no information about medications procured from pharmacy sources not included in the database (e.g. some patients also use mail-order pharmacy - which are not included in the IMS data - to get their medications and some pharmacies do not submit data to IMS). This could affect the spending amounts that were used to determine whether a beneficiary entered the gap in 2007 or not.

Sun and Lee studied prescription claims data for beneficiaries aged 65 years or older who were continuously enrolled in either PDPs or non-Part D commercial plans from January 1, 2006 through December 31, 2006 as presented in a large pharmacy benefit management database[65]. The study used a pre-post with control group study design. Cases were beneficiaries enrolled in standard PDPs who reached the coverage gap by June 30, 2006. Controls were those enrolled in non-Part D commercial plans. Direct analysis of medication utilization and costs were done for both groups for two time periods: January 1, 2006 through June 30, 2006 (pre-period) and July 1,

2006 through December 31, 2006 (post-period). Among cases, the number days of therapy decreased by 15.85% while OOP spending increased by 88.94% after reaching the gap. Among controls days of therapy increased by 1.77% while OOP spending decreased by 5.54%. Using difference-in-difference models, the study found that being in the coverage gap decreased medication utilization by 187.49 days of therapy and increased OOP spending by $796.49. This study is of significance because it estimated the impact of the coverage gap on beneficiaries enrolled in PDPs and used a quasi-experimental study design which helped account for a number of biases. However, the results of this study need to be interpreted with caution because the PDP was a part of a large pharmacy benefit management program which may not have represented the nationally enrolled Medicare population.

Raebel and colleagues analyzed pharmacy claims data of beneficiaries enrolled in one of the several MA-PD plans offered by the Kaiser Permanente of Colorado from January 1, 2006 through December 31, 2006[60]. The researchers measured medication refill adherence (MRA) for oral medications used for treating diabetes, hypertension, depression and anti-hyperlipidemics as well as beta-blockers and diuretics. In this study, cases were defined as those who reached the coverage gap at some time in 2006 and controls were those who either did not have a gap in coverage or those who did not reach the coverage gap in 2006. The two groups were matched using propensity scores and the controls were then assigned index dates to indicate the pre and post-periods corresponding to the matched cases. The findings suggest that being in the coverage gap significantly reduced MRA rates (p-value < 0.05) for all the therapeutic classes except anti-diabetics and beta-blockers. The largest significant decrease in adherence (defined as MRA > 80%) was observed for patients taking diuretics (8.3% $\pm$ 29.2), followed by those using antidepressants (6.8% $\pm$ 26.3), and anti-hypertensives (5.3% $\pm$ 24.7). The smallest change in

33

adherence was observed for patients using statins or other anti-hyperlipidemic agents (3.6% ±

22.4). However, the study also found that the adherence rates decreased for the control group as

well. Comparing the findings after matching, it was observed that the decreases in adherence for

cases using anti-hyperlipidemics and anti-hypertensive agents were significantly greater than the

decline in adherence rates for corresponding controls (p-value = 0.031 and 0.006 respectively).

Additionally, compared to the corresponding matched cohort, beneficiaries reaching the gap also

experienced greater decreases for beta-blockers (4.9% vs. 3.2% for controls), diuretics (9.7% vs.

7.7% for controls), and anti-diabetic medications (4.0% vs. 2.8% for controls); however, these

differences were not statistically significant.

In another examination, Zhang et al. compared medication usage of beneficiaries enrolled

in the MA-PD program of a large Pennsylvania health insurer to that of beneficiaries enrolled in

employer sponsored programs[66]. The MA-PD program offered coverage through two plans: one

plan offered some coverage for prescription drugs in the coverage gap while the other plan did

not offer any drug coverage while in the coverage gap (cases). The employer sponsored

programs did not have a gap in coverage throughout the year (controls). The control group was

assigned index dates to correspond with the cases' pre-gap and within-gap periods. Medication

utilization was measured as the number of prescriptions filled before and after reaching the

$2,250 threshold where the coverage gap began in 2006. After adjusting for underlying

characteristics like socio-demographics and chronic conditions, the researchers found that those

beneficiaries who reached the coverage gap and had no coverage reduced their medication use by

14% compared to those beneficiaries who did not experience gap. By comparison, beneficiaries

with coverage for generic prescriptions during the gap decreased their medication use by only

3%.

A recent exploration by Fung et al. utilized information on beneficiaries with diabetes from two different MA-PD sponsors who employed different delivery systems and offered different plans to beneficiaries[67]. One of the two sponsors used an integrated delivery system setting and offered a single plan without gap coverage. The responses of beneficiaries in this group were compared to those of beneficiaries in an employer sponsored plan with no gap in coverage throughout the year. The other was a network-model HMO that offered two plans: one with coverage for generic drugs during the gap and another plan without drug coverage during the gap. The study population comprised beneficiaries continuously enrolled in the plan from January 1, 2005 through December 31, 2006, 65 years of age or older and having used 1 or more anti-diabetic medications in 2005. The study examined the drug spending as well as OOP expenditure faced by beneficiaries in the two settings during the coverage gap. In addition, the study also measured adherence to oral anti-diabetic, hypertension and lipid-lowering medications using the Proportion of Days Covered (PDC), which was calculated from the pharmacy dispensing data. Adherence was defined as having PDC $\geq$ 80% for the entire regimen. The study found that the drug spending was 3% and 4% lower among beneficiaries with a gap compared to beneficiaries with no gap and generic coverage respectively. Within the integrated system MA-PD, beneficiaries with a gap had 189% higher OOP expenditures compared to those without gap (employer sponsored group) whereas for the network model HMO system, the difference was less pronounced (14% higher OOP costs for beneficiaries without coverage compared to those with coverage for generic drugs only). The study further found that odds of being adherent were significantly lower for beneficiaries reaching the gap versus employer sponsored group who had no gap within the integrated MA-PD setting for all the three therapeutic drug classes: OR= 0.83, 95% CI (0.79 − 0.88) for oral anti-diabetic drugs, OR = 0.78, 95% CI (0.74, 0.83) for

35

hypertension drugs and OR = 0.69, 95% CI (0.65, 0.73) for lipid lowering agents. However, no significant decrease in the odds of adherence to these medications was found between the two groups using the network-model MA-PD setting.

A common strength of the three studies using MA-PD plan data is that they used quasi-experimental designs with matched control groups that helped account for a number of biases. However, they also share a common limitation that the generalizability of their findings is limited by the use of data from a managed care program that has greater control over utilization of medications by its enrollees. The generalizability of these results is further limited by the fact that most Part D enrollees are part of stand-alone PDPs and not MA-PDs.

All the aforementioned studies utilized data from drug plans. Another set of studies analyzed pharmacy chain dispensing data. Schneeweiss et al. analyzed data generated from computerized pharmacy dispensing information of three large pharmacy chains[47]. Among their many aims was to study the impact of Medicare Part D coverage gap on medication adherence measured using Defined Daily Doses (DDD) and on OOP spending in 2006. The study reported that among patients who reached the coverage gap, use of study drugs (clopidogrel, statins, PPIs and warfarin) decreased significantly compared to their usage in previous months. This decrease ranged from 4.8% for statins to 6.3% for warfarin. There was also an increase in OOP spending among these patients from $12 per 30 DDDs of warfarin to $65 per 30 DDDs of clopidogrel.

Another study using data from pharmacy chains was conducted by Pedan and colleagues[63]. This study analyzed data for prescription drugs dispensed to beneficiaries aged 65 years and older from November 2006 through February 29, 2008 as obtained from 2 large

pharmacy chains. The study reported that among the beneficiaries reaching the coverage gap in 2007, medication use decreased by 9.47% compared to their pre-gap usage.

Both studies mentioned above merit attention because they used pharmacy dispensing data irrespective of the insurance plans in which the beneficiaries were enrolled. This increases the generalizability of the findings. The studies, however, have many limitations. The datasets used in both the studies did not contain plan related information which limited the ability to determine when a beneficiary entered the coverage gap. As a proxy, the researchers assigned a beneficiary to the gap when they had total spending more than the threshold for the start of coverage gap in the respective years and when there was a change in copayments from 25% to 90%. This, however, is an important limitation because most Part D plans are required to offer a drug benefit similar to that proposed by the Government but not necessarily use the same thresholds. In such a situation, some beneficiaries classified as being in the gap might not actually be in the gap and vice versa. The datasets also did not contain information about prescriptions received by mail-order or other pharmacies. In addition, though the studies used a pre-post time trend design, the lack of a control group to account for the underlying temporal trends in medication use requires that the results be interpreted with caution. Despite this, these results continue to indicate that being in the coverage gap adversely affects medication utilization and OOP spending for Medicare Part D beneficiaries.

The coverage gap and cost-cutting strategies

Two studies explored the cost-cutting strategies used by Medicare beneficiaries to cope with prescription drug expenditures after reaching the coverage gap. Cronk and colleagues conducted a review of electronic medical and pharmacy records of members continuously

enrolled in Kaiser Permanente Colorado MA-PD plans in 2006 to identify beneficiaries with and without a gap in coverage[68]. The researchers then surveyed enrollees who reached the coverage gap by October 1, 2006 (cases) and compared their responses to those of beneficiaries enrolled in a retiree drug subsidy plan that did not include a gap in coverage and had total spending corresponding to the threshold for the gap (i.e. $2,250 or more) by October 1, 2006 (controls). The questionnaire comprised 14 questions adapted from a questionnaire developed by Tseng and colleagues to identify the cost-lowering strategy/ies used to cope with high drug expenditures. The study concluded that the cases were three times more likely to report using a cost-lowering strategy compared to the controls (42% vs. 14%, p-value < 0.001). In particular, beneficiaries experiencing a gap in coverage were significantly more likely to use mail-order pharmacy (59.7% vs. 18.0%, p-value < 0.001) or switch to other medications because of cost (32.1% vs. 10.9%, p-value < 0.001). In addition, a significantly greater proportion of the cases reported using less medication than prescribed because of cost (29.1% vs. 11.0%, p-value < 0.001), that they stopped taking a medication because of cost (20.1% vs. 4.6%, p-value < 0.001) or that they did not fill a new prescription because of cost (21.8% vs. 6.1%, p-value < 0.001). An equal number of respondents in both groups reported receiving free samples or buying medications outside the US because of cost. Significantly greater proportions of the cases also reported cutting back on other activities (e.g. enjoyment, paying bills) or not receiving other medical care because of their drug costs compared to the control group. In terms of predictors of using a cost-lowering strategy, the study results indicate that younger beneficiaries with limited drug coverage, lower household income and poorer health status were at a higher risk of adopting one or more strategies to lower their prescription drug cost.

In another investigation, Duru et al. estimated the effect of having coverage for generic medications during the gap on self-reported CRN by beneficiaries with diabetes who were enrolled in various MA-PD and PDP plans and who did and did not use insulin. The study setting utilized administrative claims information on generic drugs utilized by beneficiaries aged 65 years or older in 2005 and 2006 and then administered a computer-assisted telephone interview (CATI) to eligible beneficiaries. The responses were compared for beneficiaries using insulin to those of beneficiaries not using insulin. After adjusting for demographic and clinical characteristics as well as non-response rates, the researchers observed that among insulin users, generic-only coverage was associated with significantly lower rates of self-reported CRN than those with no coverage in the gap (16% vs. 29%, p-value = 0.03). Among the insulin users, no significant differences were observed for reporting the use of cost-cutting strategies like switching to other medications, or shop around for lower prices. By contrast, for the group that did not use insulin, there was no significant difference in the rates of reported CRN but beneficiaries without gap coverage in this group were significantly more likely to switch to a cheaper alternative (46% vs. 36%, p-value = 0.01) and shop around for lowest prices (36% vs. 22%, p-value < 0.001).

Although both these studies indicate that beneficiaries enrolled in a Part D plan with a gap in coverage were more likely to adopt undesirable cost-lowering strategies, it is important to note that these behaviors were not assessed separately after reaching the gap and therefore, it cannot be concluded that the coverage gap was the cause of patients' utilizing more cost-lowering strategies. In addition, the studies were cross-sectional surveys and therefore suffer from limitations related to response and recall biases.

Gaps in Literature

The preceding review of the literature indicates that although Medicare Part D has increased utilization of prescription medications and decreased OOP costs, the coverage gap poses a significant challenge to beneficiaries' adherence. A few studies provide evidence that having partial coverage during the coverage gap is better than having no drug coverage during the coverage gap. However, there are several limitations to the studies reviewed that need to be addressed in future research. For example, several studies lacked use of control groups to account for selection bias introduced by the choice of enrolling in a plan that suits the beneficiary's requirements. For those studies that attempted to overcome this limitation, the design included use of comparison groups (e.g. non-elderly) that could not be considered as being equal to beneficiaries enrolled in Medicare Part D.

In addition, the studies have primarily focused on MA-PD plans and therefore lack generalizability since a majority of the beneficiaries are enrolled in PDPs. Those using a more diverse population through pharmacy chains fail to account for variability introduced by being enrolled in plans that offer different benefit structures.

Most studies have looked at either the difference in number of medications used after reaching the coverage gap or the difference in beneficiaries considered to be adherent after reaching the coverage gap. While these findings are significant, it is also important to understand the extent to which beneficiaries change their medication adherence patterns during the coverage gap using a standardized measure of medication adherence. For example, a 5% change in use of a medication is significantly different from a 50% change in use and this effect is not taken into account by studying the change in number of medications used.

Our study attempts to overcome these limitations by using a quasi-experimental study design with a control group for comparison. In addition, the study utilizes data from a nationally

40

representative sample of Medicare beneficiaries enrolled in PDPs and also accounts for variability introduced by the availability of plans that offer coverage using different benefit structures. The following chapter describes the objectives and specific aims of this research, followed by a chapter presenting the detailed methods used in the conduct of this study before presenting the study results.

RESEARCH OBJECTIVES AND SPECIFIC AIMS

This chapter presents the main objectives of this research as well as the specific aims to meet each objective. In this study, the 'overall final sample' is defined as those who meet the general inclusion and exclusion criteria as outlined in Chapter 4. The "No Gap Coverage" group is defined as those who had no drug coverage when they reached the coverage gap; i.e. they had a complete gap in drug coverage during the coverage gap. The "Some Gap Coverage" group is defined as those who had coverage for some drugs when in the coverage gap; i.e. they had a 'partial' gap in drug coverage during the coverage gap.

<u>Objective 1: To identify characteristics of beneficiaries reaching and not reaching the coverage gap in 2008</u>
Specific Aims:

1. To review the overall demographic characteristics of the final sample of beneficiaries

2. To compare the demographic characteristics of beneficiaries who did and did not have coverage for prescription drugs during the gap

3. To compare the demographic characteristics of beneficiaries who did and did not reach the coverage gap

4. To examine the medication related characteristics (i.e. total number of medications taken, total number of medications from the 7 classes being evaluated, total number of classes under evaluation across which medications are taken, total duration for which the beneficiaries should have been taking the medication since the first fill date) of the overall sample of beneficiaries

42

5. To compare the medication related characteristics of beneficiaries who did and did not have coverage for prescription drugs during the gap

6. To compare the medication related characteristics of beneficiaries who did and did not reach the coverage gap

7. To examine the plan enrollment characteristics of the final sample of beneficiaries

8. To compare the plan enrollment characteristics of beneficiaries who did and did not have coverage for prescription drugs during the gap

9. To compare the plan enrollment characteristics of beneficiaries who did and did not reach the coverage gap

10. To compare the changes in Out-Of-Pocket expenses of beneficiaries in the overall sample who did or did not reach the coverage gap

11. To compare the changes in Out-Of-Pocket expenses of beneficiaries in the "No Gap Coverage" group who did or did not reach the coverage gap

12. To compare the changes in Out-Of-Pocket expenses of beneficiaries in the "Some Gap Coverage" group who did or did not reach the coverage gap

13. To examine the demographic characteristics of beneficiaries for each therapeutic class of medications being evaluated (ACE inhibitors, beta-blockers, calcium channel blockers, diuretics, oral anti-diabetic agents, oral anti-hyperlipidemic agents, and proton pump inhibitors)

14. To examine the medication related characteristics of beneficiaries for each therapeutic class of medications being evaluated

15. To examine the plan enrollment characteristics of beneficiaries for each therapeutic class of medications being evaluated

16. To compare the demographic, medication, and plan related characteristics of beneficiaries in the "No Gap Coverage" group who did or did not reach the coverage gap for each therapeutic class of medications being evaluated before and after matching

17. To compare the demographic, medication, and plan related characteristics of beneficiaries in the "Some Gap Coverage" group who did or did not reach the coverage gap for each therapeutic class of medications being evaluated before and after matching

18. To compare the demographic, medication, and plan related characteristics of beneficiaries who did reach the coverage gap in the "Some Gap Coverage" group to those of beneficiaries who did reach the coverage gap in the "No Gap Coverage" group for each therapeutic class of medications being evaluated before and after matching

Objective 2: To study the entry and exit times from the coverage gap in 2008
Specific Aims:

1. To estimate the proportion of beneficiaries reaching the coverage gap in the overall final sample

2. To estimate the proportion of beneficiaries reaching the coverage gap for the "No Gap Coverage" and the "Some Gap Coverage" groups

3. To estimate the proportion of beneficiaries reaching the coverage gap for each therapeutic class under evaluation in the "No Gap Coverage" group

4. To estimate the proportion of beneficiaries reaching the coverage gap for each therapeutic class under evaluation in the "Some Gap Coverage" group

5. To identify the month by which most beneficiaries reached the coverage gap in the final sample

6. To identify the month by which most beneficiaries reached the coverage gap within each therapeutic class being evaluated for the "No Gap Coverage" group

7. To identify the month by which most beneficiaries reached the coverage gap within each therapeutic class being evaluated for the "Some Gap Coverage" group

Objective 3: To study the impact of a complete gap in coverage on beneficiaries' adherence to prescription medications

Specific Aims:

1. To compare the change in medication adherence during the coverage gap for the beneficiaries of "No Gap Coverage" group who did or did not reach the coverage gap in each therapeutic class before and after matching

2. To examine the proportion of beneficiaries who stopped taking medications during the coverage gap for each therapeutic class in the "No Gap Coverage" group after matching

3. To examine the proportion of beneficiaries considered adherent before and during the coverage gap for each therapeutic class in the "No Gap Coverage" group after matching

Objective 4: To study the impact of a 'partial' gap in coverage on beneficiaries' adherence to prescription medications

Specific Aims:

1. To compare the change in medication adherence during the coverage gap for the beneficiaries of "Some Gap Coverage" group who did and did not reach the coverage gap in each therapeutic class before and after matching

45

2. To examine the proportion of beneficiaries who stopped taking medications during the coverage gap for each therapeutic class in the "Some Gap Coverage" group after matching

3. To examine the proportion of beneficiaries considered adherent before and during the coverage gap for each therapeutic class in the "Some Gap Coverage" group after matching

METHODS

This chapter describes the methods used in the conduct of this study. It highlights the study design and the data sources used in the study followed by sample preparation and data analysis to meet each objective.

Study Design

This investigation employs a quasi-experimental study design with a "before-after" intervention and matched control groups. In an experimental setting, the investigator selects a group of people with similar characteristics and divides them into two groups: one receiving the intervention and the other not. However, in our analysis we retrospectively explore the effect of a "natural intervention" (the Medicare Part D coverage gap) that could have effects on beneficiaries' medication usage. The following section presents the source of data used in this study.

Database Preparation

This was a retrospective analysis of claims and denomination (demographic and enrollment) data of a 5% random sample of all Medicare beneficiaries as provided by the CMS through its Research Data Assistance Center (ResDAC) located at University of Minnesota. The study utilizes four different data files from the entire database: 5% Beneficiary Summary File with Part D denomination, 5% Beneficiary Annual Summary File, 5% Part D Event Data File with drug characteristics (16 or less variables), and the Plan Characteristics Files for 2008. The following sections describe the variables used from each of these data files for further analyses.

47

The Beneficiary Summary File

The Beneficiary Summary File provides demographic and enrollment information about beneficiaries. Beginning in 2006, this file also provides Part D enrollment information. Table 1 shows the variables utilized from this file.

Although the Beneficiary Summary File provides information about most of the demographic characteristics of the patients, it does not contain information about their income. Therefore, the next section outlines the methods to determine beneficiaries' median household income.

Table 1: Variables used from the Beneficiary Summary File

Variable Name	*Description*
BENE_ID	Encrypted beneficiary ID
SSA_STATE_CD	State code of the residence of a beneficiary
BENE_ZIP_CD	Zip code of the mailing address of a beneficiary
BENE_SEX_IDENT_CD	gender of the beneficiary
BENE_RACE_CD	race of the beneficiary
ESRD_SW	presence or absence of End-Stage Renal Disease
BENE_AGE_AT_END_REF_YR	Chronological age of the beneficiary at the end of the year
CST_SHR_GRP_CD_01 – 12	Beneficiary's subsidy and/or co-pay status for each month
RDS_IND_01 – 12	Retiree drug subsidy for each month
DUAL_STUS_CD_01 – 12	Medicaid eligibility by state for each month
PLAN_CVRG_MOS_NUM	Total number of months of Part D plan coverage
BENE_HMO_CVRAGE_TOT_MONS	Total number of months in HMO coverage

48

Calculating Median Household Income

The median household income for the beneficiary's zip code was calculated from the US Census 2000 data. The paragraphs that follow present the methods to generate the income information based on the beneficiary characteristics.

The zip code level information compatible with the CMS Beneficiary Summary File was not directly available through the Census website. Therefore, we used the ZCTA 2000 File available through the Research Triangle Institute (RTI) website at https://rtispatialdata.rti.org/Download/Data/tabid/56/Default.aspx.[69] Although this data file is created from various sources, the median household income by zip code is extracted from the Census 2000 data. We used three variables from this file: P056007, median household income in 1999 dollars age $65 - 74$ years and P056008, median household income in 1999 dollars age 75+ years, and Location_Code; the 5-digit zip code. The zip code variable in The Beneficiary Summary File (Bene_Zip_Cd) provided the full 9 digit mailing zip code of a beneficiary. Therefore, it was re-formatted to retain the first 5 digits to correspond with the 5-digit zip code available from the RTI datafile. This new variable was named Location_Code to maintain the same variable name as available from the RTI datafile. The Beneficiary Summary File and the income file generated from the RTI database were then sorted and merged by zip code (variable: Location_Code) to include the two income variables in the denomination file.

A new income variable (variable: Income) was then created using the age information from the denomination file and the two income variables used from the RTI file. This new income variable contained information representing the beneficiary's median household income based on their zip code and age. These income values were then converted to 2008 dollar values

using the Consumer Price Index (CPI) values for years 2000 through 2008 as explained in the next paragraph.

The CPI is a measure of the average change over time (generally a year) in the prices paid by urban consumers for a market basket of consumer goods and services[70] (e.g. food and beverages, transportation, housing, and medical expenses). The average annual change is calculated as a percentage; therefore, each value representing the percent change was converted to a number representing the proportional change adjusted for inflation over the last year. For example, the CPI value for 2000 was 3.4%. This means that the inflation-adjusted equivalent of 1999 dollars in 2000 would be 103.4% of the 1999 value. In other words, in order to purchase the same product (that was worth $100 in 1999) in 2000, one needs to pay $103.4. For simplicity of calculation, we have converted all the percent change values to proportions. For example, if 1999 dollar value is 1, then with a 3.4% annual inflation rate, the 2000 value would be 1.034. Since we wish to convert 1999 dollars to 2008, we need to account for annual inflation rates throughout this period (Table 2).

Table 2: Consumer Price Index 2000-2008

Year	Annual %	Annual Proportion
2000	3.4	1.034
2001	2.8	1.028
2002	1.6	1.016
2003	2.3	1.023
2004	2.7	1.027
2005	3.4	1.034
2006	3.2	1.032
2007	2.8	1.028
2008	3.8	1.038

Source: Bureau of Labor Statistics Available at http://www.bls.gov/cpi/data.htm[71]

The following equation represents the formula used to obtain the 2008 dollar values.

$$2008 \, Dollar \, Value$$

$$= 1999 \, Dollar \, Value$$

$$\times (CPI'00 \times CPI'01 \times CPI'02 \times CPI'03 \times CPI'04 \times CPI'05 \times CPI'06$$

$$\times CPI'07 \times CPI'08)$$

$$= 1999 \, Dollar \, Value \times 1.292$$

The Beneficiary Annual Summary File (BASF)

     The BASF provides diagnosis and date of diagnosis of 21 chronic conditions. This file is used to identify whether a beneficiary was suffering from chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and/or any type of cancer. Specifically, the variables presented in Table 3 were scanned for a date of diagnosis and if there was a date of diagnosis for either of these variables for a beneficiary, then they were excluded from further analyses.

Table 3: Variables used to identify beneficiaries with COPD/CKD/Cancer

Variable	*Description*
CNCRBRSE	Earliest indication of Female Breast Cancer
CNCRCLRE	Earliest indication of Colorectal Cancer
CNCRPRSE	Earliest indication of Prostate Cancer
CNCRLNGE	Earliest indication of Lung Cancer
CNCENDME	Earliest indication of Endometrial Cancer
CHRNKDNE	Earliest indication of Chronic Kidney Disease
COPDE	Earliest indication of Chronic Obstructive Pulmonary Disease

51

The Part D Event Data File and the Plan Characteristics File

The Part D event (PDE) data and the Drug and Plan Characteristics Files contain elements that provide information on beneficiary demographics, plan characteristics, drug characteristics (e.g. NDC number, days of supply, quantity supplied, and fill number) and payment characteristics (e.g. patient paid amount, and Part D paid amount). The PDE data come directly from the plan sponsors; however, they are not the same as individual drug claim transactions recorded by the plan sponsors. Instead, these data are summary extracts using CMS-defined standard fields to facilitate payments to the plan sponsors. Table 4 lists the variables used from the PDE data and the drug characteristics files. These variables were required to determine the beneficiary's gap status, adherence, and costs incurred by the beneficiary. In addition, the drug characteristics file was used to determine the generic equivalency of different medications as determined by the First Databank, whereas the plan characteristics file helped us identify the variation in benefit structures across plans. Specifically, the plan characteristics file was used to determine whether a particular plan was PDP or MA-PD, whether it offered coverage for some or all drugs during the coverage gap or not, whether it charged a deductible, used standard or self determined coverage gap threshold and the type of cost-sharing used before reaching the coverage gap. All the data files noted above can be linked using the de-identified variable called Bene_ID. The Part D utilization files, however, did not identify a drug's therapeutic class. This information was obtained from the First Databank proprietary classification system using the NDC information provided in the Part D utilization files[72].

Table 4: Variables included from Part D utilization file

Variable Name	Description
BENE_ID	Encrypted Beneficiary ID
SRVC_DT	Date on which the prescription was filled
PROD_SRVC_ID	National Drug Code (NDC) number
QTY_DSPNSD_NUM	Number of dosage units dispensed (Quantity dispensed)
DAYS_SUPPLY_NUM	Number of days' supply of medication dispensed
FILL_NUM	Fill number of the current dispensed supply
DRUG_CVRG_STUS_CD	Drug Coverage status code (Part D covered or not)
CTSTRPHC_CVRG_CD	Catastrophic coverage code
PTNT_PAY_AMT	Non-reimbursed beneficiary paid amount
OTHR_TROOP_AMT	Payments that contribute to True Out of Pocket amount
CVRD_D_PLAN_PD_AMT	Net amount paid by Medicare Part D for a 'covered' drug
BENEFIT_PHASE	Benefit Phase of the Part D event
Drug Characteristics	
BN	Brand Name of drug reported from First Data Bank
GNN	Generic Name of the drug reported from First Data Bank
GCDF	Dosage Form Code
GCDF_DESC	Dosage form code description
Plan Characteristics	
ORGANIZATION_TYPE	Type of organization (PDP, MA-PD etc.)
GAP_COVERAGE_TYPE	Type of coverage offered in the gap
DRUG_BENEFIT_TYPE	Medicare Standard benefit or an equivalent benefit
DED_APPLY	How the deductible applies (if any)
PRE_ICL_APPLY	How the pre-coverage gap cost-sharing applies
ICL_APPLY	How the coverage gap cost-sharing applies

The following figure summarizes the steps involved in preparing the database for sample selection
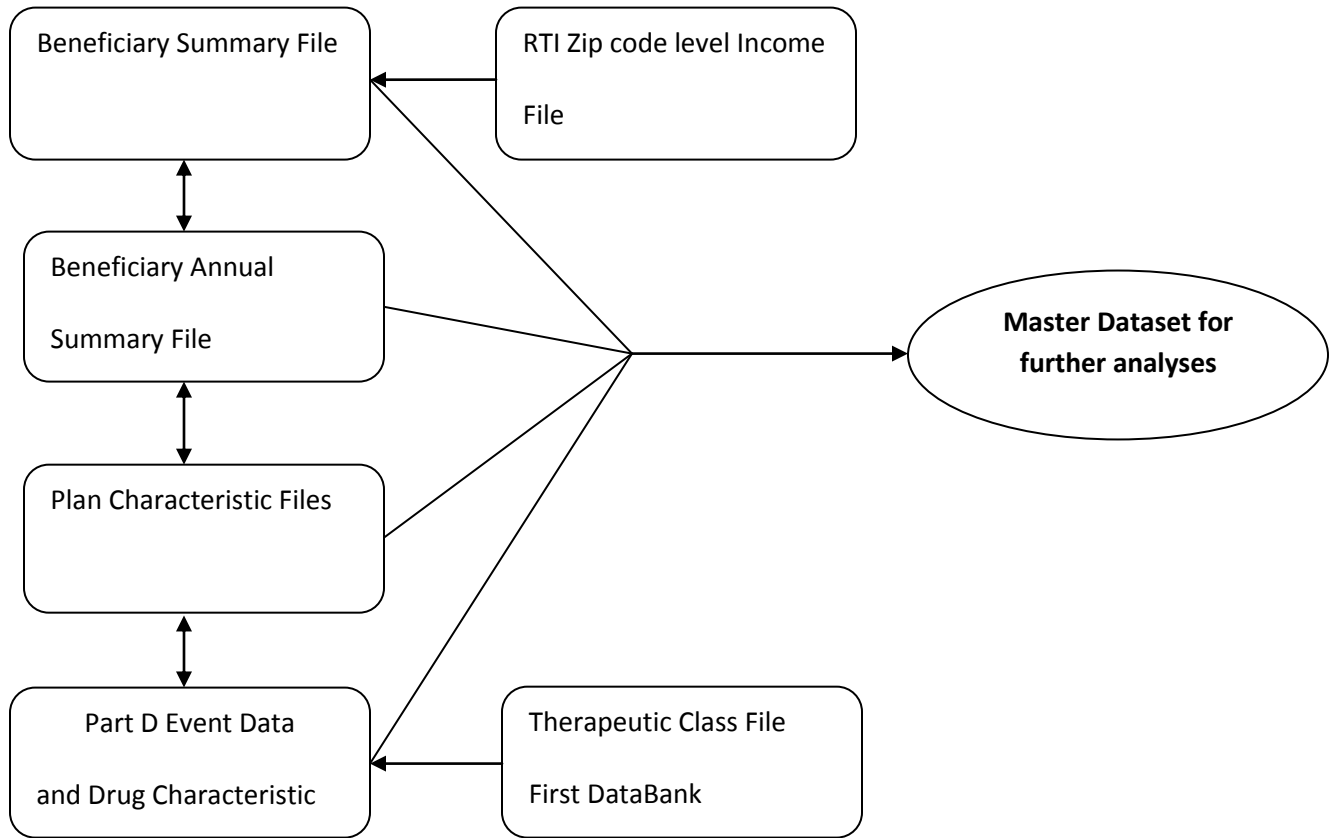
Figure 3: Methods to prepare the Dataset for sample selection

Selecting the sample of beneficiaries: general inclusion and exclusion criteria

The study examined the sampled beneficiaries' prescription drug usage of orally administered drugs from the following seven therapeutic classes: anti-diabetic agents, anti-hyperlipidemic agents, beta-blockers, diuretics, angiotensin converting enzyme (ACE) Inhibitors, calcium channel blockers, and proton-pump inhibitors (PPIs). These classes have been identified by the Centers for Disease Control and Prevention (CDC) as a part of the 15 most widely used classes of medications among community-dwelling seniors aged 65 years and over[73]. The remaining classes of medications in this group could be used for either acute or chronic purposes (e.g. pain medications, thyroid hormones, sex hormones, anti-histamines, anti-convulsants and anxiolytics and antidepressants). The last class of drugs identified in this list by CDC is 'bronchodilators' which are generally used in aerosol format and hence excluded from analysis. Beneficiaries were included in the analysis if they met the following inclusion criteria

- Age 67 years and older: We include beneficiaries who were aged at least 67 years by the end of the 2008. In other words, only those beneficiaries who are aged 66 years or more in 2008 are included in our sample. By doing so, we ensured that the study population had at least one full year of Medicare enrollment.

- Enrolled in stand-alone prescription drug programs (PDPs) from January 1, 2008 through December 31, 2008 (in other words, no MA-PD enrollees).

- Non-subsidy recipients: The study aims to quantify the change in adherence rates after entering the coverage gap and hence does not include beneficiaries who are dually eligible for Medicare and Medicaid or who receive low-income subsidies (LIS) because these beneficiaries are not subject to the coverage gap.

- Alive at the end of 2008

- Do not have cancer, COPD or end stage renal disease (ESRD): these beneficiaries are excluded from our analysis because they have a different medication utilization and spending pattern compared to the beneficiaries with other disease conditions

- The specific medication related criteria for inclusion was that the beneficiary be taking at least one oral medication (defined as either tablet or capsule) from one or more of the above mentioned therapeutic classes for more than 90 days (at least 2 fills).

Following the selection of beneficiaries who met the above criteria, the sample was further divided into groups based on presence of drug coverage during the gap ('Gap_Coverage_type' = 10, and 20, 30, or 40). This resulted into creation of two groups: One with some coverage in the gap (the 'Some Gap Coverage' group with N = 8,529) and another without any coverage in the gap (the "No Gap Coverage" group with N = 164,551). Within these two groups, beneficiaries were further divided into individual 7 therapeutic classes based on their medication use.

Within each class of medication evaluated, beneficiaries included for final analyses must have had the first prescription in the class filled by March 31, 2008. Since no information was available for the dates of diagnoses for most diseases treated by medications in the above mentioned therapeutic classes, this criterion serves as a proxy to identify 'established chronic users' of medications only. We intended to include "established chronic users" only because research has shown that the medication utilization pattern differs with the duration since the disease is diagnosed[74-76]. We extended the first fill date to March 31, 2008 instead of January 1, 2008 to account for the receipt of a 90 day supply of a drug by December 31, 2007. i.e. if a beneficiary refilled a prescription on December 31, 2007 for a 90 day supply, that medication would last till March 30, 2008 and the beneficiary would need to refill it by March 31, 2008.

If a beneficiary took medications from more than one class then he or she was included in the analysis of all applicable classes. Figure 4 summarizes the creation of the required datasets from the Master Dataset. The sections following Figure 4 present the methods of selecting and preparing the sample to study the effect of losing all or some coverage while in the coverage gap on medication adherence of beneficiaries meeting the general inclusion and exclusion criteria.
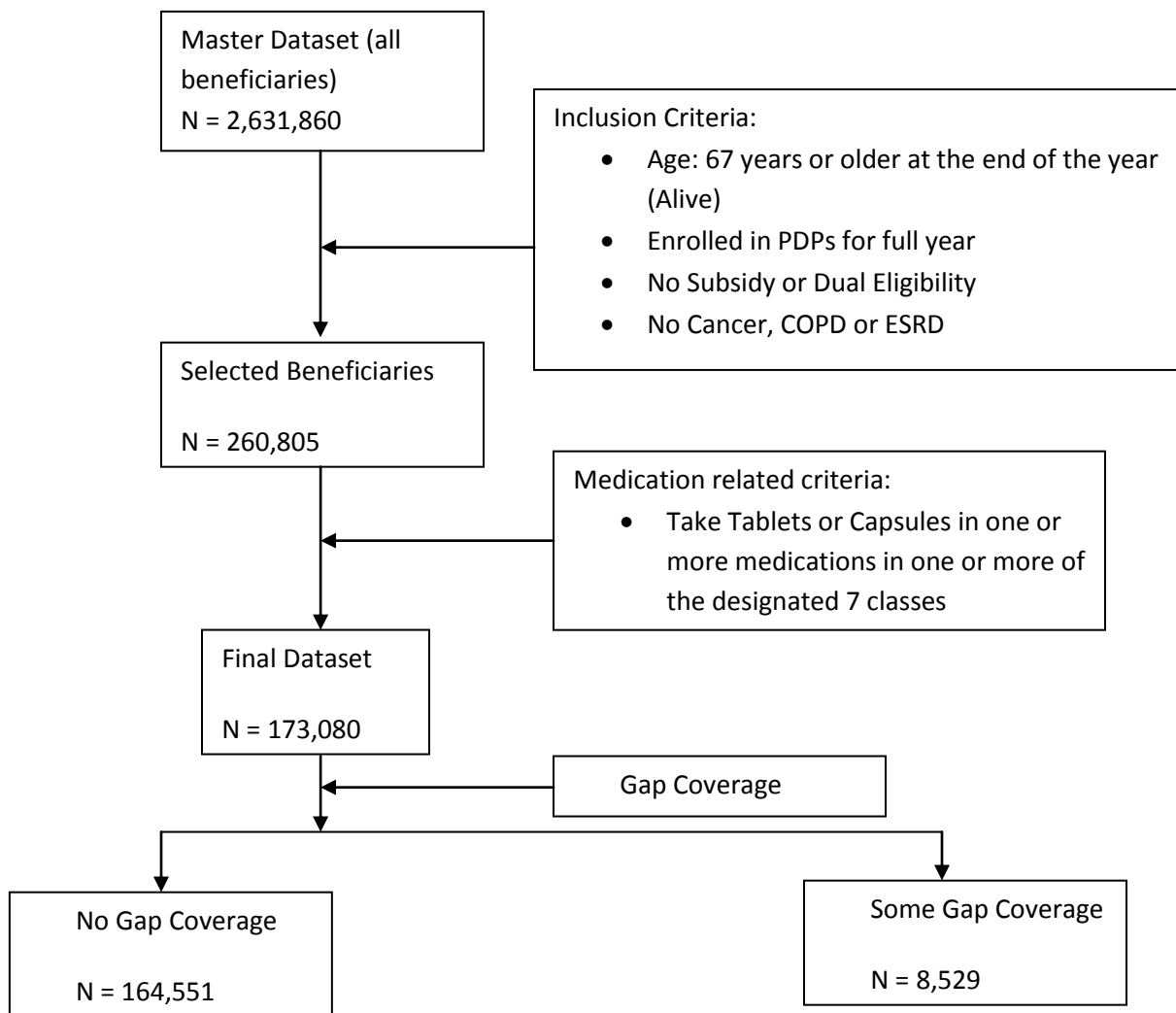
Figure 4: Methods for selecting the samples for the study

Methods to prepare the sample for each analysis

To test the different hypotheses of this study, it was necessary to create different comparison groups from the overall sample at a therapeutic class level based on whether or not the beneficiaries had coverage for drugs while in the coverage gap. For each comparison, the cohort of selected beneficiaries was divided into an intervention group and a matched control group. A control group is required in the study to account for biases introduced by variation in the baseline characteristics of the beneficiaries as well as their choice of enrolling in different plans. Patients in the intervention group (for each analysis) were identified from the claims database as those who met the afore-mentioned criteria and had at least one record of 'PI', or II' values (indicating coverage gap) for the variable 'benefit_phase' in the Part D event file. The remaining records were used as potential controls. Thus, the potential control group consisted of beneficiaries who did not experience the coverage gap during the year ('Benefit_Phase' = 'DD', 'DP' or 'PP'), and those who were catastrophically high spenders and skipped the coverage gap by entering the catastrophic coverage phase after the initial coverage ('Benefit_Phase' = 'PC'). The latter are excluded from further analysis. The two groups (who did and did not reach the coverage gap for each analysis) were then analyzed individually and also after being matched using a propensity score technique.

Propensity Scoring

Propensity scores are useful in controlling for selection bias in situations where the experimental units are not allotted to the treatment groups in a random fashion and therefore have different distributions of the baseline covariates. A propensity score for an individual is "the conditional probability of his or her treatment given the observed pretreatment covariates"[77].

58

Thus, units with similar propensity scores will tend to have similar levels of the covariates; thereby removing bias due to the covariates from the estimates[77].

Generally, a logistic regression is performed to calculate one's propensity to get one treatment over the other with the dependent variable being the treatment received (variable with 1 and 0 values depending on the group they are in)[78]. While there is considerable debate about which variables should be included as independent variables, a recent study done by Austin et al.[79] employed Monte Carlo simulations and found that "including only the true confounders (those that are associated with both treatment assignment and outcome) resulted in greater precision in estimating the treatment effect compared to the model that included variables associated with treatment assignment or outcome alone." The researchers concluded that this was because the model that included scores calculated using the true confounders had the lowest Mean Square Error (MSE) estimate among all the four models and also resulted in 24% more matched pairs compared to any other model[79]. Therefore, only the 'true confounders' will be included in estimating the propensity scores in our study.

Following the calculation of propensity scores, the selection bias can be accounted for in one or more of the following three ways: stratification, adjustment in the regression analysis and matching[78]. Each of these techniques is a way to make an adjustment prior to or while calculating the treatment effect. Matching helps in removing the bias before calculating the effect whereas regression adjustment is made during the calculation. Stratification can be used in either way. The following sections provide brief description for each method.

Stratification involves ranking of the observations based on the propensity scores and dividing them into various strata based on their scores. Thus, in this method, observations with

similar propensity scores are grouped together for the analysis. The outcome is then analyzed by strata and a weighted estimated mean is obtained per stratum. The results for each stratum are then combined and analyzed. Another method to analyze the information using stratification is to incorporate the strata in the multivariate analysis [77, 78].

Another technique is to use the propensity score as an additional variable during the regression analysis and not use the variables used to generate this estimate. This can take into account the bias created by non-equivalent distribution of the variables between the two groups.

Matching is generally employed when the sample size is large and when there are sufficient number of controls to match with the intervention group. If the sample size is not large enough, then removing those cases and controls that do not match will reduce the size of the sample and result in loss of power[77, 78]. If this technique can be used, then the procedure is to match the observations in the two groups on their propensity scores and then analyze the significance of differences in outcomes between the two groups using techniques for non-independent samples (or matched pairs).

Objective: To quantify the change in medication adherence among beneficiaries who had "No drug coverage" during the coverage gap

Within the "No Gap Coverage" group, for each therapeutic class of medications to be analyzed, the beneficiary records were classified as being in the gap versus. not being in the gap using the criteria mentioned earlier. The purpose of this analysis was to study the impact of completely losing drug coverage during the coverage gap as compared to having stable coverage throughout the year. Ideally, to attain this aim, we needed to have a control group that reached the coverage gap and had no change in the coverage during the gap. Since our data did not

60

permit the use of such a control group, we compared the effects of losing coverage to those who did not reach the gap in 2008. This is because it can be inferred that by not reaching the coverage gap at any point in 2008, the beneficiaries maintained continuous coverage for their medications throughout the year.

To account for the variation introduced by baseline characteristics as well as for the bias introduced by the voluntary enrollment in the Medicare Part D programs, the two groups were matched based on the propensity of a beneficiary to fall in the coverage gap (treatment assignment). This was calculated by performing a logistic regression with Dependent variable = "gap status" where (0 = No Gap and 1 = Gap) and covariates mentioned in a later section.

Objective: To quantify the change in medication adherence among beneficiaries who had "some drug coverage" during the coverage gap

For this part of the analyses, we compared the group that reached the coverage gap and continued to have some coverage for their prescription drug expenses to two groups. First the group that retained some coverage during the gap was compared to the group that did not reach the gap from the "Some Gap Coverage" group. The purpose of this comparison is to compare the effectiveness of having some coverage during the gap to not losing the coverage throughout the year. Again, as with the analysis to study the effect of losing complete coverage during the gap; we needed to adjust for selection bias as well as variation introduced by differences in beneficiaries' baseline characteristics. To do so, we again calculated the propensity of reaching the gap (dependent variable = 'Gap' where 0 = No Gap and 1 = Gap) and the independent variables being those described in the next section.

61

For the second part of the analyses, the change in these beneficiaries' adherence patterns was compared to the change in adherence patterns of the group that reached the gap and lost all coverage upon reaching the gap. Here, both the groups reached the coverage gap at some point in the year; however, we did have to account for the selection bias introduced by the choice to enroll in a plan with or without gap coverage rather than being randomly assigned to each plan. In addition, the variation introduced by the baseline characteristics of the two groups also needed to be adjusted for. Therefore, for this part of the analyses, we estimated the propensity of a beneficiary being enrolled in a plan that offered some coverage during the gap (treatment assignment dependent variable = 'Gap_Coverage' where (0 = No Coverage and 1 = Coverage)) based on the independent variables explained in a later section.

Independent variables for propensity score calculation

In this study, the propensity scores were separately calculated for all comparison groups for all therapeutic classes based on age, race, gender, income, the Chronic Disease Score (CDS), total number of medications taken by the beneficiary, the duration of prescribed medication, drug benefit type, and type of cost sharing in each phase of Part D. These variables are identified as those that are known to be associated with experiencing the coverage gap (treatment) as well as medication adherence (outcome). The effect of these variables on reaching the coverage gap has been described elsewhere. The following paragraphs briefly describe how these variables affect adherence to medications

Socio-demographic factors

Age: The effect of age on medication adherence is not clear. Some studies conclude that younger patients are likely to be less adherent than older patients[75, 80-83], whereas several others conclude that age is not a significant predictor of adherence [84-87].

Gender: Gender is found to be uncorrelated with adherence in general, with the exception of a few studies that did find differences in adherence rates among males and females[28, 81, 85].

Race: Race is a significant predictor of adherence with non-Caucasian race being significantly associated with lower adherence[76, 80, 83, 86, 88-91]. For example, Steinman et al. [20] found that non-Caucasian Americans were almost 3 times more likely to report reduction in medication use when faced with higher costs compared to Caucasians after controlling for income, drug coverage and health status variables.

<u>Financial factors</u>

The literature indicates that low income translates into more cost related medication adherence [21, 22, 41, 92, 93]. Additionally, it has been established that absence of insurance coverage, as well as having caps or gaps in coverage, leads to medication non-adherence[9].

<u>Medical factors</u>

Disease-Related: The literature on effects of co-morbidities on medication adherence is less conclusive. Some articles conclude that co-morbidity is not a significant predictor of medication adherence[85, 86] but others conclude that higher numbers of disease conditions led to higher rates of non-adherence[21, 41, 92, 93]. Depression is also often cited as a predictor associated with significantly lower adherence rates among patients across a range of different chronic conditions[83, 94-96].Studies also suggest that the longer the duration of diagnosis of a disease, the more likely a patient is to adhere to the therapy[75, 76, 97]

Medication-Related: Evidence clearly suggests that an increase in the frequency of administration of medications decreases adherence rates[74, 75, 82, 98, 99] . In other words, regimens that require taking medications several times a day leads to lower adherence rates. However, the effect of number of prescriptions taken is not clear. For example, Col et al.[28], Coons et al.[85],

63

Donnan et al.[75] as well as Mateo et al.[97] report that the rates of non-adherence increase with an increase in the number of prescriptions taken, whereas Grant et al.[100] and Shalansky et al.[101] conclude that non-adherence decreases with an increase in the number of prescription medications taken.

Most of the above mentioned variables were directly available from the database. The following paragraphs present the methods to calculate the variables that were not obtained from the database.

1.   Calculating the CDS

Von Korff et al. used automated pharmacy data from an HMO for one year to calculate a measure of severity of chronic diseases based on consensus of a multidisciplinary team of physicians, pharmacists, epidemiologists and health service researchers[102]. This measure is called the Chronic Disease Score or CDS. The CDS is calculated by grouping individual medications to their respective therapeutic classes and then assigning weights (scores) to the classes depending on the severity of the disease for which the class of medications is primarily used. The CDS assigns greater scores to potentially life-threatening and advanced disease conditions that require simultaneous use of medications from several therapeutic classes. By doing so, the CDS provides a measure of severity of illness by taking complexity of regimen and progress of the disease condition into account[102].

Originally, the CDS was developed to represent 30 therapeutic classes and was validated to predict hospitalization as well as mortality. From the results of their analyses, Von Korff et al. concluded that a CDS of 7 or greater was associated with a 5 fold increase in risk of hospitalization and a 10 fold increase in risk of mortality compared to CDS of 0[102]. The CDS

64

was found to be a significant predictor of hospitalization and death even after adjusting for age, gender and ambulatory care visits. Several studies have replicated and/or extended the validity of the CDS since its development in 1991. Over time, the CDS has been shown to have good test-retest reliability, construct validity with the RAND-36 instrument, and good predictive validity for hospitalizations, mortality and health care visits[103-109]. Since we are assessing the adherence patterns for selected classes of medications, the computation of the CDS for our study required modification of the original algorithm (which was based on 30 therapeutic classes[102]). Table 5 describes the classes and associated weights involved in the calculation of the CDS for this study.

Table 5: Chronic Disease Score Calculation

Disease Indicator	*Therapeutic Class*	*Score/Weight*
Heart Disease	ACE Inhibitors	3
Hypertension	Calcium channel blockers	2
	Beta-blockers	1
	Diuretics	1
Diabetes	Oral Anti-diabetic Agent	2
High Cholesterol	Anti-hyperlipidemics	1
Peptic Ulcers	Proton Pump Inhibitors	1

2. <u>Calculating total number of medications taken</u>

The total number of medications was calculated as the total number of distinct generic medications taken by a beneficiary who meets the inclusion criteria for this study. Thus the total number of medications taken by a beneficiary included the medications taken within the 7

therapeutic classes evaluated as well as medications from other classes not being evaluated for adherence.

3. Calculating the total duration of prescribed medication

The total duration of a medication prescribed in any class was calculated as the number of days between the first fill date and December 31, 2008. Thus, for example, if a beneficiary had their first fill on January 1, 2008 then the total number of days that they should be taking the medication was calculated as (days between January 1, 2008 and December 31, 2008) irrespective of whether or not they reached the coverage gap.

Propensity Score Matching

Following calculation of propensity scores, for each comparison in this study, we matched the two comparison groups (e.g. those reaching the coverage gap were matched to those who did not in the "No Gap Coverage" group) using the propensity score based Greedy 5 → 1 digit matching technique for SAS[110]. In this technique, propensity scores are arranged in decreasing order and then observations are attempted to be matched on the first 5 digits of the score. If all cases are not matched, then a four digit match is attempted. This process is repeated until matches are attempted on the first digit of the propensity score. This maximizes the number of matched pairs formed while minimizing error. Observations that cannot be matched using this technique are excluded from the analysis.

Observations in the matched control group were then allotted index dates to match the time of entrance into the coverage gap for the corresponding case. Thus, for example, if a beneficiary in the intervention group entered the coverage gap on August 1, 2008, and remained

66

in the gap for the rest of the year, he or she would have a "before" the intervention (coverage gap) period of January 1, 2008 until July 31, 2008 and an "after" the intervention period of August 1, 2008 through December 31, 2008. The matched control is then assigned an index date of August 1, 2008 and in this particular example, his or her "before" period was from January 1, 2008 through July 31, 2008 and the "after" period was from August 1, 2008 through December 31, 2008. This design allowed analyses of the two groups controlling for variation in baseline characteristics as well as potential secular trends that can affect adherence rates irrespective of a beneficiary's gap status. The methods used to calculate medication adherence are outlined in the next section.

67

Measuring Medication Adherence

Methods to assess medication adherence include self-reporting, pill counting, patient diaries and using claims data[111]. In this study, pharmacy claims data were used to measure beneficiaries' adherence to prescribed medications in 2008. The use of retrospective claims data for assessing adherence generally requires slight alteration of the theoretical definition presented earlier, because claims data do not provide information on the act of taking the medication as indicated. Thus, for assessing adherence from claims data, the definition was operationalized as "the number of doses dispensed in relation to the dispensing period"[19].

Several methods of measuring adherence to medications using retrospective claims data have been proposed so far; however, the superiority of one method over the other is yet to be ascertained. These methods include but are not limited to calculating gaps in filling prescriptions, proportions of days covered and Medication Possession Ratio[111]. This study uses the most popular measure of calculating medication adherence using claims data: Medication Possession Ratio (MPR)[112].

MPR is calculated using the formula noted below:

$$MPR = \frac{Number\ of\ days\ of\ medication\ supplied\ within\ the\ refill\ interval}{Number\ of\ days\ in\ the\ refill\ interval}$$

This is usually calculated by summing the number of days supplied for all but the last refill, divided by the number of days between the first and the last refill. Therefore, at least two fill dates are required to calculate this ratio.

Since we wanted to assess adherence levels before and during the coverage gap for each comparison group in each therapeutic class, we calculated different MPR values for each period for both the cohorts in each therapeutic class. The MPR for the time when a beneficiary was not in the coverage gap was calculated as follows: The numerator equaled the total days of supply

between the first fill in 2008 and the last refill before the date that the beneficiary entered the coverage gap plus the days of supply between the last fill and the first date of reaching the coverage gap. The latter was calculated by splitting the days of supply obtained with the last fill to match the number of days left before reaching the coverage gap and carrying forward the remaining into the coverage gap phase calculations (the same time period was used for the matched control). The denominator was calculated as the total number of calendar days between the day the beneficiary first reached the coverage gap and the date of first fill.

The MPR within the period when the beneficiary was in the coverage gap was calculated as follows: the numerator equaled the total days of supply between the refill when the beneficiary reached the coverage gap in 2008 and the refill when the beneficiary reached catastrophic coverage or December 31 in 2008; whichever came first (the same time period is used for the matched control). The denominator equaled the maximum of total number of calendar days between the two fill dates used in the numerator and the total number of days a beneficiary spent in the coverage gap. This is because when beneficiaries reach catastrophic coverage, they are no longer in the coverage gap. However, if beneficiaries do not reach catastrophic coverage by the end of December, they are still out of the coverage gap because they re-enroll in the plan beginning January of every year. Again, the excess days of supply before and during the coverage gap is split to match the corresponding days in that phase and the remaining are carried over into the next phase. If a beneficiary ended the year in the coverage gap phase but did have days of supply more than the days in the gap, then the excess days of supply were excluded from the analysis

In this study we calculated adherence to solid oral dosage forms (tablets and capsules) from one or more of the therapeutic classes mentioned earlier only. Generic drugs are

69

therapeutically equivalent to the corresponding brand name drugs. Hence, if a beneficiary switched from a brand name drug within a therapeutic class to a therapeutically equivalent generic drug in the same class during the study period (e.g. from Zocor® to simvastatin), he or she was considered as continuing with the same therapy in the calculation of MPR. Additionally, the study examines changes in adherence rates by therapeutic class and hence substitution to a chemically different but therapeutically equivalent drug within the same class (e.g. from Lipitor® to Zocor®) was also considered as continuing with the same therapy in the calculation of the MPR. However, switching between classes (e.g. from beta-blockers to diuretics for hypertension) was not considered as being adherent. Beneficiaries taking medications from multiple therapeutic classes were included in the analysis of every applicable class.

Measuring proportion of beneficiaries considered adherent before and during the coverage gap

MPR can be presented as a continuous measure of adherence or dichotomized into "adherent" or "non-adherent" groups. We used the most common threshold for this dichotomization: MPR value ≥80% was classified as adherent and those with MPR < 80% were classified as non-adherent.

The first use of 80% as a cut-point was a study done by Psaty et al. in 1990[23]. This study examined the relation between adherence to hypertensive medications and risk of developing myocardial infarction. The researchers did not mention any rationale for selection of this cut-off, just that 'it was assumed to be 80%'. This was a randomized clinical trial that found that patients with less than 80% adherence to their medication (as measured by calculating MPR from a computerized pharmacy database) have a 4 fold increase in risk of developing acute cardiac events. As it appears, this was a disease specific measure.

Over the last decade, there has been an increasing interest to evaluate whether being adherent to medications more than 80% of the time provided any clinical benefit. Several studies done in this time period have concluded that having MPR value ≥ 80% significantly improved clinical outcomes and/or reduced healthcare utilization and costs for specific disease condition and studies indicate that there are significant improvements at and beyond this threshold. For example, a study by Lau et al. found that among patients taking oral hypoglycemic agents to control their diabetes, those who had MPR values less than 80% had higher odds of being hospitalized compared to those who had MPR ≥ 80% (odds ratio: 2.53, with significant 95% CI)[113]. A recent study by Karve et al. examined the validity of different cut-off values of MPR in terms of predicting hospitalizations in a large Medicaid population database (predictive

71

validity)[114]. This study found that the optimal cut-off value for MPR to predict any cause hospitalization ranged between 0.63 and 0.89 and for disease specific hospitalization, the values ranged from 0.58 to 0.85. Thus, it concluded that it is reasonable to select 0.80 as the cut-off point. Hansen et al. [115] attempted to measure the convergent validity of the measure with other measures of adherence (patient self-report and electronic adherence measures) at different cut-off points. This study found that at the widely used cut-point (80%), there was a balance between the sensitivity and specificity in classifying the subjects with heart failure or hypertension for all measures and that they correlate well with each other at this point. This study has limited generalizability because it was conducted on patients with a specific disease condition. However, both of these studies provide an empirical basis for using 80% as the cut-off value in classifying patients as being adherent and non-adherent

Thus, we expect that using 80% as the cut-off in our study provides information of practical relevance for policy makers and define a beneficiary as being adherent if their MPR value is 0.8 or greater. This analysis is done by therapeutic class and by presence or absence of drug coverage during the coverage gap after matching for both the groups that did or did not reach the coverage gap.

Measuring proportion of beneficiaries who stopped taking their medications during the coverage gap

In this analysis, we examined the proportion of beneficiaries who stopped taking their medications after reaching the coverage gap for each therapeutic class. This analysis was done after matching to examine the effect on the matched control group as well. For this purpose, we defined a person to have stopped taking their medications in the coverage gap phase if they were found to have reached the coverage gap but had no days of supply (as calculated earlier) of medications for that time. For example, if we assume that a person reached the coverage gap on December 1, 2008 but had a 90 day supply of medications dispensed to him/her on October 1, 2008 This was included in the analysis by splitting the 90 day supply received on October 1 into a 60 day supply before the gap and 30 day supply in the gap. Thus, it would not appear as if the beneficiary discontinued the medication during the coverage gap phase. However, if the beneficiary received a 30 day supply on October 1 and did not have any refill thereafter, then it would indicate that s/he stopped taking his/her medications.

73

Data Analyses

The following sections describe our data analysis:

Descriptive analyses

We performed several types of descriptive analyses. First, we studied the entire final sample in terms of their demographics (age, race, gender, income), total number of medications used, and out of pocket costs. The results were reported as means and standard deviations for the following variables: age, income, total number of medications used and out-of-pocket costs. The variables 'race' and 'gender' are reported as percentage of Caucasian population and percentage of males and females respectively.

Next, we identified the percentage of beneficiaries who entered the coverage gap in 2008 overall and for each therapeutic class as well as months spent in the coverage gap. Following this, within each therapeutic class, we studied the characteristics of beneficiaries who reached the coverage gap in 2008 to understand their demographics, month of entry in the coverage gap, CDS, total duration for which they should have taken their medication and total number of medications as well as plan characteristics. For all variables except the median annual household income (which was reported as median), results were reported as means and standard deviations for all the continuous variables (age, total medications, total duration and CDS). As before, race and gender are expressed as percentages. In addition, the percentage of beneficiaries having no deductible, tiered cost-sharing and Medicare defined standard gap threshold were also reported for each therapeutic class.

We performed similar analyses for the group that did not reach the coverage gap to study the differences in the baseline characteristics of the two groups before matching. Appropriate tests for significance in differences are reported in the next chapter depending on the variable

type. In general, the significance of differences between the two groups for the categorical variables was assessed by chi-square tests whereas that for the continuous variables was assessed using the Wilcoxon Rank Sum Test.

The two groups were reassessed on the same variables after matching to check the quality of matching. However, since the two groups were now matched pairs, the underlying assumption of using independent samples in comparisons using the Wilcoxon Rank Sum test as well as Chi-square test is violated. Therefore, we used the appropriate tests of significance for paired data. For continuous variables, we used the Wilcoxon Signed Rank Test whereas for categorical variables the significance of difference was assessed using the McNemar's test.

Measuring the Impact of Coverage Gap on Adherence

We studied the impact of coverage gap on adherence rates to medications prescribed in different therapeutic classes mentioned earlier. The main outcome of interest was change in adherence to prescription medications after reaching the coverage gap. This was measured as a difference of MPR before and MPR after reaching the gap. This value was obtained for each beneficiary for both the treatment and the control group. The statistical significance was then measured using the Wilcoxon signed rank test which tests for a significant difference between the paired data. The test was performed by therapeutic classes of the drugs for both the treatment and the control group. In other words, this first set of analysis tested for significance in change in adherence rates using the paired data of beneficiaries who entered the coverage gap and similar analysis was done for their matched controls. Thus, here, the beneficiaries in each group served as their own controls.

The second set of analyses was done to account for the baseline characteristics of the beneficiaries and changing time trends using the simple difference in difference (DD) technique.

75

This technique involves comparison of differences in the difference between the before and after values of the outcome variable (here MPR values) for the treatment and control group. Thus, we calculated the difference in MPR values before and after reaching the coverage gap for each group and then calculated the difference of these differences.

Let Mt,b and Mt,a respectively represent the MPR value before and after reaching the coverage gap for the treatment group and Mc,b and Mc,a respectively represent the MPR values for matching time for the control group. Then, the DD estimator was calculated as:

$$DD = (Mt, b - Mt, a) - (Mc, b - Mc, a)$$

We employed this simple analysis technique instead of using a regression that can control for other baseline characteristics because we had already matched the two groups on other baseline characteristics using the propensity score technique. The matched control group was allotted index dates that correspond to the times before and within the coverage gap for the matched case. Thus, the DD estimate obtained in our analysis accounted for both observed and unobserved factors that can affect the change in adherence rates during the coverage gap and hence provide a more robust association between the coverage gap status and change in adherence rates[116]. The statistical significance of the differences between the groups was again assessed using the Wilcoxon signed rank test for paired data. This analysis was done at therapeutic class level for the groups depending on whether or not they had drug coverage during the coverage gap.

CHAPTER 5

RESULTS

This chapter presents the sample size and the results obtained for each objective.

Sample Size

The master dataset created after merging all the CMS datasets as well as those created for income and therapeutic class consisted of claims, demographic and enrollment information of 2,631,860 unique beneficiaries enrolled in Medicare in 2008. After applying the general inclusion and exclusion criteria, the dataset comprised 250,890 unique beneficiaries. Upon application of medication related criteria (i.e. taking one or more oral medications in one or more of the 7 therapeutic classes), the final sample contained information of 173,080 beneficiaries. These beneficiaries were then separated into two groups based on their enrollment in plans that did or did not offer drug coverage in the coverage gap. Thus, the two groups were a) beneficiaries enrolled in plans that did not offer any coverage during the coverage gap (No Gap Coverage Group (N = 164,551) and b) beneficiaries enrolled in plans that offered some coverage during the coverage gap (Some Gap Coverage Group N = 8,529).

Within each of these two groups, beneficiaries were separated into therapeutic classes being evaluated in this study. If a beneficiary took medications from more than one class among those evaluated, then they are included in each applicable class. However, within each class, if the first fill date was after March 31, 2008, then that record was deleted from further analyses. Due to this criterion, although several beneficiaries took medications from the classes being evaluated at some point in 2008, only those with a presumed full year of usage were included in

77

further analyses. For example, in the 'No Gap Coverage group, 40,060 beneficiaries were taking ACE inhibitors in 2008; however, only 34,477 beneficiaries had records of filling the first medication by March 31, 2008. Therefore, the rest were excluded from further analyses in the study. Among the overall sample of beneficiaries included in the subsequent analyses, the most widely used class of drugs was anti-hyperlipidemic agents, followed by beta-blockers, diuretics, ACE inhibitors and calcium channel blockers. The classes of drugs used by a lesser proportion of beneficiaries were PPI and oral anti-diabetic agents. Table 6 shows the sample sizes for each therapeutic class being evaluated by the type of coverage during the gap.

Table 6: Sample Size by Therapeutic Class

Therapeutic Class	No Gap Coverage	Some Gap Coverage
ACE inhibitors	34,477	1,499
Beta-blockers	47,911	2,295
Calcium channel blockers	29,229	1,384
Diuretics	47,711	2,275
Oral anti-diabetic agents	17,500	845
Oral anti-hyperlipidemic agents	69,178	3,407
Proton pump inhibitors	23,925	1,117

The following section presents the descriptive characteristics of the overall sample as well as by therapeutic class.

Descriptive Characteristics

All beneficiaries (N = 173,080)

Overall, our sample was found to be older and predominantly Caucasian. The mean age of the beneficiaries in our sample was 77.43 ($\pm$ 7.05) years. A little over 90% of the sample was found to be Caucasian and almost three - quarters of the sample (73.35%) comprised females. The sample had a median household income of $33,646. On average, beneficiaries in our sample took 7.94 ($\pm$ 4.30) unique medications, and were predominantly enrolled in stand-alone Prescription Drug Plans (PDPs) that offered coverage using some modification of the standard Medicare Part D benefit structure (58.10%).

For the sample in our study, a majority were enrolled in plans that did not charge a deductible (75.93%), had tiered cost-sharing (in contrast to Medicare defined coinsurance of 25%), had coverage gap and catastrophic coverage beginning at the Medicare defined amount ($2,510 in total spending and $4,050 in OOP spending respectively) and did not offer coverage for any drugs in the coverage gap (95.07%).

Presence or absence of coverage during the gap

As with the overall sample, both groups (with or without coverage in the gap) were found to be older, predominantly Caucasian, female and on several medications. The group with some coverage in the gap was similar to the group without coverage in the gap in terms of demographics. However, there were significant differences in the benefit structures offered by the plans in the two groups. The beneficiaries in the "Some Gap Coverage" group were enrolled in plans that offered drug coverage through 'enhanced alternative' structure that did not charge a deductible. By comparison, beneficiaries in the "No Gap Coverage" group were enrolled in plans

that offered drug coverage through a variety of benefit structures. Only about a third of these plans offered an 'enhanced alternative' benefit structure, and a quarter of all plans charged a deductible. In spite of these variations, it was interesting to note that plans in both the groups had tiered cost sharing for covered prescription drugs and had coverage gap begin and end thresholds that were the same as those defined by Medicare. Table 7 lists the characteristics of the overall sample and of the two groups.

Table 7: Characteristics of beneficiaries overall and by type of coverage in the coverage gap

Characteristic	Total N=173,080	No Gap Coverage N = 164,551	Some Gap Coverage N = 8,529
Age(Mean (Std. Dev*))	77.43(7.05)	77.42(7.05)	77.8(7.01)
Race (%Caucasian)	91.92	91.88	92.73
Gender (% Females)	73.35	73.29	74.58
Income** (Median)	33,646	33,662	33,259
Total # of medications	7.94(4.3)	7.92(4.29)	8.31(4.41)
Drug benefit type (% Standard or equivalent)	58.1	61.11	0
Deductible (% No)	75.93	74.68	99.99
Initial Coverage Limit (% beneficiaries with Medicare defined amount)	98.78	98.72	99.91
Initial cost sharing (% beneficiaries with tiers)	99.24	99.2	99.99
% beneficiaries with drug coverage in coverage gap	4.93	N/A	100

Note: * Std. Dev means Standard Deviation, ** Income = median household income of beneficiaries' zip-code

Characteristics of beneficiaries by class

1.   **No Gap Coverage Group (N = 164, 551)**

(a)   Demographic Characteristics

As observed with the overall dataset, the mean age of the sample in each class was close to 78 years of age. Additionally, approximately 90% of the sample in each therapeutic class was Caucasian with most being females. Table 8 presents the demographic characteristics of the sample by therapeutic class.

Table 8: Demographic characteristics of beneficiaries with no drug coverage in the coverage gap by therapeutic class

Class	N	Age Mean (Std.Dev*)	Race %Caucasian	Gender %Males	%Females	Income** Median $
ACE inhibitors	34,477	77.49(7.06)	91.76	31.69	68.31	32,704
Beta-blockers	47,911	77.89(7.02)	93.17	26.47	73.53	32,612
Calcium channel blockers	29,229	78.52(7.29)	89.37	22.63	77.37	32,609
Diuretics	29,229	78.36(7.31)	91.53	20.66	79.34	31,896
Oral anti-diabetic agents	17,500	75.99(6.37)	85.38	34.75	65.25	32,867
Oral anti-hyperlipidemic agents	69,178	76.39(6.41)	92.18	30.57	69.43	34,453
Proton pump inhibitors	23,925	77.04(7.01)	91.92	23.27	76.73	33,132

Note: * Std. Dev means Standard Deviation, ** Income = median household income of beneficiaries' zip-code

(b)   Medication Related Characteristics

As with the overall sample, the beneficiaries from each therapeutic class took at least 8 unique medications. In addition, a majority of the beneficiaries in each class concurrently took at least 4 medications from an average of three of the classes being evaluated in this study. For each class studied, the total duration that the beneficiaries were supposed to take the medications was around 345 days. The medication related characteristics of the beneficiaries in each class are outlined in Table 9 below:

Table 9: Medication related characteristics of beneficiaries with no drug coverage in the coverage gap by therapeutic class

Class	Total Rx* Mean (Std.Dev**)	Total Class† Mean (Std.Dev)	Total Rx from classes†† Mean(Std.Dev)	Total Duration††† Mean (Std.Dev)
ACE inhibitors	7.70(3.71)	3.11(1.29)	3.43(1.60)	346.79(19.82)
Beta-blockers	7.94(3.79)	3.06(1.25)	3.32(1.54)	345.32(20.96)
Calcium channel blockers	8.13(3.67)	3.11(1.32)	3.46(1.82)	345.53(21.01)
Diuretics	8.35(3.91)	3.04(1.27)	3.37(1.53)	345.76(20.59)
Oral anti-diabetic agents	8.18(3.73)	3.27(1.34)	3.86(1.72)	350.01(16.18)
Oral anti-hyperlipidemic agents	7.45(3.67)	2.77(1.29)	3.09(1.59)	344.29(21.67)
Proton pump inhibitors	9.08(4.17)	2.98(1.36)	3.38(1.59)	342.89(22.89)

Note: * Rx = Prescription Medications, ** Std. Dev = Standard Deviation, †Total Class = number of classes under evaluation from which the beneficiaries took medications simultaneously, †† Total Rx from classes = number of medications from the 7 classes evaluated, ††† Total Duration = number of days beneficiaries were supposed to take their medication since the first fill date

(c)   Plan Characteristics

Less than 1% of all enrollees in the No Gap Coverage group were enrolled in plans that offered coverage through the standard Medicare Part D benefit structure. Most beneficiaries were enrolled in plans that offered drug coverage through benefit structures that are considered equivalent or enhanced when compared to the standard Part D design. A majority of plans did not charge a deductible and had tiered cost-sharing as opposed to the standard 25% co-insurance during the initial coverage period. As with the overall sample, almost all plans imposed Medicare defined spending limits to determine a beneficiary's gap entry and exit times. Table 10 presents these results in detail.

Table 10: Plan characteristics of beneficiaries with no drug coverage in the coverage gap by therapeutic class

Class	Drug Benefit Type			Deductible Applied (%No)	Pre-Gap Cost-sharing (%Tiers)	Gap Threshold (%Std.amt*)
	Actuarially Equivalent	Basic Alt.**	Enhanced Alt.			
ACE inhibitors	20.79	40.49	38.71	75.72	99.26	98.77
Beta-blockers	21.41	39.17	39.42	75.37	99.17	98.64
Calcium channel blockers	21.48	40.25	38.27	74.92	99.16	98.67
Diuretics	22.09	39.02	38.89	74.74	99.27	98.73
Oral anti-diabetic agents	21.67	40.18	38.15	74.28	99.13	98.67
Oral anti-hyperlipidemic agents	20.63	40.19	39.18	76.10	99.36	98.85
Proton pump inhibitors	21.19	39.94	38.87	75.64	99.15	98.71

Note: *Std.amt = Medicare defined Standard amount ($2,510 for 2008) ** Alt. = Alternative

83

2. Some Gap Coverage Group (N = 8,529)

(a)   Demographic and Medication related characteristics

The demographic characteristics of the beneficiaries in this group were in concordance with the findings for the overall sample. In other words, within each therapeutic class, beneficiaries with some drug coverage during the coverage gap were also older, predominantly Caucasian and female. In addition, the medication taking behavior of the beneficiaries in this group was also similar to that of the overall sample and the "No Gap Coverage" group. Tables 11 and 12 present the demographic and medication related characteristics of the beneficiaries in this group.

Table 11: Demographic characteristics of beneficiaries with some drug coverage in the coverage gap by therapeutic class

Class	N	Age Mean (Std.Dev*)	Race %Caucasian	Gender %Males	%Females	Income** Median($)
ACE inhibitors	1,499	77.67(6.87)	92.66	31.49	68.51	32,489
Beta-blockers	2,295	78.13(6.92)	93.99	25.66	74.34	32,507
Calcium channel blockers	1,384	78.92(7.12)	89.74	20.66	79.34	31,827
Diuretics	2,275	78.77(7.26)	93.23	19.74	80.26	32,211
Oral anti-diabetic agents	845	76.41(6.45)	87.22	34.67	65.33	33,241
Oral anti-hyperlipidemic agents	3,407	76.75(6.36)	93.01	29.26	70.74	33,915
Proton pump inhibitors	1,117	77.40(6.86)	92.87	23.46	76.54	32,531

Note: * Std.dev = Standard Deviation, ** Income = the median household income of the beneficiaries' zip-code

Table 12: Medication related characteristics of beneficiaries with some drug coverage in the coverage gap by therapeutic class

Class	Total Rx* Mean (Std.Dev**)	Total Class† Mean (Std.Dev)	Total Rx from classes†† Mean(Std.Dev)	Total Duration††† Mean (Std.Dev)
ACE inhibitors	7.83(3.61)	3.32(1.28)	3.54(1.60)	346.94(20.05)
Beta-blockers	8.07(3.78)	3.03(1.24)	3.39(1.54)	344.31(21.31)
Calcium channel blockers	8.21(3.87)	3.21(1.29)	3.48(1.57)	344.14(21.67)
Diuretics	8.33(3.74)	3.08(1.23)	3.38(1.56)	345.12(21.39)
Oral anti-diabetic agents	8.35(3.68)	3.43(1.33)	3.96(1.67)	343.12(23.26)
Oral anti-hyperlipidemic agents	7.51(3.59)	2.76(1.28)	3.15(1.59)	343.18(22.37)
Proton pump inhibitors	9.02(4.06)	3.02(1.36)	3.33(1.69)	341.77(23.89)

Note: * Rx = Prescription Medications, ** Std. Dev = Standard Deviation, †Total Class = number of classes under evaluation from which the beneficiaries took medications simultaneously, †† Total Rx from classes = number of medications from the 7 classes evaluated, ††† Total Duration = number of days beneficiaries were supposed to take their medication since the first fill date

(b) Plan Characteristics

Since this group of beneficiaries are documented to have coverage for some drugs while in the coverage gap, as expected, all the beneficiaries were enrolled in plans that offered coverage through an 'enhanced alternative' benefit design. In addition, no plan in this group charged a deductible and all had tiered cost-sharing structures during the initial coverage limit phase. In spite of these 'enhanced' offerings, all the plans had a coverage gap starting at the Medicare defined amount of $2,510 in total spending and catastrophic limits starting at $4,050 in total OOP spending. It was interesting to note that although these beneficiaries had coverage for drugs when in the coverage gap, this benefit was limited to some or all generic drugs only.

85

Specifically, 54% of all beneficiaries in this group had all generic drugs covered during the coverage gap, 38% had coverage limited to 'preferred generics' and the remaining 8% had coverage limited to only 'a few' generic drugs when in the coverage gap. No plan in our sample offered coverage for any brand name drugs during the coverage gap for this group.

Characteristics of beneficiaries based on whether or not they reached the coverage gap

1. Overall (N = 173,080)

Overall, 24.42% (N = 42,264) of our sample reached the coverage gap in 2008. Of these, only 6.29% beneficiaries (N = 2,660) had some coverage for their prescription medications during the coverage gap. The remaining 93.71% beneficiaries had no coverage for their prescription drugs during the coverage gap. Among the "No Gap Coverage" group, 24.07% reached the coverage gap. By comparison, 31.19% of those with some gap coverage reached the coverage gap in 2008 (Figure 5). Overall, a little over half of the beneficiaries reaching the coverage gap (59.92%) did so by September and spent about 97 days ($\pm$ 67 days) in the coverage gap. Of these, 12.10% (3% of the total sample) reached the catastrophic coverage phase. It was found that those reaching the catastrophic coverage phase were primarily beneficiaries reaching the coverage gap in the first half of the year. In addition, beneficiaries receiving catastrophic coverage spent approximately 83 days ($\pm$ 72 days) in that phase, which is consistent with the finding that a majority of these beneficiaries reached the phase early in the year. Irrespective of the level of analysis, the beneficiaries reaching the coverage gap did not have different demographic characteristics when compared to those who did not reach the coverage gap. Figure 6 presents the demographic characteristics of the two groups by level of analysis.
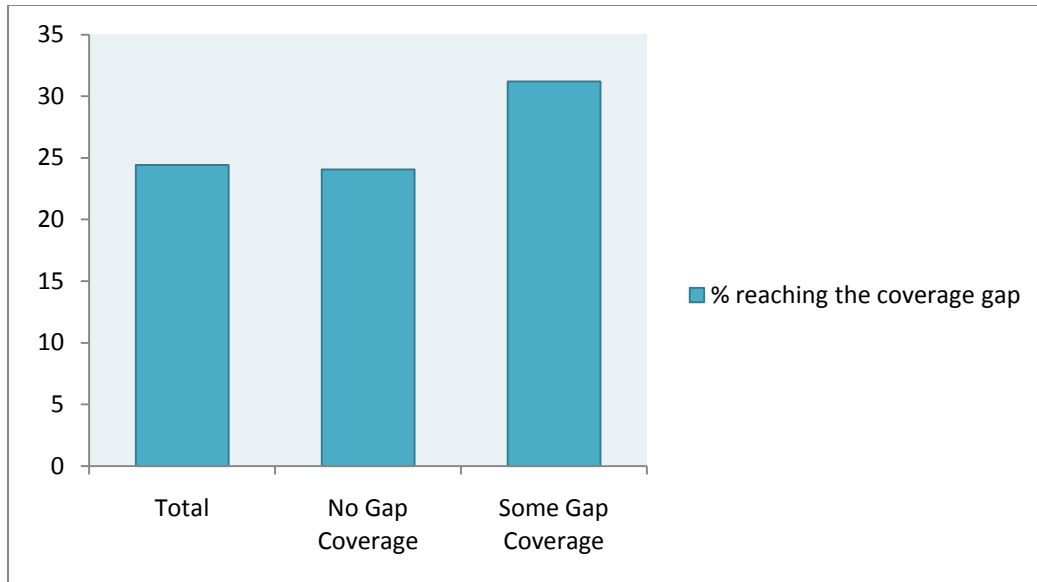
Figure 5: Percentage of beneficiaries reaching the coverage gap in 2008
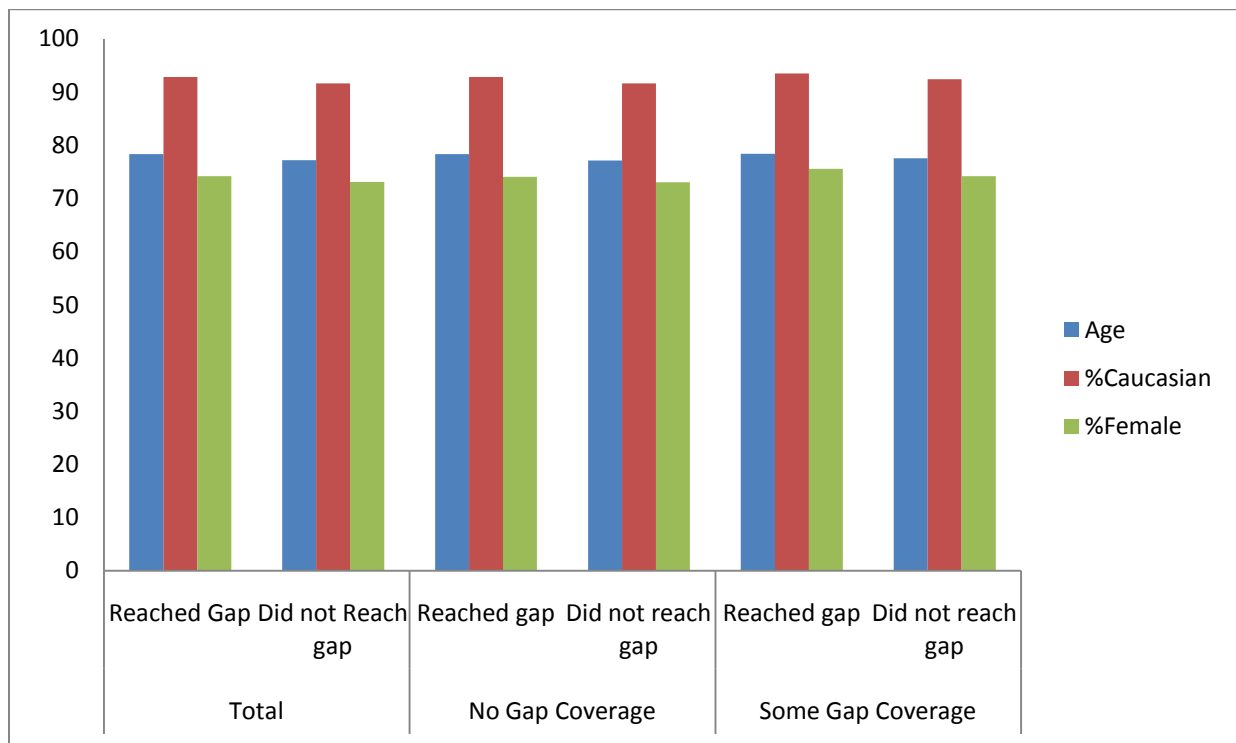
Figure 6: Demographic characteristics by gap and gap coverage status

Although the two groups had similar demographic attributes, those who did reach the coverage gap had higher prescription medication use and OOP spending compared to those that did not reach the coverage gap in 2008. An average beneficiary reaching the coverage gap took 11.25 ($\pm$ 4.63) different medications compared to 7.39 ($\pm$ 3.75) medications taken by a beneficiary not reaching the coverage gap throughout the year. The OOP spending for a beneficiary reaching the gap was found to be higher during both the pre-gap as well as the coverage gap periods compared to stable lower spending experienced by beneficiaries not reaching the coverage gap. Beneficiaries reaching the coverage gap spent an average \$763.95 ($\pm$ \$330.46) before reaching the coverage gap and \$945.70 ($\pm$ \$986.22) during the coverage gap. By comparison, beneficiaries not reaching the coverage gap had an average OOP spending of only \$400.00 ($\pm$ \$286.59) throughout the year. These numbers were similar when the groups were compared based on presence or absence of gap coverage during the gap. For instance, for those reaching the coverage gap in the "No Gap Coverage" group, the pre-gap spending was \$768.30 ($\pm$ \$329.50) and the 'during gap' spending was \$951.65 ($\pm$ \$987.13) compared to an average \$396.00 ($\pm$ \$285.85) in annual OOP spending for those who did not reach the coverage gap in this group. Similarly, for those reaching the coverage gap in the "Some Gap Coverage" group, the pre-gap as well as the 'during gap' spending were found to be higher than the annual OOP spending for those who did not reach the coverage gap in this group (\$699.14 $\pm$ \$337.91 and \$857.07 $\pm$ \$968.34 respectively vs. \$418.17 $\pm$ \$301.36).

Similar proportions of beneficiaries in both the groups were enrolled in coverage designs considered to be equivalent or enhanced adaptations of the standard Medicare Part D benefit structures. Figure 7 summarizes the enrollment statistics for each plan benefit design based on presence or absence of drug coverage in the gap.

89
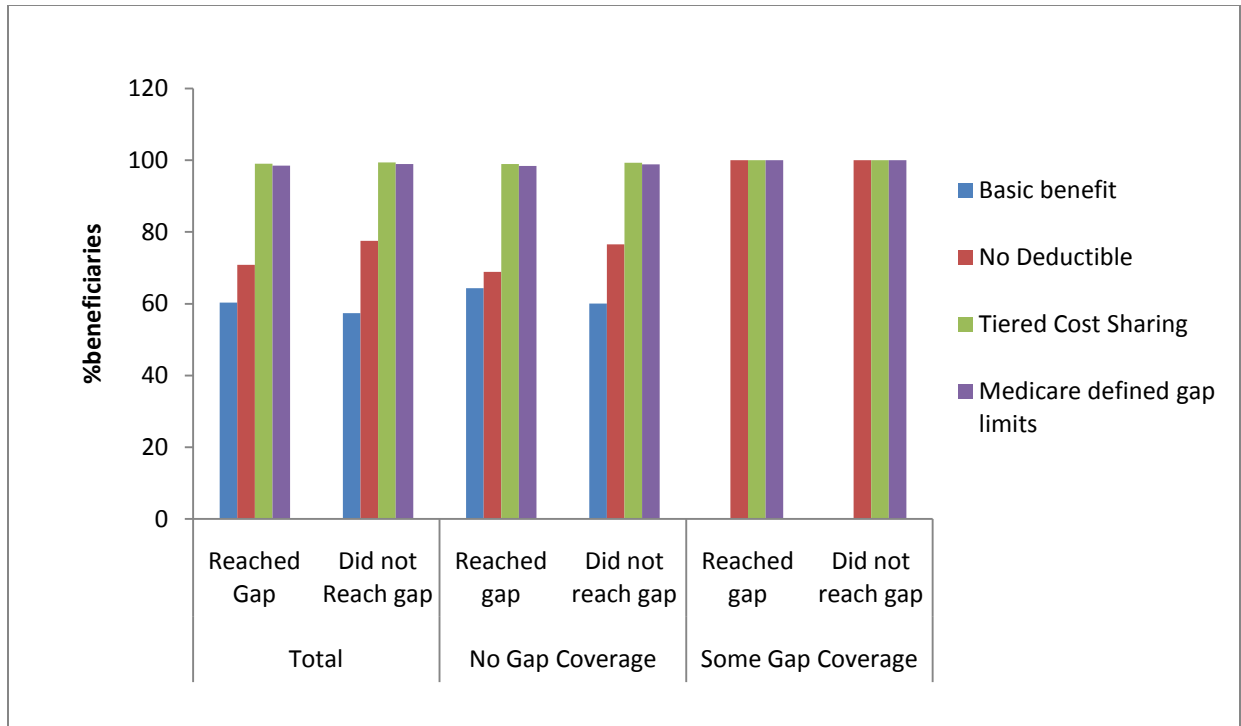
Figure 7: Plan Characteristics of beneficiaries by gap and gap coverage status

2. Characteristics by therapeutic class before and after matching

No Gap Coverage Group

The comparison groups comprised those who did and did not reach the coverage gap in the "No Gap Coverage" group. Within the "No Gap Coverage" group, the beneficiaries were divided into 7 therapeutic classes being studied and within each therapeutic class they were further divided into two groups based on whether or not they reached the coverage gap in 2008. The beneficiaries in the two groups in each class shared a few similar characteristics but there was also variability with respect to some other baseline attributes. In order to generate reliable estimates of the effect of losing all coverage in the coverage gap on beneficiaries' adherence measures, it was necessary to make the two groups more comparable in terms of their baseline characteristics. Therefore, the beneficiaries reaching the coverage gap were matched to those not reaching the coverage gap on a variety of variables. These variables were: age, race, gender, income, number of medications taken, duration of therapy, severity of disease as calculated using CDS, type of benefit design, presence or absence of deductible, type of cost sharing before reaching the coverage gap, and coverage gap threshold amount. The following paragraphs outline the characteristics of the groups that did and did not reach the coverage gap by therapeutic class before and after matching.

(a)   Oral anti-hyperlipidemic agents

This was the most widely used class of medications in the sample; with around 80,000 beneficiaries using one or more medications from this class at some point in 2008. However, the proportion of beneficiaries having usage beginning in the first quarter of 2008 was less; only 69,178 beneficiaries were prescribed the medication since the beginning of the year. From this

pool, 7,636 beneficiaries (11.04%) reached the coverage gap in 2008. A majority of beneficiaries reached the coverage gap by November, with the largest proportion doing so between October and November (41% and 70% respectively). However, only two of beneficiaries reached the catastrophic phase and therefore the results after reaching the catastrophic phase are not shown.

Although the two groups were similar in a few characteristics (e.g. income and disease severity), there were a number of other attributes that differed between the two (p-value < .05). A greater proportion of the beneficiaries reaching the gap were Caucasians and male compared to those not reaching the coverage gap (93.07% vs. 92.08% and 32.24% vs. 30.40% respectively). In addition, beneficiaries reaching the coverage gap were a little older compared to those not reaching the coverage gap in 2008. Beneficiaries reaching the coverage gap took about 10 different medications (vs. 7 for those not reaching the gap) over a relatively short duration of time (312 days vs. 349 for those not reaching the gap). Greater proportions of beneficiaries reaching the coverage gap were enrolled in plans that offered no additional benefit over a standard benefit structure (61.38% vs. 60.75%) and that charged a deductible (26.9% vs. 23.53% from those not reaching the gap). The use of propensity score matching resulted in 5,041 matched pairs (66.02% of the beneficiaries reaching the gap) that were similar to each other in all the observed characteristics. Table 13 presents these results in detail.

Table 13: Characteristics of beneficiaries in the "No Gap Coverage" group taking oral anti-hyperlipidemic agents before and after matching

Variable	Before matching			After matching		
	Treatment N = 7,636	Control N = 61,542	p-value	Treatment N = 5,041	Control N = 5,401	p-value
Age Mean(Std.dev**)	76.52 (6.47)	76.19 (6.33)	0.0002*	76.19 (6.32)	75.98 (6.33)	0.0886
Race (%Caucasian)	93.07	92.08	0.0328*	92.82	92.44	0.9964
Gender (% Females)	67.76	69.60	0.0010*	66.46	66.55	0.9150
Income†(Median)	34,022	34,259	0.543	34,677	34,700	0.3500
# Medications taken (Mean (Std.Dev))	9.63 (3.93)	7.19 (3.51)	<0.0001*	8.43 (3.34)	8.29 (3.91)	0.0594
CDS†† Mean(Std.dev)	3.62 (2.12)	3.41 (1.92)	0.23	3.48 (2.11)	3.42 (2.15)	0.1060
Total Duration††† Mean(std.dev)	311.57 (24.28)	349.35 (17.47)	<0.0001*	321.37 (22.84)	319.71 (24.32)	0.1344
Benefit Type (% Basic Design)	61.38	60.75	<0.0001*	61.20	61.79	0.3114
Deductible (% No)	73.1	76.47	<0.0001*	74.49	75.76	0.0580
Pre-Gap Costsharing (% Tiers)	99.28	99.38	0.3176	99.35	99.39	0.7995
Gap Threshold (% Std. amt***)	98.73	98.85	0.3435	98.73	98.97	0.2611

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

(b) Beta-blockers

Out of 53,315 users of beta-blockers in this sample, 47,911 unique beneficiaries had documented usage beginning by March 31. Among these beneficiaries, 11.06% reached the coverage gap three-quarters of these did so by November. Only four beneficiaries reached the catastrophic coverage; the remainder either stayed in the coverage gap for the rest of the year or stopped taking the medication in this class.

Beneficiaries reaching the coverage gap in this group were found to be similar to those not reaching the coverage gap in terms of age, race, income and disease severity; but had different gender, medication and plan related characteristics. Beneficiaries reaching the coverage gap had a significantly higher medication use for a significantly shorter duration of therapy. In addition, a greater proportion of these beneficiaries were enrolled in plans that offered coverage through basic alterations of the Standard Part D benefit design and that charged a deductible. Again, the differences between the two groups were eliminated by matching those reaching the coverage gap to those not reaching the coverage gap. However, in the process, we lost 18% of the beneficiaries reaching the coverage gap because no match was found from the group not reaching the coverage gap. Table 14 presents the characteristics of these beneficiaries before and after matching.

Table 14: Characteristics of beneficiaries in the "No Gap Coverage" group taking Beta-blockers before and after matching

Variable	Before matching			After matching		
	Treatment N = 5,928	Control N = 42,613	p-value	Treatment N = 3,821	Control N = 3,821	p-value
Age Mean(Std.dev**)	77.94 (6.97)	77.88 (7.02)	0.5148	77.74 (6.93)	77.75 (6.96)	0.9200
Race (%Caucasian)	93.74	93.03	0.3746	93.54	92.25	0.5578
Gender (% Females)	71.64	73.75	0.0012*	71.32	70.43	0.3791
Income†(Median)	32,905	32,590	0.1020	32,975	32,401	0.2907
# Medications taken (Mean (Std.Dev))	10.24 (3.88)	7.66 (3.67)	<0.0001*	9.38 (3.34)	9.31 (5.14)	0.4276
CDS†† Mean(Std.dev)	3.80 (2.05)	3.63 (2.11)	0.0900	3.74 (2.04)	3.71 (2.17)	0.4586
Total Duration††† Mean(std.dev)	313.51 (24.14)	349.27 (16.73)	<0.0001*	322.59 (21.31)	322.38 (26.45)	0.4548
Benefit Type (% Basic Design)	62.74	60.32	<0.0001*	62.68	62.21	0.1999
Deductible (% No)	71.03	75.91	<0.0001*	72.10	73.38	0.3769
Pre-Gap Costsharing (% Tiers)	98.81	99.28	<0.0001*	98.98	99.24	0.2184
Gap Threshold (% Std. amt***)	98.33	98.73	0.0766	98.46	98.93	0.069

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

(c)   <u>Diuretics</u>

Although 47,900 beneficiaries used a diuretic at some point in 2008, 47,711 had used a medication from this class since the first quarter of the year. Of these, 10.37% reached the coverage gap; a majority of which (70.78%) did so by November. Only two of these beneficiaries reached the catastrophic coverage. Beneficiaries reaching the coverage gap were found to be slightly older compared to those who did not reach the coverage gap. They took almost 11 unique medications compared to 8 medications taken by beneficiaries not reaching the coverage gap. As with the other groups, a greater proportion of beneficiaries reaching the coverage gap were enrolled in plans that charged a deductible and offered coverage through a benefit design considered equivalent to the standard Part D benefit structure (Table 15).

Table 15: Characteristics of beneficiaries in the "No Gap Coverage" group taking Diuretics before and after matching

Variable	Before matching			After matching		
	Treatment N = 4,948	Control N = 42763	p-value	Treatment N = 3530	Control N = 3,530	p-value
Age Mean(Std.dev**)	78.59 (7.28)	78.37 (7.29)	0.0129*	78.31 (7.26)	78.17 (7.25)	0.3661
Race (%Caucasian)	92.91	91.28	0.0011*	92.46	90.85	0.1344
Gender (% Females)	78.35	79.52	0.0556	78.75	78.64	0.9065
Income† (Median)	32,120	31,838	0.2517	32,460	33,035	0.0556
# Medications taken (Mean (Std.Dev))	10.99 (3.98)	8.05 (3.78)	<0.0001*	10.03 (3.47)	9.99 (5.33)	0.6397
CDS†† Mean(Std.dev)	3.97 (2.11)	3.81 (2.13)	0.6100	3.94 (2.11)	3.93 (2.23)	0.8084
Total Duration††† Mean(std.dev)	314.04 (24.14)	349.43 (16.62)	<0.0001*	323.48 (21.19)	323.23 (27.23)	0.4879
Benefit Type (% Basic Design)	62.91	60.9	<0.0001*	62.35	62.04	0.5917
Deductible (% No)	70.17	75.27	<0.0001*	71.42	73.06	0.2075
Pre-Gap Costsharing (% Tiers)	98.77	99.32	0.0034*	98.95	98.98	0.9955
Gap Threshold (% Std. amt*)**	98.45	98.76	0.3961	98.56	98.87	0.2489

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

(d)   <u>ACE Inhibitors</u>

Among all beneficiaries using ACE inhibitors (N = 40,060), 34,477 had usage beginning in the first quarter of 2008 and hence were included in further analyses. In this group, only 5.64% reached the coverage gap in 2008; 61% of whom did so by November. None of these beneficiaries reached catastrophic coverage in 2008. A lesser proportion of those reaching the coverage gap were females compared to those who did not reach the coverage gap (65.26% vs. 68.57% respectively). In addition, a greater proportion of those reaching the coverage gap were enrolled in plans with basic benefit designs that charged a deductible. The beneficiaries reaching the coverage gap also took a significantly greater number of medications compared to beneficiaries who did not reach the coverage gap (10.17 vs. 7.55). In addition, the severity of disease in the group reaching the coverage gap was greater compared to those not reaching the coverage gap. The differences between the two groups were eliminated by creating propensity score based matched groups (Table 16).

98

Table 16: Characteristics of beneficiaries in the "No Gap Coverage" group taking ACE inhibitors before and after matching

Variable	Before matching			After matching		
	Treatment N = 1,943	Control N = 32,534	p-value	Treatment N = 1,373	Control N = 1,373	p-value
Age Mean(Std.dev**)	77.55 (7.21)	77.39 (7.04)	0.5640	77.26 (7.08)	77.17 (7.21)	0.7390
Race (%Caucasian)	92.57	91.61	0.3761	92.28	90.68	0.1060
Gender (% Females)	65.26	68.57	0.0023*	65.33	65.77	0.8023
Income† (Median)	32,232	32,710	0.2312	32,838	34,213	0.1126
# Medications taken (Mean (Std.Dev))	10.17 (3.92)	7.55 (3.67)	<0.0001*	9.06 (3.47)	8.96 (4.45)	0.2052
CDS†† Mean(Std.dev)	5.71 (1.62)	5.34 (1.53)	<0.0001*	5.61 (1.61)	5.56 (1.69)	0.4032
Total Duration††† Mean(std.dev)	306.22 (22.78)	349.22 (16.77)	<0.0001*	314.14 (21.83)	313.46 (26.74)	0.1808
Benefit Type (% Basic Design)	63.05	61.18	<0.0001*	62.35	62.78	0.6011
Deductible (% No)	70.87	76.01	<0.0001*	72.91	73.05	0.8939
Pre-Gap Costsharing (% Tiers)	99.54	99.24	0.1900	99.42	99.56	0.5930
Gap Threshold (% Std. amt***)	99.28	98.76	0.0521	99.05	98.76	0.4328

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

(e)   Calcium channel blockers

From an aggregate of 31,346 beneficiaries taking calcium channel blockers at sometime in 2008; 29,229 beneficiaries had a full year of medication use according to our criteria. Of these, 3482 beneficiaries (11.91%) reached the coverage gap in 2008 and only two beneficiaries reached the catastrophic coverage. Almost three quarters (73%) of beneficiaries reaching the coverage gap did so by November.

A significantly greater proportion of beneficiaries reaching the coverage gap were Caucasians (91.51% vs. 89.07%) and had a higher median annual household income compared to those who did not reach the coverage gap ($32,933 vs. $31,971). In addition, beneficiaries reaching the coverage gap were of similar age and gender but used significantly larger number of prescription medications over a significantly shorter duration of therapy compared to those who did not reach the coverage gap. Most of the beneficiaries reaching the coverage gap were enrolled in plans offering coverage through actuarially equivalent Part D benefit with a deductible. The propensity score matching resulted in 2,373 matched pairs with similar characteristics beneficiaries who reached the coverage gap (68.15%). Table 17 presents the results in detail:

100

Table 17: Characteristics of beneficiaries in the "No Gap Coverage" group taking Calcium channel blockers before and after matching

Variable	Before matching			After matching		
	Treatment N = 3,482	Control N = 25,747	p-value	Treatment N = 2,373	Control N = 2,373	p-value
Age Mean(Std.dev**)	78.59 (7.32)	78.48 (7.27)	0.4916	78.38 (7.21)	78.14 (7.26)	0.2699
Race (%Caucasian)	91.51	89.07	<0.0001*	90.86	91.45	0.9972
Gender (% Females)	76.88	77.43	0.4641	76.53	77.08	0.6536
Income† (Median)	32,933	31,971	.0013*	33,269	33,309	0.6284
# Medications taken (Mean (Std.Dev))	10.41 (3.85)	7.82 (3.71)	<0.0001*	9.46 (3.45)	9.39 (5.04)	0.5319
CDS†† Mean(Std.dev)	4.57 (1.92)	4.54 (2.01)	0.0535	4.61 (1.95)	4.54 (2.02)	0.2415
Total Duration††† Mean(std.dev)	313.81 (24.46)	349.82 (16.29)	<0.0001*	324.16 (21.71)	323.57 (26.29)	0.1115
Benefit Type (% Basic Design)	63.3	61.53	.0011*	63.55	61.53	0.6328
Deductible (% No)	71.86	75.34	<0.0001*	72.69	74.04	0.2988
Pre-Gap Costsharing (% Tiers)	99.05	99.28	0.2754	98.99	99.21	0.4458
Gap Threshold (% Std. amt***)	98.62	98.79	0.4028	98.76	98.48	0.4602

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

    (f)   <u>Proton-Pump Inhibitors (PPI)</u>

Approximately 25,000 beneficiaries took PPIs during 2008 and 23,925 had used them since the first quarter of the year. Almost 18% of these beneficiaries (N=4,204) reached the coverage gap and four beneficiaries reached the catastrophic coverage phase. Three-quarters (74%) of the beneficiaries using PPIs reached the coverage gap by November. As with the other

groups, the existing differences between the characteristics of beneficiaries in the two groups were eliminated after employing propensity score matching technique which yielded 2,678 matched pairs (Table 18).

Table 18: Characteristics of beneficiaries in the "No Gap Coverage" group taking Proton Pump Inhibitors before and after matching

Variable	Before matching			After matching		
	Treatment N = 2,492	Control N = 11,355	p-value	Treatment N = 2,068	Control N = 2,068	p-value
Age Mean(Std.dev**)	77.43 (7.28)	76.95 (6.99)	<0.0001*	77.08 (6.99)	76.89 (6.92)	0.3113
Race (%Caucasian)	92.84	91.73	0.0140*	92.61	92.98	0.9926
Gender (% Females)	76.15	76.73	0.4271	75.43	74.38	0.3788
Income† (Median)	33,226	33,107	0.2851	33,523	34,029	0.2306
# Medications taken (Mean (Std.Dev))	10.74 (4.36)	8.67 (4.04)	<0.0001*	9.73 (3.85)	9.59 (4.63)	0.2778
CDS†† Mean(Std.dev)	3.37 (2.01)	3.35 (2.12)	0.0348*	3.32 (1.98)	3.27 (2.19)	0.1845
Total Duration††† Mean(std.dev)	313.11 (24.11)	349.23 (16.83)	<0.0001*	324.85 (20.81)	324.24 (24.77)	0.4230
Benefit Type (% Basic Design)	62.02	60.96	<0.0001*	61.69	61.46	0.7878
Deductible (% No)	71.97	76.42	<0.0001*	73.00	73.49	0.4691
Pre-Gap Costsharing (% Tiers)	99.04	99.20	0.4084	98.99	98.98	0.7893
Gap Threshold (% Std. amt*)**	98.62	98.72	0.5939	98.81	98.81	1

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

(g)   Oral anti-diabetic agents

An aggregate of 22,836 beneficiaries from the overall sample took one or more oral anti-diabetic agents in 2008. However, only 17,500 beneficiaries had a full year of medication use and were included in further analyses. Almost 13% of these beneficiaries experienced the coverage gap in 2008; 73% of whom did so by November and only one passed into the catastrophic coverage phase.

The two groups within this therapeutic class were significantly different from each other (Table 19). Those reaching the coverage gap were older beneficiaries who used more medications in a shorter duration of time. The severity of their disease, however, was similar to their peers who did not reach the coverage gap. As with other groups, greater proportions of beneficiaries reaching the coverage gap were enrolled in plans that charged a deductible and offered no additional benefit over the standard Part D structure. These differences were accounted for after finding appropriate matched pairs from the two groups. However, in doing so, 36.67% of beneficiaries who reached the coverage gap were not matched to anyone not reaching the gap and were therefore excluded from the analyses.

103

Table 19: Characteristics of beneficiaries in the "No Gap Coverage" group taking oral anti-diabetic agents before and after matching

Variable	Before matching			After matching		
	Treatment N = 2,613	Control N = 14,887	p-value	Treatment N = 1,655	Control N = 1,655	p-value
Age Mean(Std.dev**)	76.69 (6.31)	76.08 (6.42)	0.0190*	75.58 (6.11)	75.55 (6.03)	0.9291
Race (%Caucasian)	88.52	84.83	<0.0001*	87.37	87.43	0.7893
Gender (% Females)	63.57	65.61	0.0439*	63.14	64.77	0.2855
Income† (Median)	33,053	32,839	0.0269*	33,304	34,238	0.229
# Medications taken (Mean (Std.Dev))	10.45 (4.12)	8.18 (3.27)	<0.0001*	9.46 (3.57)	9.48 (4.69)	0.5353
CDS†† Mean(Std.dev)	5.09 (1.99)	5.08 (2.03)	0.7705	5.07 (2.07)	5.08 (2.16)	0.7129
Total Duration††† Mean(std.dev)	312.73 (24.34)	350.01 (16.19)	<0.0001*	324.28 (21.69)	324.28 (25.41)	0.9962
Benefit Type (% Basic Design)	63.91	61.48	<0.0001*	63.26	64.77	0.5518
Deductible (% No)	71.18	74.82	0.0002*	73.11	72.57	0.8658
Pre-Gap Costsharing (% Tiers)	98.74	99.19	0.0030*	99.03	99.27	0.4497
Gap Threshold (% Std. amt*)**	98.55	98.69	0.5525	98.85	98.79	0.8658

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Within the "Some Gap Coverage" group, the beneficiaries were divided into 7 therapeutic classes being studied and within each therapeutic class they were further divided into two groups based on whether or not they reached the coverage gap in 2008. The beneficiaries in the two groups in each class shared similar demographic and plan enrollment characteristics but there was variability with respect to their medication taking behavior. As with the analyses for the "No Gap Coverage" group, it was necessary to make the two groups more comparable in terms of these characteristics before making reliable estimates of the effect of being in the coverage gap on the beneficiaries' adherence to medications. The following paragraphs outline the characteristics of the groups that did and did not reach the coverage gap by therapeutic class before and after matching.

As with the "No Gap Coverage" group, oral anti-hyperlipidemic agents were the most frequently used class of medications in this group, followed by beta-blockers, diuretics and ACE inhibitors. Again, the least frequently used classes of medications were calcium channel blockers, followed by PPIs and oral anti-diabetic agents. The greatest impact was seen in the group taking PPIs; with almost a fifth (19.96%) of the beneficiaries in that group reaching the coverage gap in 2008. This was followed by beneficiaries taking oral anti-diabetic agents (16.33%), calcium channel blockers (14.81%), oral anti-hyperlipidemic agents (13.09%), beta-blockers (12.68%) and diuretics (11.34%). Only 6% of beneficiaries using ACE inhibitors reached the coverage gap in this group.

As with the "No Gap Coverage" group, between 40% of beneficiaries reaching the coverage gap (for all therapeutic classes) did so by October and 70% did so by November. As

105

mentioned earlier, all the beneficiaries in this group had similar demographic and plan enrollment characteristics, irrespective of whether or not they reached the coverage gap in 2008. However, beneficiaries reaching the coverage gap were more likely to use a greater number of prescription medications over a shorter duration of time compared to those who did not reach the coverage gap. Detailed characteristics of beneficiaries by therapeutic class evaluated are presented in Tables 20-26.

Table 20: Characteristics of beneficiaries in the "Some Gap Coverage" group taking anti-hyperlipidemic agents before and after matching

Variable	Before matching			After matching		
	Treatment N = 446	Control N = 2,961	p-value	Treatment N = 235	Control N =235	p-value
Age Mean (Std.dev**)	76.81 (6.08)	76.86 (6.41)	0.9992	76.67 (6.01)	77.27 (6.19)	0.1854
Race (%Caucasian)	95.07	92.71	0.3500	97.02	93.62	0.058
Gender (% Females)	70.19	70.82	0.7814	72.77	71.70	0.0903
Income† (Median)	32,945	34,039	0.0546	33,915	33,208	0.8216
#Medications taken (Mean (Std.dev))	9.74 (3.99)	7.17 (3.43)	<0.0001*	8.46 (3.54)	8.15 (3.98)	0.3878
CDS†† Mean(Std.dev)	2.89 (1.87)	2.66 (1.78)	0.0101*	2.82 (1.93)	2.69 (1.81)	0.4597
Total Duration††† Mean(std.dev)	310.65 (23.79)	348.05 (17.53)	<0.0001*	324.79 (21.53)	323.67 (25.75)	0.2425

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 21: Characteristics of beneficiaries in the "Some Gap Coverage" group taking beta-blockers before and after matching

Variable	Before matching			After matching		
	Treatment N = 291	Control N = 2,004	p-value	Treatment N = 163	Control N =163	p-value
Age Mean (Std.dev)**	78.21 (6.78)	78.08 (7.19)	0.6651	78.49 (6.88)	76.97 (6.46)	0.0535
Race (%Caucasian)	94.16	93.96	0.3736	94.48	90.80	0.6398
Gender (% Females)	73.88	74.41	0.8500	74.85	70.55	0.3621
Income† (Median)	31,784	32,662	0.2447	31,641	32,133	0.1948
#Medications taken (Mean (Std.dev))	10.43 (4.24)	7.71 (3.58)	<0.0001*	9.17 (3.53)	8.69 (4.47)	0.1217
CDS†† Mean(Std.dev)	3.01 (2.03)	2.84 (1.81)	0.3921	2.87 (1.95)	2.85 (1.99)	0.8282
Total Duration††† Mean(std.dev)	312.55 (22.52)	348.65 (16.71)	<0.0001*	323.62 (20.33)	323.32 (24.81)	0.5417

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 22: Characteristics of beneficiaries in the "Some Gap Coverage" group taking diuretics before and after matching

Variable	Before matching			After matching		
	Treatment N = 258	Control N = 2,017	p-value	Treatment N = 128	Control N =128	p-value
Age Mean (Std.dev**)	78.89 (7.39)	78.63 (7.21)	0.6055	79.51 (7.29)	78.43 (6.95)	0.3291
Race (%Caucasian)	94.57	93.06	0.4856	95.31	92.62	0.5998
Gender (% Females)	84.11	79.77	0.0994	83.59	79.87	0.6949
Income† (Median)	33,060	31,752	0.7989	30,920	31,798	0.863
#Medications taken (Mean (Std.dev))	10.99 (3.95)	7.99 (3.58)	<0.0001*	10.05 (4.11)	10.23 (3.58)	0.3075
CDS†† Mean(Std.dev)	3.26 (1.98)	2.97 (1.87)	0.0359*	3.25 (1.85)	3.21 (1.97)	0.4563
Total Duration††† Mean(std.dev)	312.59 (24.04)	349.28 (17.05)	<0.0001*	328.51 (19.59)	336.16 (34.85)	0.3852

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 23: Characteristics of beneficiaries in the "Some Gap Coverage" group taking ACE inhibitors before and after matching

Variable	Before matching			After matching		
	Treatment N = 86	Control N = 1,413	p-value	Treatment N = 36	Control N =36	p-value
Age Mean (Std.dev**)	79.09 (7.06)	77.57 (6.84)	0.0435*	79.37 (7.99)	79.25 (6.22)	0.952
Race (%Caucasian)	94.19	92.57	0.8954	90.63	90.63	1
Gender (% Females)	72.09	68.29	0.4615	65.63	81.25	0.1317
Income† (Median)	29,573	32,589	0.0976	29,708	30,631	0.3024
#Medications taken (Mean (Std.dev))	9.64 (3.76)	7.72 (3.54)	<0.0001*	8.22 (3.58)	9.41 (3.92)	0.1403
CDS†† Mean(Std.dev)	5.57 (1.96)	4.07 (1.91)	<0.0001*	4.88 (2.09)	4.59 (1.96)	0.872
Total Duration††† Mean(std.dev)	304.21 (20.94)	349.55 (16.77)	<0.0001*	318.93 (21.72)	318.41 (31.66)	0.9345

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 24: Characteristics of beneficiaries in the "Some Gap Coverage" group on calcium channel blockers before and after matching

Variable	Before matching			After matching		
	Treatment N = 205	Control N = 1179	p-value	Treatment N = 97	Control N =97	p-value
Age Mean (Std.dev**)	78.69 (7.08)	78.78 (7.14)	0.9411	78.65 (6.85)	78.42 (6.96)	0.8230
Race (%Caucasian)	93.17	89.14	0.4717	91.75	85.57	0.1537
Gender (% Females)	79.02	79.39	0.9052	79.38	78.35	0.8575
Income† (Median)	32,587	31,744	0.3939	30,954	31,093	0.1601
#Medications taken (Mean (Std.dev))	10.05 (3.93)	7.88 (3.57)	<0.0001*	8.68 (2.98)	8.84 (4.52)	0.7605
CDS Mean†† (Std.dev)	3.74 (1.82)	3.57 (1.81)	0.1437	3.44 (1.55)	3.62 (2.02)	0.4591
Total Duration††† Mean(std.dev)	312.86 (21.73)	349.58 (16.42)	<0.0001*	326.32 (19.05)	327.24 (26.46)	0.6155

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

110

Table 25: Characteristics of beneficiaries in the "Some Gap Coverage" group taking PPIs before and after matching

Variable	Before matching			After matching		
	Treatment N = 223	Control N = 894	p-value	Treatment N = 108	Control N =108	p-value
Age Mean (Std.dev**)	77.98 (7.14)	77.24 (6.64)	0.2106	78.39 (7.25)	77.54 (6.37)	0.2824
Race (%Caucasian)	94.17	92.81	0.8098	93.26	89.81	0.1060
Gender (% Females)	79.37	75.84	0.2653	80.56	75.00	0.3428
Income† (Median)	32,531	32,548	0.8039	33,312	32,259	0.4872
#Medications taken (Mean (Std.dev))	10.57 (4.22)	8.54 (3.88)	<0.0001*	9.68 (3.96)	9.32 (4.15)	0.6281
CDS†† Mean(Std.dev)	2.56 (1.87)	2.67 (1.87)	0.5034	2.72 (1.98)	2.66 (1.98)	0.7924
Total Duration††† Mean(std.dev)	316.37 (24.94)	348.85 (17.53)	<0.0001*	331.16 (20.92)	330.47 (25.21)	0.5952

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

111

Table 26: Characteristics of beneficiaries in the "Some Gap Coverage" group on oral anti-diabetic agents before and after matching

Variable	Before matching			After matching		
	Treatment N = 138	Control N =707	p-value	Treatment N = 61	Control N =61	p-value
Age Mean (Std.dev**)	76.55 (6.52)	76.37 (6.52)	0.9536	76.52 (7.38)	75.85 (5.77)	0.9343
Race (%Caucasian)	89.86	86.70	0.2548	93.44	90.33	0.2531
Gender (% Females)	65.70	65.49	0.8223	68.85	62.3	0.4927
Income† (Median)	33,942	33,213	0.8287	33,068	34,133	0.4236
#Medications taken (Mean (Std.dev))	10.14 (4.06)	8.08 (3.71)	<0.0001*	9.16 (3.51)	8.49 (3.57)	0.2850
CDS†† Mean(Std.dev)	4.35 (2.05)	3.95 (1.95)	0.0673	4.11 (1.96)	4.09 (2.29)	0.9149
Total Duration††† Mean(std.dev)	311.66 (25.52)	349.26 (17.01)	<0.0001*	329.48 (22.02)	327.89 (26.33)	0.4150

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation, † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

To study the effect of having "Some Gap Coverage" compared to not having any coverage during the gap, we compared, within each therapeutic class, those beneficiaries from the "Some Gap Coverage" group who reached the coverage gap and those from the "No Gap Coverage" group who also reached the coverage gap. For almost every therapeutic class, the two groups were similar in terms of demographics and medication related behavior except the CDS. In addition, beneficiaries from both the groups were primarily enrolled in plans that had tiered cost-sharing and coverage gap starting at the Medicare defined amount. The only major difference was in the type of benefit structure used by the plans in which the beneficiaries were enrolled. For the "Some Gap Coverage" everyone was enrolled in plans that offered coverage through an 'enhanced' alternative to the standard structure whereas a greater proportion of beneficiaries with "No Gap Coverage" were enrolled in plans that offered coverage through basic alteration of the standard Part D structure. In addition, no beneficiary from the "Some Gap Coverage" group had a deductible whereas a significant proportion of beneficiaries in the "No Gap Coverage" group were enrolled in plans that charged a front-end deductible.

Ideally, as with other analyses, it would be useful to eliminate these differences using the propensity score matching technique. However, the sample size restriction as well as the variables on which the two groups differed prevented the use of the matching technique. For example, in the group that took oral anti-hyperlipidemic agents, 446 had "Some Gap Coverage" whereas 7,636 had "No Gap Coverage". Among the latter, only 38.62% (295) beneficiaries were enrolled in an 'enhanced alternative' benefit structure and even that did not offer coverage during the gap. Thus, the sample sizes of the two groups were so similar that it would be difficult to perform a match. In addition, since the benefit structure is what defines and differentiates them into these two groups, there would not be any additional utility to match on this particular

113

variable even if there was sufficient sample size. Therefore, no matching was performed for this analysis. Tables 27-33 present the characteristics of the two comparison groups used for this analysis by therapeutic class.

Table 27: Characteristics of beneficiaries on oral anti-hyperlipidemic agents based on "gap coverage" status

Variable	Some Gap Coverage N=446	No Gap Coverage N = 7,636	p-value
Age Mean(Std.dev**)	76.81(6.08)	76.52(6.47)	0.2185
Race (%Caucasian)	95.07	93.07	0.3701
Gender (% Females)	70.19	67.76	0.2871
Income† (Median)	32,945	34,022	0.0239*
# Medications taken (Mean (Std.Dev))	9.74(3.99)	9.63(3.93)	0.8055
CDS†† Mean(Std.dev)	2.89(1.87)	3.62(2.12)	<0.0001*
Total Duration††† Mean(std.dev)	310.65(23.79)	311.57(24.28)	0.4963
Benefit Type (% Basic Design)	0	61.38	<0.0001*
Deductible (% No)	100	73.1	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	99.28	0.0721
Gap Threshold (% Std. amt***)	100	98.73	0.0299

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

114

Table 28: Characteristics of beneficiaries on beta-blockers based on "gap coverage" status

Variable	Some Gap Coverage N=291	No Gap Coverage N = 5,298	p-value
Age Mean(Std.dev**)	78.21(6.78)	77.94(6.97)	0.3879
Race (%Caucasian)	94.16	93.74	0.8676
Gender (% Females)	73.88	71.64	0.4138
Income† (Median)	31,784	32,905	0.1466
# Medications taken (Mean (Std.Dev))	10.43(4.24)	10.24(3.88)	0.7948
CDS†† Mean(Std.dev)	3.01(2.03)	3.80(2.05)	<0.0001*
Total Duration††† Mean(std.dev)	312.55(22.52)	313.51(24.14)	0.6400
Benefit Type (% Basic Design)	0	62.74	<0.0001*
Deductible (% No)	100	71.03	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	98.81	0.0614
Gap threshold (% Std. amt***)	100	98.33	0.0553

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 29: Characteristics of beneficiaries on diuretics based on "gap coverage" status

Variable	Some Gap Coverage N=198	No Gap Coverage N = 2,899	p-value
Age Mean(Std.dev**)	78.89(7.39)	78.59(7.28)	0.5334
Race (%Caucasian)	94.57	92.91	0.5045
Gender (% Females)	84.11	78.35	0.0279*
Income† (Median)	33,060	32,120	0.8454
# Medications taken (Mean (Std.Dev))	10.99(3.95)	10.99(3.98)	0.9870
CDS†† Mean(Std.dev)	3.26(1.98)	3.97(2.11)	<0.0001*
Total Duration††† Mean(std.dev)	312.59(24.04)	314.04(24.14)	0.3642
Benefit Type (% Basic Design)	0	62.91	<0.0001*
Deductible (% No)	100	70.17	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	98.77	0.0887
Gap Threshold (% Std. amt***)	100	98.45	0.0599

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 30: Characteristics of beneficiaries using ACE inhibitors based on "gap coverage" status

Variable	Some Gap Coverage N=86	No Gap Coverage N = 1,943	p-value
Age Mean(Std.dev**)	79.09(7.06)	77.55(7.21)	0.0319
Race (%Caucasian)	94.19	92.57	0.8106
Gender (% Females)	72.09	65.26	0.1919
Income† (Median)	29,573	32,232	0.2192
# Medications taken (Mean (Std.Dev))	9.64(3.76)	10.17(3.92)	0.2306
CDS†† Mean(Std.dev)	5.57(1.96)	5.71(1.62)	0.3773
Total Duration††† Mean(std.dev)	304.21(20.94)	306.22(22.78)	0.5540
Benefit Type (% Basic Design)	0	63.05	<0.0001*
Deductible (% No)	100	70.87	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	99.54	0.5270
Gap Threshold (% Std. amt***)	100	99.28	0.4296

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

117

Table 31: Characteristics of beneficiaries on calcium channel blockers based on "gap coverage" status

Variable	Some Gap Coverage N=205	No Gap Coverage N = 3,842	p-value
Age Mean(Std.dev**)	78.69(7.08)	78.59(7.32)	0.6456
Race (%Caucasian)	93.17	91.51	0.7706
Gender (% Females)	79.02	76.88	0.4785
Income† (Median)	32,587	32,933	0.9296
# Medications taken (Mean (Std.Dev))	10.05(3.93)	10.41(3.85)	0.1083
CDS†† Mean(Std.dev)	3.74(1.82)	4.57(1.92)	<0.0001*
Total Duration††† Mean(std.dev)	312.86(21.73)	313.81(24.46)	0.7814
Benefit Type (% Basic Design)	0	63.30	<0.0001*
Deductible (% No)	100	71.86	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	99.05	0.1615
Gap Threshold (% Std. amt***)	100	98.62	0.1109

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 32: Characteristics of beneficiaries using PPIs based on "gap coverage" status

Variable	Some Gap Coverage N=223	No Gap Coverage N = 4,204	p-value
Age Mean(Std.dev**)	77.98(7.14)	77.43(7.28)	0.2251
Race (%Caucasian)	94.17	92.84	0.9463
Gender (% Females)	79.37	76.15	0.2707
Income† (Median)	32,531	33,226	0.2563
# Medications taken (Mean (Std.Dev))	10.57(4.22)	10.74(4.36)	0.3955
CDS†† Mean(Std.dev)	2.56(1.87)	3.37(2.01)	<0.0001*
Total Duration††† Mean(std.dev)	316.37(24.94)	313.11(24.11)	0.9256
Benefit Type (% Basic Design)	0	62.02	<0.0001*
Deductible (% No)	100	71.97	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	99.04	0.2629
Gap Threshold (% Std. amt***)	100	98.62	0.1187

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Table 33: Characteristics of beneficiaries using oral anti-diabetic agents based on "gap coverage" status

Variable	Some Gap Coverage N=138	No Gap Coverage N = 2,613	p-value
Age Mean(Std.dev**)	76.55(6.52)	76.69(6.31)	0.2542
Race (%Caucasian)	89.86	88.52	0.5560
Gender (% Females)	65.7	63.57	0.8256
Income† (Median)	33,942	33,053	0.7402
# Medications taken (Mean (Std.Dev))	10.14(4.06)	10.45(4.12)	0.2793
CDS†† Mean(Std.dev)	4.35(2.05)	5.09(1.99)	<0.0001*
Total Duration††† Mean(std.dev)	311.66(25.52)	312.73(24.34)	0.5342
Benefit Type (% Basic Design)	0	63.91	<0.0001*
Deductible (% No)	100	71.18	<0.0001*
Pre-Gap Costsharing (% Tiers)	100	98.74	0.1841
Gap Threshold (% Std. amt***)	100	98.55	0.1537

Note: * indicates significant differences between the groups as p-value <0.05, ** means Standard Deviation and *** indicates Medicare Defined Standard amount ($2,510 in 2008), † Income = Median household income of the beneficiaries' zip-code, †† CDS = Chronic Disease Score, ††† Total Duration = total number of days beneficiaries were supposed to take the medications since the first fill date

Medication Adherence

1. <u>Impact of having 'No Drug Coverage' during the coverage gap on beneficiaries' adherence</u>

To determine whether the coverage gap affected the extent to which beneficiaries having no coverage during the coverage gap remained adherent to their prescribed regimen, the medication possession ratios of beneficiaries reaching the coverage gap are first compared with themselves before and after reaching the coverage gap and then with that of matched beneficiaries that did not reach the coverage gap. Initially, the beneficiaries serve as their own controls and any change in the adherence can be attributed to factors other than the observed demographic, medication related and plan enrollment related characteristics. These 'other factors' can be being in the coverage gap or situations that cannot be captured in the database (e.g. selection into specific plans or sudden changes in economic conditions).

Before matching the beneficiaries reaching the coverage gap to those who did not reach the coverage gap, it was found that beneficiaries in most of the therapeutic classes exhibited significantly less adherent behavior in the gap compared to their own filling pattern before reaching the gap. The significance of the difference in the two values is estimated using the Wilcoxon Signed Rank Test for paired data. The decrease in MPR ranged from 11% for oral anti-diabetic agents to 38% for PPIs. Table 34 presents the MPR values before and after reaching the coverage gap among beneficiaries with "No Gap Coverage" as well as for those who did not reach the coverage gap in 2008.

121

Table 34: Decrease in MPR† in the "No Gap Coverage" group before matching

Class	Did not reach the gap	Reached the Gap			
		Pre-Gap	In Gap	Difference	p-value
ACE inhibitors	0.73	0.86	0.59	0.27	<0.0001*
Beta-blockers	0.88	0.95	0.61	0.34	<0.0001*
Calcium channel blockers	0.86	0.96	0.60	0.36	<0.0001*
Diuretics	0.88	0.95	0.59	0.36	<0.0001*
Oral anti-diabetic agents	0.98	0.98	0.87	0.11	<0.0001*
Oral anti-hyperlipidemic agents	0.79	0.99	0.75	0.24	<0.0001*
Proton pump inhibitors	0.68	0.96	0.58	0.38	<0.0001*

Note: † MPR = Medication Possession Ratio* indicates significant differences between the groups at p-value <0.05

To reliably attribute the change in adherence values to the fact that the beneficiary was in the coverage gap and not some other mediator, it was necessary to compare the change in medication usage patterns of those reaching the coverage gap to those not experiencing the coverage gap throughout the year. Therefore, for this part of the analyses, the change in beneficiaries' adherence during the coverage gap phase was compared to the change in adherence experienced by corresponding matched beneficiaries who did not reach the coverage gap. After performing the match as specified earlier, the matched pairs were analyzed for the change in adherence before and during the gap. Then these differences were compared using the Wilcoxon Signed Rank Test.

The results indicate that for the most part, both groups experienced significant decreases in adherence (Table 35). However, compared to those who did not reach the coverage gap, the beneficiaries reaching the coverage gap decreased their adherence to medications to a greater extent. For example, the decrease in adherence to beta-blockers after reaching the coverage gap

122

was 3% greater than the decrease in adherence observed for the corresponding beneficiaries not reaching the coverage gap during the same period. In absolute terms, beneficiaries using beta-blockers who reached the coverage gap decreased their adherence by 33% while in the gap; whereas beneficiaries not reaching the coverage gap experienced a decrease of 30% in their MPR for the same period (p-value = 0.006). Similar results were obtained for beneficiaries using oral anti-diabetic agents (difference-in-difference = 9%, p-value < 0.0001), oral anti-hyperlipidemic agents (difference-in-difference = 7%, p-value < 0.0001) and PPIs (difference-in-difference = 7%, p-value < 0.0001).

Beneficiaries using ACE inhibitors, calcium channel blockers or diuretic agents also experienced greater reductions in adherence values compared to those reaching the coverage gap, but these differences were not statistically significant. Among those who used calcium channel blockers, the decrease in adherence for those reaching the coverage gap was 1% more than the decrease observed for those not reaching the coverage gap (p-value 0.1906). The decrease in adherence was 2% higher among those using diuretic medications and reaching the coverage gap compared to those that did not reach the coverage gap (p-value 0.1572). However, the results were reversed for beneficiaries taking ACE inhibitors. In this group, beneficiaries reaching the coverage gap experienced a 1% smaller reduction in adherence compared to those who did not reach the gap (p-value .3888).

Table 35: Difference-In-Difference analyses of the decreases in MPR†s in the "No Gap Coverage" group by therapeutic class after matching

Class	Reached the Gap	Did not reach the Gap	Diff-in-Diff**	p-value
ACE inhibitors (N = 1,373 pairs)	0.25	0.26	-0.01	0.3888
Beta-blockers (N = 3,821 pairs)	0.33	0.30	0.03	0.006*
Calcium channel blockers (N = 2,373 pairs)	0.33	0.32	0.01	0.1572
Diuretics (N = 3,530 pairs)	0.35	0.33	0.02	0.1906
Oral anti-diabetic agents (N = 1,655 pairs)	0.41	0.32	0.09	<0.0001*
Oral anti-hyperlipidemic agents (N = 5,041 pairs)	0.33	0.26	0.07	<0.0001*
Proton pump inhibitors (N = 2,678 pairs)	0.36	0.29	0.07	<0.0001*

Note: † MPR = Medication Possession Ratio, * indicates significant differences between the groups as p-value <0.05 ** means Difference-In-Difference, calculated as (Change in MPR after reaching the gap for the 'Reached Gap') – (Change in MPR after reaching the gap for 'Did not reach the Gap'),

In a second set of analyses, the percentage of beneficiaries found to have stopped taking their medications after reaching the coverage gap was estimated for the matched pairs. In addition, we compared the proportion of beneficiaries considered to be adherent (MPR $\geq$ 0.80) before and after reaching the coverage gap for each therapeutic class.

The results indicate that a greater proportion of beneficiaries not reaching the coverage gap appeared to have stopped taking their medications at the time corresponding to the coverage gap. Overall, the group taking PPIs was most likely to stop taking the medications during the coverage gap. A little over one fifth (21.51%) of the beneficiaries reaching the gap and 28.90% of beneficiaries not reaching the gap in this group stopped taking their medications in the time corresponding to the coverage gap. Beneficiaries using diuretics was another group in which

12.85% and 23.40% of the beneficiaries who did and did not experience the coverage gap stopped taking the medication during the time corresponding to the coverage gap. For all other groups, the proportion of beneficiaries who discontinued taking medications during the time corresponding to the coverage gap was in the range of 9% - 19%. The differences in the proportion of beneficiaries stopping medications from the groups that did and did not reach the coverage gap were statistically significant for all the classes evaluated. Table 36 presents these results in detail.

Table 36: Percent of beneficiaries in the "No Gap Coverage" group stopping medications during the coverage gap

Class	Reached the gap (%)	Did not reach the gap (%)	p-value
ACE inhibitors (N = 1,373 pairs)	15.37	18.43	<0.0001*
Beta-blockers (N = 3,821 pairs)	10.49	15.18	<0.0001*
Calcium channel blockers (N = 2,373 pairs)	12.85	18.71	<0.0001*
Diuretics (N = 3,530 pairs)	18.53	23.40	<0.0001*
Oral anti-diabetic agents (N = 1,655 pairs)	9.49	13.41	<0.0001*
Oral anti-hyperlipidemic agents (N = 5,041 pairs)	11.60	16.43	<0.0001*
Proton pump inhibitors (N = 2,678 pairs)	21.51	28.90	<0.0001*

The proportion of beneficiaries considered adherent before and during the coverage gap decreased for both the groups in all classes of medications evaluated. For example, among beneficiaries using beta-blockers, 80.81% of the beneficiaries reaching the coverage gap were considered adherent before reaching the coverage gap. However, only half of these beneficiaries (44.21%) were found to be adherent during the coverage gap phase. For beneficiaries not reaching the coverage gap, the numbers were 72.52% in the pre-gap period and 42.97% in the

125

'during gap' period. These findings were consistent across all the remaining therapeutic classes being evaluated. Table 37 presents these results in detail.

Table 37: Percentage of beneficiaries in the "No Gap Coverage" group considered adherent* in the Pre-Gap and the During Gap periods by therapeutic class

Class	Reached gap		Did not Reach Gap	
	%adherent Pre-Gap	% adherent During Gap	%adherent Pre-Gap	% adherent During Gap
ACE inhibitors (N = 1,373 pairs)	72.54	44.51	70.12	40.64
Beta-blockers (N = 3,821 pairs)	80.81	44.21	72.52	42.97
Calcium channel blockers (N = 2,373 pairs)	82.68	46.08	71.35	40.18
Diuretics (N = 3,530 pairs)	72.27	42.72	64.43	40.37
Oral anti-diabetic agents (N = 1,655 pairs)	84.65	68.61	72.71	48.88
Oral anti-hyperlipidemic agents (N = 5,041 pairs)	78.82	49.64	76.86	42.99
Proton pump inhibitors (N = 2,678 pairs)	66.43	36.45	46.11	30.85

Note: * considered adherent = beneficiaries whose Medication Possession Ratio (MPR) ≥ 0.80

Further, we evaluated the differences in percentage of beneficiaries considered adherent before and after reaching the coverage gap in both the groups for statistical significance. The tests indicate that the differences between the groups were statistically significant for all therapeutic classes except ACE inhibitors. The decrease in percentages of beneficiaries considered adherent was greater among those taking beta-blockers, calcium channel blockers, diuretics or PPIs and reaching the coverage gap compared to those not reaching the coverage gap. However, greater percentages of beneficiaries taking ACE inhibitors, oral anti-diabetic agents, or oral anti-hyperlipidemic agents and not reaching the coverage gap were found to be non-adherent at the time corresponding to the matched group's coverage gap (Table 38).

126

Table 38: Difference-in-difference of decreases in percentages of beneficiaries in the "No Gap Coverage" group considered adherent† during the coverage gap

Class	Reached the Gap	Did not reach the Gap	Diff-in-Diff**	p-value
ACE inhibitors (N = 1,373 pairs)	28.03	29.48	-1.45	0.4010
Beta-blockers (N = 3,821 pairs)	36.60	29.55	7.05	<0.0001*
Calcium channel blockers (N = 2,373 pairs)	36.60	31.17	5.43	<0.0001*
Diuretics (N = 3,530 pairs)	29.55	24.06	5.49	<0.0001*
Oral anti-diabetic agents (N = 1,655 pairs)	16.04	23.83	-7.79	<0.0001*
Oral anti-hyperlipidemic agents (N = 5,041 pairs)	29.18	33.87	-4.69	<0.0001*
Proton pump inhibitors (N = 2,678 pairs)	29.98	15.26	14.72	<0.0001*

Note: † considered adherent = beneficiaries whose Medication Possession Ratio (MPR) $\geq$ 0.80 * indicates significant differences between the groups as p-value <0.05 ** means Difference-In-Difference, calculated as (decrease in percent adherent after reaching the gap for the 'Reached the Gap') – (decrease in percent adherent after reaching the gap for 'Did not reach the Gap')

These results indicate that among the beneficiaries taking beta-blockers and PPIs, those reaching the coverage gap were more likely to reduce their medication usage to some extent (inferred from the reduction in percentage considered adherent) rather than stopping it completely as compared to those who did not reach the coverage gap. The net effect was that the observed decrease in adherence (in other words, MPR) during the coverage gap for those reaching it was significantly greater than for those not reaching the coverage gap. However, for those taking oral anti-diabetic agents and oral anti-hyperlipidemic agents, the results indicate that though beneficiaries reaching the coverage gap were less likely to stop taking their medications altogether, there is still a significantly greater decrease in their MPR values compared to those not reaching the coverage gap. Among those taking calcium channel blockers and diuretics, a lesser proportion of beneficiaries reaching the coverage gap stopped the medications during that

127

time compared to those not reaching the coverage gap. This was nullified by the fact that a greater proportion of beneficiaries not reaching the coverage gap became non-adherent (MPR < 0.80) during the coverage gap period compared to those who reached the coverage gap. In other words, there was no significant difference in the decrease in adherence (MPR) values between the two groups for these therapeutic classes.

128

2. <u>Impact of having 'Partial Drug Coverage' during the coverage gap on beneficiaries' adherence</u>

To study the impact of having partial drug coverage during the gap, comparisons of changes in MPR values before and after reaching the coverage gap were made with themselves in the "Some Gap Coverage" group. It was found that the decrease in beneficiaries' adherence to medications during the coverage gap was significant compared to their adherence values before reaching the coverage gap for all therapeutic classes being studied. The greatest decline in adherence was exhibited by the group taking PPIs (41%) whereas the smallest decrease was in the group using oral anti-diabetic agents (18%). An analysis of the changes in adherence after adding the comparison group that did not reach the coverage gap revealed that the percent decrease in adherence in the group reaching the coverage gap was not significantly different than the percent decrease experienced by the corresponding comparison group for any therapeutic class. Tables 39 and 40 present these results in detail.

Table 39: Decreases in MPR in the "Some Gap Coverage" Group by gap status before matching

Class	Did not reach the gap	Reached the Gap			
		Pre-Gap	In Gap	Difference	p-value
ACE inhibitors	0.73	0.81	0.49	0.32	<0.0001*
Beta-blockers	0.88	0.96	0.66	0.30	<0.0001*
Calcium channel blockers	0.89	0.96	0.62	0.34	<0.0001*
Diuretics	0.88	0.95	0.59	0.36	<0.0001*
Oral anti-diabetic agents	0.98	1.02	0.84	0.18	<0.0001*
Oral anti-hyperlipidemic agents	0.79	0.98	0.67	0.31	<0.0001*
Proton pump inhibitors	0.67	0.86	0.45	0.41	<0.0001*

Note: * indicates significant differences between the groups at p-value <0.05

Table 40: Difference-In-Difference analyses of decreases in MPR†s in the "Some Gap Coverage" group by therapeutic class after matching

Class	Reached the Gap	Did not reach the Gap	Diff-in-Diff**	p-value
ACE inhibitors (N = 36 pairs)	0.18	0.17	0.01	0.8935
Beta-blockers (N = 163 pairs)	0.3	0.29	0.01	0.9786
Calcium channel blockers (N = 97 pairs)	0.32	0.36	-0.04	0.5614
Diuretics (N = 128 pairs)	0.32	0.2	0.12	0.6842
Oral anti-diabetic agents (N = 61 pairs)	0.47	0.29	0.18	0.0512
Oral anti-hyperlipidemic agents (N = 235 pairs)	0.34	0.32	0.02	0.2426
Proton pump inhibitors (N = 108 pairs)	0.42	0.2	0.22	0.0015

Note: † MPR = Medication Possession Ratio, * indicates significant differences between the groups as p-value <0.05 ** means Difference-In-Difference, calculated as (Change in MPR after reaching the gap for the 'Reached Gap') – (Change in MPR after reaching the gap for 'Did not reach the Gap')

130

As with the "No Gap Coverage" group, we estimated the proportion of beneficiaries who stopped taking medications from a particular therapeutic class while in the coverage gap. We also estimated the change in proportion of beneficiaries considered to be adherent (MPR $\geq$ 0.80) before and during the coverage gap phases. Among those with some gap coverage, a considerable percentage of beneficiaries stopped taking medications during the coverage gap phase. These percentages in this group ranged from 7.98% for beta-blockers to 30.56% for PPIs. However, unlike the "No Gap Coverage" group, the percentage of beneficiaries not reaching the coverage gap but stopping the medications was greater among those taking beta-blockers, calcium channel blockers, diuretics and oral anti-hyperlipidemic agents; but less among those taking ACE inhibitors, PPIs or oral anti-diabetic agents. None of these differences (except ACE inhibitors), however, was statistically significant (Table 41).

Table 41: Percent of beneficiaries in the "Some Gap Coverage" group stopping medications during the time corresponding to the coverage gap

Class	Reached the gap (%)	Did not reach the gap (%)	p-value
ACE inhibitors (N = 36 pairs)	28.13	6.25	0.0102
Beta-blockers (N = 163 pairs)	7.98	11.66	0.2628
Calcium channel blockers (N = 97 pairs)	9.28	14.43	0.2670
Diuretics (N = 128 pairs)	17.97	19.53	0.7490
Oral anti-diabetic agents (N = 61 pairs)	11.48	3.28	0.0802
Oral anti-hyperlipidemic agents (N = 235 pairs)	10.64	11.91	0.6600
Proton pump inhibitors (N = 108 pairs)	30.56	27.78	0.6528

The proportion of beneficiaries considered adherent during the coverage gap decreased from the pre-gap values for both groups (those who did and did not reach the coverage gap). A greater proportion of those taking ACE inhibitors, beta-blockers, calcium channel blockers and oral anti-diabetic agents and not reaching the coverage gap were considered non-adherent at the time corresponding to the matched group's coverage gap while the results were opposite for the other classes evaluated. Only the difference for those taking PPIs was statistically significant. Table 42 and 43 presents these results in detail.

Table 42: Percentage of beneficiaries considered adherent* in the Pre-Gap and the During Gap periods by therapeutic class

Class	Reached gap		Did not Reach Gap	
	%adherent Pre-Gap	% adherent During Gap	%adherent Pre-Gap	% adherent During Gap
ACE inhibitors	59.38	46.88	74.19	47.88
Beta-blockers	88.34	54.6	89.76	47.24
Calcium channel blockers	82.47	49.48	81.45	45.36
Diuretics	73.44	45.31	67.72	49.22
Oral anti-diabetic agents	85.25	57.48	85.25	57.27
Oral anti-hyperlipidemic agents	78.3	44.25	71.55	42.13
Proton pump inhibitors	58.33	30.55	34.58	26.85

Note: * considered adherent = beneficiaries whose Medication Possession Ratio (MPR) $\geq$ 0.80

Table 43: Difference-in-difference of decreases in percentages of beneficiaries in the "Some Gap Coverage" group considered adherent† during the coverage gap

Class	Reached the Gap	Did not reach the Gap	Diff-in-Diff**	p-value
ACE inhibitors (N = 36 pairs)	12.50	26.31	-13.81	0.1310
Beta-blockers (N = 163 pairs)	33.74	42.42	-8.78	0.1032
Calcium channel blockers (N = 97 pairs)	32.99	36.09	-3.10	0.6528
Diuretics (N = 128 pairs)	28.13	18.50	9.63	0.0672
Oral anti-diabetic agents (N = 61 pairs)	27.77	27.98	-0.21	0.9760
Oral anti-hyperlipidemic agents (N = 235 pairs)	34.05	29.42	4.63	0.2846
Proton pump inhibitors (N = 108 pairs)	27.78	7.73	20.05	<0.0001*

Note: † considered adherent = those with MPR $\geq$ 0.80* indicates significant differences between the groups as p-value <0.05 ** means Difference-In-Difference, calculated as (decrease in percent adherent after reaching the gap for the 'Reached the Gap') – (decrease in percent adherent after reaching the gap for 'Did not reach the Gap')

The results for those with "Some Gap Coverage" indicate that the proportions of beneficiaries considered adherent or stopping the medications did not differ between those who did and did not reach the coverage gap for all therapeutic classes except PPIs. For those taking PPIs, similar proportions of beneficiaries stopped taking medications at the time of the coverage gap but a greater proportion of those reaching the coverage gap were considered non-adherent compared to those not reaching the coverage gap. Therefore, overall, it appears that there is a significantly greater reduction in adherence (MPR) for those reaching the coverage gap in this group compared to those not reaching the coverage gap.

From the previous analyses, it can be concluded that the decreases in adherence to medications for beneficiaries reaching the coverage gap relative to the decreases in adherence of

beneficiaries not reaching the coverage gap varied across therapeutic classes. Further, it is found that the extent to which beneficiaries' MPR decreased within a therapeutic class also varied by presence or absence of drug coverage in the gap. To study the significance of this variability within the groups reaching the coverage gap, the differences in beneficiaries' adherence values (i.e. MPRs) before and after reaching the coverage gap based on their "gap coverage" status were compared using the Wilcoxon Rank Sum Test. As can be noted from Table 44 below, the decreases in adherence values during the coverage gap were not significantly different between groups for any of the therapeutic classes.

Table 44: Decreases in MPR†s during the coverage gap by gap coverage type and therapeutic class

Class	Some Gap Coverage N	Decrease	No Gap Coverage N	Decrease	p-value
ACE inhibitors	86	0.32	1,943	0.27	0.2918
Beta-blockers	291	0.30	5,298	0.34	0.0727
Calcium channel blockers	205	0.34	3,842	0.36	0.4529
Diuretics	198	0.36	2,899	0.36	0.9123
Oral anti-diabetic agents	138	0.18	2,613	0.11	0.2918
Oral anti-hyperlipidemic agents	446	0.31	7,636	0.24	0.9006
Proton pump inhibitors	223	0.41	4,204	0.38	0.1911

Note: † MPR = Medication Possession Ratio, * indicates significant differences between the groups as p-value <0.05

Main Conclusions

A significant proportion of beneficiaries reached the coverage gap in 2008. However, most did so late in the year and spent the rest of the year in the gap. Also, the impact of coverage gap on beneficiaries' adherence is mixed depending on whether or not they had coverage for some drugs during the gap. The following chapter discusses the results as well as the study strengths and limitations in detail. It also highlights the practical applications of these results.

CHAPTER 6

DISCUSSION

This chapter discusses the results of the study as well as the strengths and limitations of the study design. It also presents an overview of practical implications of the study results, concluding remarks, and ideas for future research.

Objective 1:

The sample for our analysis was older, sicker and predominantly Caucasian. Almost three-quarters of the sample comprised females and the median annual household income ranged around $33,000. Most seniors in our sample took several medications simultaneously and used at least 3 classes of medications being evaluated. A greater proportion of beneficiaries from our sample were enrolled in stand-alone PDP plans and 95.07% did not have any coverage for drugs during the coverage gap. Moreover, these beneficiaries were enrolled in plans that did not charge a deductible and in those that had tiered cost-sharing structures rather than the standard 25% coinsurance rate set by Medicare. Beneficiaries with drug coverage in the gap were limited to coverage for generic drugs only. These socio-demographic characteristics as well as plan enrollment profile are similar to the national estimates indicating that our sample was a representative sample of all Medicare beneficiaries[117].

Overall, the beneficiaries in our sample were found to have similar socio-demographic characteristics irrespective of whether or not they reached the coverage gap or whether or not they had coverage during the gap. This indicates that the socio-demographic characteristics of beneficiaries that were included in this study are not significant in determining whether or not

136

beneficiaries reached the coverage gap in a given year. These results are consistent with prior findings that socio-demographic characteristics are not significant predictors of reaching the coverage gap threshold[64]. The results however, do indicate that beneficiaries reaching the coverage gap used significantly greater numbers of unique medications and had higher OOP spending before and during the gap. The use of greater numbers of medications can be used as a proxy for having greater number/severity of co-morbidities. In addition, though the differences between the socio-demographic and plan enrollment characteristics varied by therapeutic class, the number of medications and CDS were consistently higher among those who reached the coverage gap compared to those who did not. These results are in accordance with prior estimations that the likelihood of reaching the coverage gap increases with increases in co-morbidity[64, 66, 118].

Objective 2:

Almost a quarter of all beneficiaries in our sample reached the coverage gap in 2008. This finding is similar to prior estimates by researchers at Kaiser Family Foundation[62]. However, this proportion is greater than found by other studies that estimated that between 6 and 19% of their samples reached the coverage gap in a given year[118-121]. It should be noted, however, that the study done by Kaiser Family Foundation used data from a representative sample of beneficiaries enrolled in PDPs whereas the other studies used data from beneficiaries enrolled in MA-PD plans, which are inherently different from PDPs.

When comparing beneficiaries with some drug coverage during the gap to those without any drug coverage during the gap, we found that the two groups were similar in terms of their demographic and medication taking behavior, but that a greater proportion of beneficiaries with "Some Gap Coverage" reached the coverage gap. These results hold at the therapeutic class level

137

analyses as well. In our opinion, these findings are consistent with the basic economic theory of insurance and demand; the presence of some drug coverage during the gap may lead to an increased utilization of medications before the gap, and therefore increase the chances of reaching the coverage gap.

At the therapeutic class level, the greatest proportion of beneficiaries reaching the gap were those who took proton pump inhibitors group, followed by those taking oral anti-diabetic agents, beta-blockers and oral anti-hyperlipidemic agents. Beneficiaries using ACE inhibitors were the least likely to have experienced the coverage gap. These results were consistent in groups with and without gap coverage.

A majority of our sample reaching the coverage gap did so by September which is a month later than the previous estimates of beneficiaries reaching the gap by August[62]. This could be due to adaptation to the benefit structure. To the best of our knowledge this is the first study to estimate the effect of coverage gap two years into its implementation and we hypothesize that since the beneficiaries were exposed to the Part D benefit design for at least a couple of years, they would have been able to adjust their medication usage accordingly. A study by Hsu et al.[122] tested a similar assumption and found that those who were aware of having a gap in coverage were significantly more likely to adopt one or more cost-cutting strategies throughout the year which could be translated as a measure to delay their entry to the coverage gap.

On average, beneficiaries reaching the coverage gap spent about three months in the phase. Only 3% of the total sample reached the catastrophic coverage phase. These beneficiaries were those who reached the coverage gap in the first quarter of the year and had quite high expenditures on medications. There was no difference in the time taken to reach the coverage

138

gap based on presence or absence of gap coverage. These estimates are also consistent with prior research indicating that a very small percentage of beneficiaries reach the catastrophic coverage level and that most of the beneficiaries reaching the coverage gap remain in that phase through the rest of the year[62, 119, 123].

Objectives 3 and 4:

Our study results indicate that the impact of experiencing a coverage gap on beneficiaries' adherence to prescription medications depends on the therapeutic class of medication evaluated as well as presence or absence of drug coverage during the coverage gap.

When compared with themselves, beneficiaries in all therapeutic classes experienced a significant reduction in their adherence during the coverage gap irrespective of the presence or absence of gap coverage. For the group with "No Gap Coverage", the decrease in MPR values during the gap ranged from 11% for those using oral anti-diabetic agents to 38% for those using PPIs. Similar results were obtained for those reaching the coverage gap and having "Some Gap Coverage" (18% for oral anti-diabetic users and 41% for PPIs). These estimates are consistent with the hypothesis that adherence would be adversely affected during the coverage gap, but are greater than previous studies[62, 66, 118].

In the "No Gap Coverage" group, the decrease in adherence (MPR) for beneficiaries reaching the coverage gap was 1% (for calcium channel blockers) to 9% (for oral anti-diabetic agents) more than the decrease in adherence for beneficiaries not reaching the coverage gap. The difference in the differences was statistically significant for those using beta-blockers, oral anti-diabetic agents, oral anti-hyperlipidemic agents or PPIs. For those in the "Some Gap Coverage" group also, MPR values declined during the time corresponding to the coverage gap irrespective

139

of whether or not they reached it, but the difference between these decreases were not statistically significant for any class except PPI, the group in which the MPR values for beneficiaries reaching the coverage gap decreased by 22% more than those not reaching the coverage gap. Overall, the findings that adherence decreased for both the groups is consistent with a prior study in which Raebel et al found that adherence decreased more for those reaching the coverage gap and, to a lesser but still substantial extent, for those who did not reach the gap[60].

In addition, the results indicate that a substantial proportion of beneficiaries stopped taking their medications during the coverage gap phase for both those who did and did not reach the coverage gap, independent of gap coverage. The extent of beneficiaries stopping their medications ranged from about 10% to 25% depending on the class and group being evaluated. This finding is consistent with that of the study by Kaiser Family Foundation that found that as many as 20% of their sample stopped taking medications during the coverage gap[62].

The proportion of beneficiaries considered to be adherent also decreased during the coverage gap phase for both those who did and did not reach the coverage gap, for all classes of medications irrespective of gap coverage. The extent of decrease in percentage of beneficiaries considered adherent during the coverage gap in both groups varied with therapeutic class and presence of gap coverage. These results, however, are counter-intuitive in the fact that the percentages of beneficiaries stopping medications or becoming non-adherent at the time of the coverage gap were greater for those not reaching the coverage gap compared to those who did reach the coverage gap for most comparisons.

140

A possible explanation for the findings that a significant proportion of beneficiaries either stopped or became non-adherent even though they did not reach the coverage gap can be drawn from the studies that estimated the impact of having a cap on spending for prescription medications. This is because the group that did not reach the coverage gap in our study did have a 'cap' of $2,510 on their drug spending and an awareness of this cap could lead to decreased utilization of medications. A study by Hsu et al. tested a similar hypothesis and found that the group not reaching the coverage gap was more aware of having a gap in coverage compared to those who did reach the coverage gap and therefore modified their medication taking behaviors accordingly[122]. Such findings have also been noted in the literature before the implementation of Medicare Part D among seniors with capped benefits[38-40, 124].

Given this, it is reasonable to state that our results indicate a greater need for providing 'uninterrupted' and/or 'uncapped' drug coverage to all Medicare beneficiaries. As proposed by the newly signed health reform law, provision of uninterrupted coverage is proposed to be achieved by phasing in subsidies for drugs during the coverage gap every few years until the gap is eliminated completely. For example, the current timeline[125] suggests provision of a rebate worth $250 to beneficiaries reaching the gap between July and December of 2010. For the following years, the manufacturers have agreed to provide 50% rebate for the brand name drugs purchased by beneficiaries in the gap. Beginning in January 2011, the Government will start offering 7% discount on generic drugs and increase the discount gradually till 2020 when the gap is proposed to be eliminated. The subsidies for brand name drugs will be offered from January 2013 till the total cost to beneficiaries reaches 25% (50% by manufacturer and upto 25% by the Government) in 2020.

141

These are a few steps in the right direction, but as is apparent from the plan, it will take several years to be fully implemented. Implementing this policy reform might not be feasible in the long run because providing coverage throughout the year will lead to increase in utilization of the medications and, in turn, increase government spending on prescription drugs. A recent publication in the Kaiser Health News bulletin, reported that the Congressional Budget Office has estimated the cost of elimination the coverage gap by 2019 to be $42.6 billion[126]. There is also a possibility of further delay in implementation of all the provisions due to political as well as financial pressures that may develop over the course of time. Thus, the beneficiaries still have to cope with having interruptions and/or caps in drug coverage for several more years to come.

An additional possible reason for finding decreases in adherence as well as percentage of beneficiaries considered adherent during the coverage gap for both the groups that did and did not reach the coverage gap can be due to financial barriers like having limited income or changing economic times like the Great Recession of 2008. However, we believe that we were able to account for these effects to some extent through techniques like propensity score matching and the difference-in-difference analysis.

Another possible reason for such findings may be the availability of non-recorded medications (e.g. cash pays for $4 generics or over the counter medications; especially for PPIs). In other words, it is possible that the beneficiaries utilized their medications as prescribed but purchased them from sources that were not recorded in the insurance claims data. The availability of such medications could have a significant beneficial effect on beneficiaries' OOP spending as well as help them delay reaching the coverage gap. As a result, there could have been significant use of such medications, especially, among those not reaching the coverage gap than those who did reach it. Therefore, together, it would appear that the beneficiaries not

142

reaching the gap stopped or reduced their medication utilization to a greater extent as compared to those reaching the gap.

In addition, a review of the literature suggests that cost-related medication non-adherence is a very complex phenomenon. A model developed by Piette et al. summarizes the known predictor/s of medication non-adherence (either alone or in combination of more than one) to be socio-demographic, complexity of regimen, drug coverage, OOP costs, number of co-morbid conditions, physical, emotional and social health status, perceived need of medications, adverse effects of medications, patient – provider relationship, effect on Health Related Quality of Life (HRQoL) and health system characteristics[127]. Therefore, it is possible that non-financial barriers to medication adherence may exist for not only those who experience a coverage gap, but also for the entire senior population enrolled in stand-alone PDP plans, due to which the entire sample in our analysis experienced varied degree of decreases in adherence during the time corresponding to the coverage gap. While we were able to account for a few of these factors (socio-demographic factors, drug coverage, co-morbid conditions, health system characteristics and complexity of drug regimen), the effect of a number of predictors (health beliefs, perceived need for medications, effects on HRQoL and physician patient relationship) remains to be explored. Therefore, it is possible that a lack of awareness among the patients, personal beliefs or other non-financial factors might increase the rates of non-adherence despite the availability of uninterrupted drug coverage through the proposed health reform.

In summary, we believe that it is reasonable to state that our study results have policy implications for all beneficiaries enrolled in Medicare Part D and beyond. Firstly, our results indicate that there is a need to provide uninterrupted and/or uncapped coverage for prescription drugs to the seniors. Secondly, we also suggest that it would be beneficial to educate all

143

Medicare beneficiaries; especially those with multiple chronic diseases and who take several medications at a time; about the importance of medication adherence as well as strategies that can help them continue taking their medications as prescribed throughout the year while enrolled in the Part D program. These strategies include choosing a plan that has providers and a formulary structure that meet the beneficiary's requirements, obtaining supplemental coverage, and switching to generic medications early in therapy.

Strengths and Limitations

Evidence from the literature suggests that beneficiaries reduce the use of medications during the coverage gap. However, the degree to which a lack of coverage in the gap reduces adherence rates remained to be explored. Ours is one of the first studies to quantify the extent to which adherence rates decreased during the coverage gap for beneficiaries taking one more of the most widely used medications among seniors. Further, most studies to date limited their analyses to data from single health plans offering MA PD drug plans and thus may have limited application to beneficiaries enrolled in stand-alone PDPs. In addition, the studies done to date are limited to data up to the year of 2007. To the best of our knowledge, ours is the first study to use the CMS claims and denomination data files to estimate the impact of Medicare Part D coverage gap on adherence of beneficiaries enrolled in stand-alone PDPs two years into the program's implementation. As a result, our findings reflect the impact of the gap after the beneficiaries have had two years to learn about the program and develop strategies to cope with it.

The study design accounts for different types of effects that can introduce biases in our estimates. First, it uses eligible beneficiaries as their own controls in assessing the change in medication adherence rates during the coverage gap. Since the same cohort of patients is observed before and after the intervention, this reduces potential bias introduced due to differences in beneficiary characteristics between the two study periods. This is further controlled by using a matched control group that did not experience a coverage gap. The second stage of analysis estimates the difference in change in adherence rates (before and during the gap) between cases and matched controls. This helps us to control biases introduced by choices in plan selection as well as potential temporal trends like the changing economy and changing

145

overall prevalence of diseases. Together, these controls help us to more accurately measure the association between the gap and change in adherence.

The study, however, also has limitations. The use of retrospective claims data implies that the study is affected by limitations related to secondary data sources. One of the main limitations is that using only the information from the database compels us to assume that all the filled prescriptions were taken as prescribed[128]. Despite this, it is known that claims data are relatively accurate measures of the dates and times at which most prescription medications are taken by a patient and therefore do provide information about 'possessing' a medication[128]. In addition, we believe that the population studied for this research had limited incentives to 'not' take their medications if they were filled because our sample included senior Medicare beneficiaries who generally have limited sources of income and several concomitant chronic diseases that require continuous use of medications.

We could not, however, account for medications taken by the beneficiaries that are not billed through Medicare as those transactions are not recorded in the claims data. Examples include free samples, over-the-counter medicines, borrowed medicines, and prescriptions paid for with cash (such as $4 generics at Wal-Mart or Target). The result of this is that we could have underestimated the adherence to medications in our sample. In other words, it is possible that some beneficiaries did not really stop treatment for their conditions, but since they moved to alternatives that are not captured in the database (e.g. $4 generics), they were considered as being non-adherent according to our definition. This supports the argument for forming a comprehensive dataset that also captures information of such drugs that are not paid for by the insurance but are still dispensed as being equivalent to the prescription medications.

146

In addition, switching between therapeutic classes of medications was not allowed in our adherence calculations which might also lead to underestimation of adherence to medications. However, we believe that since the report was generated at a therapeutic class level, allowing the switch between classes would have generated inaccurate estimates of effects of the coverage gap within a particular therapeutic class.

Our results indicate that being in the coverage gap was not a significant indicator of decrease in adherence in the group with "Some Gap Coverage". This is because among those with some drug coverage during the coverage gap, the extent of decreases in adherence for those reaching the coverage gap was similar to those not reaching the coverage gap. However, in a separate analysis, it was found that having some drug coverage during the gap was not significantly different from having no drug coverage during the gap. Previous results indicate that having some coverage during the coverage gap was beneficial for the seniors[66, 67, 129] but the impact of "Some Gap Coverage" during the coverage gap on medication adherence was not clear in our study. These results need to be interpreted with caution because the sample size of groups with some form of coverage during the coverage gap was close to about 100 beneficiaries only. In addition, even though the groups that did and did not have gap coverage were similar to each other in terms of most of their characteristics, there were differences in their plan enrollment characteristics which could affect their medication taking behavior. Owing to sample size issues, it was not possible to match these two groups with each other to generate reliable estimates.

We were not able to evaluate the effects of other known predictors of medication non-adherence (e.g. side effects or adverse reactions of the drugs, health beliefs, and patients' relationship with the physician) because this database did not collect information on these variables. These predictors could have affected our adherence values in either direction.

147

Additionally, we did not eliminate the overlaps caused by using multiple drugs in the same therapeutic class and hence we might have overestimated the adherence rates.[112]

The income and therapeutic class information were not available in the CMS database and were obtained by linking our database with other data sources. The income information was gathered from Census data which has been widely used as a measure of a person's financial status. The concern is that the Census data presents the median household income in a zip-code, not at the level of a beneficiary's individual income. The therapeutic classification was obtained from First Databank based on the NDC numbers provided in the CMS Part D event file. However, the NDC as well as the classification system used both came from First Data Bank and therefore, we are less concerned about the differences introduced by use of an external source for this information. In addition, it is reasonable to believe that all the study limitations had similar effects on the groups that did and did not reach the coverage gap. Therefore, much of the bias introduced because of these limitations would be minimized between the groups.

Conclusions and Future Research

In conclusion, the impact of 'coverage gap' in our sample is not clear. Though there are reductions in adherence values for those reaching the coverage gap independent of presence of gap coverage, medication adherence decreased for all beneficiaries as the year progressed. The reductions were greater for some therapeutic classes for those reaching the coverage gap in the "No Gap Coverage" group compared to those not reaching the coverage gap; however, the coverage gap did not seem to significantly affect the adherence values of those with "Some Gap Coverage".

Future research should study the effects of the coverage gap for the same group of beneficiaries over several years because it would provide information about whether prior experiences help beneficiaries make effective choices in subsequent years or not. In addition, it would be useful to compare the effects of being in the coverage gap with no coverage to beneficiaries who reached the coverage gap and had full coverage during the gap. As evidence from the literature suggests, decreases in adherence to medications leads to worse clinical outcomes which can increase the cost of therapy. Therefore, future research should be directed at studying the impact of Medicare Part D coverage gap on utilization of other health care services. It would also be useful to conduct studies that examine the effects of non-financial barriers like health beliefs, effects on HRQoL, patient-physician relationship and awareness about Part D on medication adherence while being in the coverage gap.

149

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154

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- Assist with teaching and grading assignments
- Creating and posting materials to Blackboard

05/2010-07/2010

Summer Internship
- Intelliject LLC, Richmond, VA
- Conduct literature based analysis to explore potential for new auto-injector device
- Create hypothetical model to evaluate the pharmacoeconomic benefits of a potential new auto-injector

04/2008-08/2008   **Other Training**
- Intelliject LLC, Richmond, VA
- Conducted a Decision- tree based Cost-Consequence Analysis to study the pharmAcoeconomic benefits of a potentially new epinephrine auto-injector for anaphylactic patients

LEADERSHIP EXPERIENCE

06/2010-05/2011   **ISPOR Student Network Chair**
- Oversee functioning of the Student Network and its activities
- Preside over all subcommittees responsible for conducting one or more activities at the Network level
- Serve as the primary liaison between the Student Body and the ISPOR Board of Directors

06/2009-05/2010   **ISPOR VCU Student Chapter President**

ISPOR Student Network Survey Committee Chair
- Supervised the design and implementation of a brief survey of the student network members
- Compiled a report and presented it at the 15th Annual International Meeting of ISPOR in Atlanta, May 2010

AWARDS and HONORS
- Victor A Yanchick Award for excellence in scholarship, research, teaching and service, 2010-2011
- SPOR Distinguished Service Award as Student Network Chair, 2010-2011
- VCU Graduate School Dissertation Award (08/2010-05/2011)
- ISPOR Distinguished Service Award as Survey Committee Chair, 2009-2010
- Honor of presenting a working model of '*Manufacturing tables by Wet Granulation'* to the then President of India Dr. APJ Abdul Kalam, January 2005

POSTER PRESENTATIONS

- Desai U., Carroll NV. A cost-consequence analysis comparing an established and a novel epinephrine autoinjector for anaphylaxis. *Value In Health* 2009;12(3):A123. 14th International Meeting of ISPOR, May 2009
- Patel D, Holdford H, Desai U, Carroll N. Economic Burden of Anaphylaxis in the United States. 15th Annual International Meeting of ISPOR, May 2010

SHORT COURSE CERTIFICATIONS

- Advanced PRO Assessment: Psychometric Methods (05/2009)
- Outcomes Research for Medical Devices and Diagnostics (05/2009)
- AHRQ's MEPS Workshop (09/2009)

VCU Memo

Office of Research Subjects Protection
BioTechnology Research Park
BioTech One, 800 E. Leigh Street, #114
P.O. Box 980568
Richmond, Virginia 23298-0568
(804) 828-0868, fax (804) 827-1448

DATE: February 8, 2010

TO: Norman Carroll, PhD
           Pharmacy
           Box 980533

FROM: Lloyd H. Byrd, MS *ℒℬ/ℵℐ*
           Chairperson, VCU IRB Panel E
           Box 980568

RE: **VCU IRB #: HM12720**
           Title: Impact of Medicare Part D Coverage Gap on Adherence to Prescription Medications

On February 1, 2010 the following research study *qualified for exemption* according to 45 CFR 46.101(b) Category 4. This approval includes the following items reviewed by this Panel:

RESEARCH APPLICATION/PROPOSAL: NONE

PROTOCOL: Impact of Medicare Part D Coverage Gap on Adherence to Prescription Medications, version 11/28/09, received 1/21/10

ADDITIONAL DOCUMENTS:
▪ None

The Primary Reviewer assigned to your research study is Janet Niemeier, PhD. If you have any questions, please contact Dr. Niemeier at jniemeier@vcu.edu and 628-1633; or you may contact Donna Gross, IRB Coordinator, VCU Office of Research Subjects Protection, at dsgross@vcu.edu or 827-2261.

Attachment – Conditions of Approval

Conditions of Approval:

In order to comply with federal regulations, industry standards, and the terms of this approval, the investigator must *(as applicable):*

1. Conduct the research as described in and required by the Protocol.

2. Obtain informed consent from all subjects without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate (unless Waiver of Consent is specifically approved or research is exempt).

3. Document informed consent using only the most recently dated consent form bearing the VCU IRB "APPROVED" stamp (unless Waiver of Consent is specifically approved).

4. Provide non-English speaking patients with a translation of the approved Consent Form in the research participant's first language. The Panel must approve the translated version.

5. Obtain prior approval from VCU IRB before implementing any changes whatsoever in the approved protocol or consent form, unless such changes are necessary to protect the safety of human research participants (e.g., permanent/temporary change of PI, addition of performance/collaborative sites, request to include newly incarcerated participants or participants that are wards of the state, addition/deletion of participant groups, etc.). Any departure from these approved documents must be reported to the VCU IRB immediately as an Unanticipated Problem (see #7).

6. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.

7. Report Unanticipated Problems (UPs), including protocol deviations, following the VCU IRB requirements and timelines detailed in VCU IRB WPP VIII-7):

8. Obtain prior approval from the VCU IRB before use of any advertisement or other material for recruitment of research participants.

9. Promptly report and/or respond to all inquiries by the VCU IRB concerning the conduct of the approved research when so requested.

10. All protocols that administer acute medical treatment to human research participants must have an emergency preparedness plan. Please refer to VCU guidance on http:/www.research.vcu.edu/irb/guidance.htm.

11. The VCU IRBs operate under the regulatory authorities as described within:
    a) U.S. Department of Health and Human Services Title 45 CFR 46, Subparts A, B, C, and D (for all research, regardless of source of funding) and related guidance documents.
    b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.
    c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).