Implications and Investigations of Pharmacy Benefit in the United States

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Abstract

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Medicaid clients are among the most at-risk members for poor health outcomes in society and this safety net health care is critical for assuring continuous access to medical care. We will describe the importance of curtailing unnecessary drug spend as well as generic utilization mechanisms already applied by payers. We will describe the background, implementation, and early findings of a prescriber feedback report card program to improve generic utilization in the Washington State Medicaid system.

We quantified the association between possession of prescription drug coverage and likelihood of experiencing an emergency room [ER] visit and hospitalization in the adult United States population with private health insurance. For the outcomes of ER visits and hospitalizations, the ORs were 1.05 (95% confidence interval [CI], 0.95 to 1.15) and 1.07 (95% CI, 0.95-1.22) respectively using propensity score matching. Indicating a non-significant increase in odds of the outcomes of ER visit and hospitalization for patients possessing drug coverage . Multiple logistic regression produced similar findings. For the outcomes of ER visit and hospitalization, the adjusted ORs were 1.03 (0.96-1.12) and 1.01 (0.91-1.21) respectively. Prescription drug coverage in the United States was not associated with a reduction in likelihood of ER visit or hospitalization in this assessment pooling ten years of cross-sectional data.

To estimate the reduction in adherence and medication supplied for patients that experience increases in average monthly copay over time for three therapeutically distinct drugs for chronic syndrome management using a nationally representative Commercial Claims databaseIncrease in $5 or more or $10 or more for average monthly copay was associated with a statistically significant reduction in MPR for all three drugs. Measured by generalized

estimating equations, change in MPR varied from a minimum loss of 0.024 for simvastatin with a $5 or more increase in copay to a maximum loss of 0.063 for insulin glargine with $10 or more increase. This equates to a minimum loss of days supply 8.8 to 23.0 for simvastatin and insulin glargine respectively. Copay increases are associated with significant reductions in adherence of chronic medications necessary for optimal disease control.

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DEDICATION

To my parents, Fumihiko and Jane Watanabe

Chapter 1: Generic Medication Utilization and Medicaid Sustainability

Chapter 1 abstract

In this essay we argue for the expansion of generic drug utilization policies to protect the Medicaid system in an era of critical budget depletion. Medicaid clients are among the most at-risk members for poor health outcomes in society and this safety net health care is critical for assuring continuous access to medical care. Medicaid coverage obviates the consumption of billions of public dollars paying the health care bills for catastrophic outcomes for the uninsured poor. We will describe the importance of curtailing unnecessary drug spend as well as generic utilization mechanisms already applied by payers. This paper will also describe the historic opportunity to arrest unsustainable drug spending due to the recent patent losses of manifold blockbuster medications. The stimulation of a robust and safe generic drug marketplace in the United States via the Drug Price Competition and Patent Term Restoration Act will also be explored. The positive implications for patient medication adherence with generic use will follow. Finally, we will describe the background, implementation, and early findings of a prescriber feedback report card program to improve generic utilization in the Washington State Medicaid system. This article is drawn from a comprehensive review of the research literature on generic medication use; research with academic policy investigators; and collaboration with policy makers in the Medicaid system of Washington State.

Medicaid patients at risk

One in every five Americans receives health care coverage through Medicaid. These 60 million Americans are provided coverage based on low-income status or disability. Medicaid covers 31 million low income children and finances 40% of all child births[1]. Medicaid is clearly a foundational societal support system both now and for the future caretakers of the US.

Repeated findings in several countries have confirmed the association between low income and poor health (Stronks, van de Mheen, and Mackenbach 1998; van de Mheen et al. 1998; Dalstra et al. 2002; Sacker et al. 2000; Lynch et al. 2000). Data suggests a death spiral in which poor health outcomes, originally propelled by low income, foster worsening

[1] Data from The Center for Medicare and Medicaid Services. http://www.medicaid.gov/Medicaid-CHIP-Program-Information/Medicaid-and-CHIP-Program-Information.html

socioeconomic status (Lynch and Smith 2005). Medicaid serves as a crucial safety net for providing medical care for those that would otherwise be without. A recent analysis found significant increases in hospitalizations for patients with chronic illness who dealt with interruptions in their Medicaid coverage. Moreover, the impact was felt quickly as the bulk of the hospitalizations occurred within 3 months in lapse of Medicaid coverage (Bindman, Chattopadhyay, and Auerback 2008)

The importance of sheltering Medicaid coverage so it may continue to offer health care to the disabled, the poverty-stricken, mothers, gestating fetuses, infants, and children cannot be overstated. Emerging research has shed light on a causal connection between childhood health problems and lower socioeconomic circumstance in adult life (Kuh et al. 2003). Sustaining an able and robust labor force is contingent on ensuring childhood health which Medicaid resources succor.

Overspending due to underuse of generic medications

While branded medications represent only 31% of prescriptions dispensed, their utilization encumbers 84% of total drug spending in the US (IMS Health 2009). According to the National Association of Chain Drugstores, last year the average retail price for a brand drug was $96.01. The average retail price of a generic drug was $28.74—a savings of nearly 70 percent per prescription (Committee on Energy and Commerce: Subcommittee on Health 2005). An Office of Inspector General (OIG) report found a similar pattern within the state Medicaid system with generic drug prices 61% less expensive than brand drugs. The OIG analysis found that only 54% of all drugs dispensed in Medicaid were generics. Based on the perceived under utilization of generic medications, the report recommended specific focus within therapeutic

categories that demonstrated greater variation in generic utilization rates across states. This variance was interpreted as a signal that states with utilization on the lower bound had potential for improvement. The report does concede that many states may have already attained their maximum generic substitution rate. For states below the median overall or below median by therapeutic category, opportunity for savings with enhanced generic use remains (OIG 2006). Although Center for Medicare and Medicaid Services (CMS) data recently showed that generic use had improved to 67% of total prescriptions in Medicaid by the year 2010, it is highly likely that much higher generic use rates can be achieved based on the levels achieved by many states (Center for Medicare and Medicaid Services 2010)

Profound cost reductions for chronic syndromes are attainable based on scenario analyses of clinical guidelines-based generic substitution. A well publicized cost effectiveness study of hypertension control medications for non-diabetic patients estimated it would require $52,983 to gain an additional quality adjusted life year (QALY) versus no treatment (Kahn et al. 2008). When this analysis was repeated substituting available generic medications for brand medications the dollars per QALY dropped from $52,983 to $7,753 (Shrank et al. 2011). Given the traditional range of $50,000 to $100,000 per QALY deemed 'cost effective' (Chambers, Neumann, and Buxton 2010), chronic care with generics is surpassingly cost effective. Analysis of 133,624 elderly patients in a Pennsylvania pharmaceutical assistance program found that $11.6 million could have been saved by increased adherence to evidence-based recommendations for hypertension management with generic medications. The study authors estimated $1.2 billion could be saved nationally for hypertension management of the elderly if these substitutions were applied (Fischer and Avorn 2004). This is an underestimate of current savings as many guideline recommended first-line hypertension drugs for patients with diabetes

and heart failure for hypertension management have lost patent protection since that analysis was performed in 2004 (Shrank et al. 2011).

To achieve blood pressure goals, The 7th report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) states that patients will often require more than one agent in addition to the initial recommended thiazide diuretic medication. These recommendations have been succored by recent clinical findings. A recent meta-analysis of 42 trials pooling findings from 11,000 subjects found a five-fold increase in blood pressure reduction when a second antihypertensive was added versus doubling the dose of the single agent (Wald et al. 2009). This has not limited the applicability of generic formulations as wide availability of generic combination drugs exists. The presence of generic combination products has bolstered the potential cost savings and reduced the number of pills taken per day if prescribed. This reduction in pill burden has been credited with improving patient adherence to therapy (Pan, Chernew, and Fendrick 2008). Generic fixed-dose combination drugs may provide additional cost savings by reducing administrative costs for multiple prescriptions and are often less expensive than the constituent drugs sold separately (Wertheimer and Morrison 2002). Moreover, cost has recently been the impetus in the development of combination drugs for cardiovascular disease treatment (Wald and Law 2003; van Gils et al.). These medications were designed with the overt goal of additive and synergistic benefits of multiple drug entities at a reduced price point by using inexpensive generic medications in array.

Increase in First-Line Generic Drugs

The last few years have seen an acceleration in availability of first line medication options due to virtually simultaneous patent losses of brand medications. Lipitor, Plavix,

Zyprexa, Zocor, and Aricept make up a truncated list of medications with individual annual sales of greater than $1 billion per year that will lose patent protection by the close of 2012. The number one and two highest revenue generating medications, Lipitor and Plavix, represent more than $13 billion in annual sales (Shrank et al. 2011). Generic drug prescribing presents a clear opportunity for dramatic drug spending reductions.

The ratio of available generic medications has also been increased based on a reduction in patent protected new molecular entities (Theodorou and Slezak 2009). The deceleration in new branded drugs reaching the market combined with the increase in available generic agents described above has increased the proportion of generic medicines in the armamentarium to control chronic disease. These phenomena are credited with blunting the overall increase in drug spend to 1% to 2% annual increases in drug spending (IMS Health 2009). The IMS report described $734 billion in savings due to generic medicines from 1999-2008 with $121 billion in savings in 2008 alone.

Viability of Generic Drugs

Recent systematic reviews and meta-analyses have confirmed the bioequivalence and clinical equivalence of generic drugs to brand name drugs (Dentali et al. ; Vlahiotis et al.). A meta-analysis of 47 cardiovascular studies that compared brand to generic medications found no evidence of clinical superiority for branded medications. The investigators parsed clinical trials of drugs with a smaller dose margin between clinical benefit and toxicity referred generally as ‘narrow therapeutic index (NTI) drugs’. Six trials involving NTI drugs such as warfarin or antiarrhythmic drugs similarly revealed no clinical differences between brand and generic medications. Interestingly, the study authors also reviewed medical journal editorials that discussed the clinical differences of brand and generic medications. Half of the editorials

reported a negative view of generics seemingly at odds with the mounting body of evidence (Kesselheim et al. 2008). These perspective pieces likely fuel the misperceptions often harbored by clinicians and patients.

The Kesselheim meta-analysis was successful in including the bulk of therapeutic categories of medications used for cardiovascular syndromes including but not limited to beta-blockers, diuretics, calcium channel blockers, statins, ACE inhibitors, and antiplatelet agents. The availability of first-line generic options is not limited to cardiovascular medications. The 5 leading chronic causes of death in order are heart disease, stroke, chronic lower respiratory diseases, Alzheimer's disease, and Diabetes (Heron 2011). The constellation of treatments for each of these is penetrated with generic medications as first-line therapy. See table 1.

Table 1. Leading Chronic Causes of Death and Availability of Generic Medicines

Heart Disease	No. 1 Chronic Disease Case of Death 616,067 annual deaths	25.4% of total annual deaths
Category	Generic Available	Example
Thiazide diuretics	Yes	hydrochlorothiazide, chlorthalidone
Beta-blockers	Yes	atenolol, metoprolol, carvedilol
Angiotensin-converting enzymes	Yes	lisinopril, benazepril
Calcium channel blockers	Yes	amlodipine, diltiazem
Angiotensin receptor blockers	Yes	losartan
Loop diuretics	Yes	furosemide, bumetanide
Peripheral vasodilator	Yes	hydralazine
Anticoagulant	Yes	warfarin
Anti-platelet agents	Yes	aspirin, clopidogrel*
Nitrates	Yes	isosorbide mononitrate, isosorbide dinitrate
Statins	Yes	simvastatin, atorvastatin, pravastatin
Fibric acids	Yes	gemfibrozil, fenofibrate
Oral direct thrombin inhibitors	No	n/a

Stroke	No. 2 Chronic Disease Case of Death 135, 952 annual deaths 5.6% of total annual deaths	
Drug categories widely overlap with heart disease drugs above		
Anti-platelet agents	Yes	aspirin, clopidogrel, dipyridamole
Anti-coagulants	Yes	heparin, enoxaparin
Chronic Lower Respiratory Disease	No. 3 Chronic Disease Case of Death 127, 924 annual deaths 5.3% of total annual deaths	
Short-acting beta agonists	Yes	nebulized albuterol
Inhaled corticosteroids	Yes	nebulized budesonide
Anticholinergics	Yes	ipratropium
Leukotriene receptor antagonists	Yes	zafirleukast
Long-acting beta agonists	No	n/a
Alzheimer's Disease	No. 4 Chronic Disease Case of Death 74, 632 annual deaths 3.1% of total annual deaths	
Cholinesterase inhibitors	Yes	donepezil, rivastigmine, galantamine
NMDA receptor antagonists	No	n/a
Monoamine oxidase inhibitor	Yes	selegiline
Diabetes Mellitus	No. 5 Chronic Disease Cause of Death 71, 382 annual deaths 2.9% of total annual deaths	

Insulins	Yes	insulin R, insulin human isophane
Sulfonylureas	Yes	glyburide, glipizide, glimepiride
Biguanides	Yes	metformin
Meglitinides	Yes	nateglinide
Thiazolidinediones	No[†]	n/a
GLP-1 receptor agonists	No	n/a

[†]Generic pioglitazone will be available in 2012

Influence of the Drug Price Competition and Patent Term Restoration Act

It is informative to describe seminal policies that have evolved to approve generic versions of medications. These efforts began in earnest with the publication in 1979 of a list (the List) of all prescription drug products that are approved by FDA for safety and effectiveness. The goal for publication of the List was to assist state health care agencies determine therapeutic substitutes that would promote cost containment efforts. To this end, the List was accompanied with therapeutic equivalence determinations for multisource prescription products (Federal Register 1979). This first iteration included only drug products FDA approved via new drug applications (NDAs) and abbreviated new drug applications (ANDAs) as stipulated in Section 505 of the Federal Food, Drug, and Cosmetic Act (the Act) (Approved Drug Products with Therapeutic Equivalents 2012). Section 505 of the Act sanctioned the use of bioequivalence stipulations that took shape as the evaluations of therapeutic equivalence for multisource drugs in

the List. A code letter system was developed that indicates the evaluation made with each addition of the List including a summary description of the meaning of each therapeutic code evaluation (Federal Register 1980). These efforts were bolstered and further codified in 1984 by the signing of President Reagan of the Drug Price Competition and Patent Term Restoration Act (The 1984 Amendments) commonly referred to as the Hatch-Waxman Act (United States Code 1984). The 1984 Amendments included a mandate that a comprehensive list of approved drug products be published by the FDA for public use. The 1984 Amendments also required the FDA to publish monthly cumulative supplements. This legal obligation was satisfied by production of The *Approved Drug Products with Therapeutic Equivalence Evaluations publication*, commonly referred to as the Orange Book (Approved Drug Products with Therapeutic Equivalents 2012).

The 1984 Amendments have played a significant role in engendering an environment favorable for generic development. The increase in available generics manufactured has been a necessary step in achieving cost savings. Prior to the 1984 Amendments generic medications were estimated to represent only 19% of all prescriptions (Congressional Budget Office 1998). The proportion has dramatically shifted as generic medications represented 75% of total prescriptions in 2009 (Berndt and Aitken 2011). The central goals of the 1984 Amendments were two fold 1) Improve patent protection for innovators of new drugs that had experienced diminished patent life post marketing due to more extensive FDA reviews. 2) Incentivize generic entry for other manufacturers to improve competition that would reduce drug costs for consumers. The first goal was achieved by providing extensions for patent life equal to the duration of the FDA review before approval plus half the number of years devoted to completion of the clinical trials. The extension could not exceed 5 years (Lourie 1989). The second goal was achieved via several provisions. The 1984 Amendments provided a route for more rapid

approval of generic entities by allowing bioequivalence tests to prove equivalence rather than completion of clinical trials for the ANDA to be submitted. The 1984 Amendments developed provisions for generic firms to challenge brand-name patents and produce their bioequivalent drug after the 5 years from innovator drug approval. Third, a successful challenge would reward this first generic manufacturer with a 180 day exclusivity period. This 6 month generic monopoly was proposed to incentivize the generic firm to bear the legal costs associated with the challenge.

Some investigators have questioned the causality between The 1984 Amendments and the increase in generic use citing the lack of challenge filings specific to the 1984 amendments to completely explain the massive increase in generic use (Kesselheim 2011). However, it is difficult to conceive the 1984 Amendments not playing a significant role in the observed increases in generic medications and the accelerated erosion of brand market share following generic entry since the 1984 Amendments ensued. Analysis of IMS Health Data from 1995 to 2008 demonstrated a reduction in years brand drugs exist on the market before a legal challenge for generic manufacture from 18.7 years in 1995 to 8.2 years in 2008. Similarly, the proportion of of new drugs that experienced generic legal challenges at any point has increased from 9% in 1995 to 64% in 2008 (Grabowski et al.). The study authors failed to account for changes in the health care market as a whole, but it is unlikely market dynamics independent of the 1984 Amendments could completely explain the observed trend. It may be that the 1984 Amendments were not immediate in effect, but required several years before the market effects could be well delineated.

The 1984 Amendments not only codified the mechanism for improving generic entry, but also stipulated regulatory framework for generic drugs to be efficacious substitutes

demonstrating therapeutic equivalence (United States Code 1984). Drug are deemed therapeutically equivalent if they are pharmaceutical equivalents. This mandates an expectation of elicitation of the same clinical effect and safety profile when patients consume the drugs under the conditions specified in the FDA approved labeling. As specifically detailed in the preface of the 32nd Orange Book (Approved Drug Products with Therapeutic Equivalents 2012):

"FDA classifies as therapeutically equivalent those products that meet the following general criteria: (1) they are approved as safe and effective; (2) they are pharmaceutical equivalents in that they (a) contain identical amounts of the same active drug ingredient in the same dosage form and route of administration, and (b) meet compendial or other applicable standards of strength, quality, purity, and identity; (3) they are bioequivalent in that (a) they do not present a known or potential bioequivalence problem, and they meet an acceptable in vitro standard, or (b) if they do present such a known or potential problem, they are shown to meet an appropriate bioequivalence standard; (4) they are adequately labeled; (5) they are manufactured in compliance with Current Good Manufacturing Practice regulations."

The statistical bioequivalence determination involves two separate one-sided t-tests. The first assay evaluates whether a brand drug substituted is significantly less bioavailable than a generic medication. The second assay reverses this procedure determining whether a generic substituted for a brand is significantly less bioavailable. The pharmacokinetic parameters of interest are the resulting area under the plasma concentration-time curve (AUC) and the maximum or peak drug concentrations (Cmax), for rate of absorption. A difference of greater than 20% for each of the two tests was determined to be significant, and therefore, undesirable for all drug products. This amounts to a range of 80% to 125% (reciprocal of 80% for second test). The criteria are fairly stringent as the confidence interval for both pharmacokinetic

parameters, AUC and Cmax, must be entirely within the 80% to 125% boundaries cited above.(Approved Drug Products with Therapeutic Equivalents 2012)

The established coding system delineates therapeutically equivalent multisource medications will carry a Therapeutic Equivalence Evaluations Codes (TE Codes) of beginning with the letter 'A' if therapeutically equivalent and therefore possibly substitutable and the letter 'B' indicating the drug has not been deemed therapeutically equivalent as described in the Orange Book. Specifically, drugs that have no suspected bioequivalence issues are designated as AA, AN, AO, AP, or AT with the second letter reflecting dosage form. In situations where potential or detected bioequivalence issues have been rectified via sanctioned studies demonstrating bioequivalence, the drugs are designated as AB.

Throughout this document 'generically available' refers to the market presence of A rated generic medications that have met the criteria described above.

Patient adherence to care regimen increases with generic medications

Improved adherence is a collateral benefit often observed in analyses of generic medications (Briesacher et al. 2009; Shrank et al. 2006; Gemmill, Thomson, and Mossialos 2008; Fairman, Motheral, and Henderson 2003). This is likely a consequence of the improved probability of medication consumption due to dramatically reduced or zero dollar patient copay for generic medications by pharmacy benefit managers (Klepser et al. 2007). Elasticity of demand for necessary medications is a natural extension of the inverse correlation between price and consumption of health services observed classically in the Rand Health Insurance Experiment (RAND-HIE) (Manning et al. 1987). The pharmacy benefit designs compared in the RAND-HIE were less developed than current tiered benefit structures. However, the findings

hold true today. The researchers found a 23% increase in prescriptions filled for participants in a free plan versus one with a 25% coinsurance (Leibowitz, Manning, and Newhouse 1985). These findings were found to be reproducible 16 years later using data from a preferred provider organization that had shifted certain clients from a two-tier to three-tier benefit plan (Motheral and Fairman 2001).

Medications must be taken as directed to provide maximal benefit. Studies have consistently demonstrated the decrease in health status for patients and increase in health utilization costs for patients with reduced adherence to their medication regimens (DiMatteo et al. 2002). A comparison of the influence of factors on treatment effectiveness and efficiency demonstrated adherence to be more influential than stage of disease, age, and gender on outcomes (Mar and Rodriguez-Artalejo 2001). The journal of the American Heart Association *Hypertension* has gone so far as to devise recommendations on the appropriate measurement of adherence for hypertension control medications because of the strong relationship to increased hospitalizations and excess medical costs inextricable when patients are not taking medications as directed (Halpern et al. 2006)

Previous Attempts to Influence Generic Utilization

As the recession has leveled state budgets in recent years, utilization control efforts have intensified. However, efforts to control medication budgets through an array of mechanisms have been unfolding over the last thirty years in the Medicaid system (Soumerai et al. 1993). Early crude Medicaid utilization controls such as monthly caps on number of prescriptions and copays have been joined by more elaborate drug utilization modifiers such as prior authorization, closed preferred drug lists, generic substitution, duration/refill limits, and step-therapy (Farley et

al. 2008; Morden and Sullivan 2005). Morden and Sullivan found in 2005 that virtually every state had developed and instituted usage control measures (Morden and Sullivan 2005).

A multitude of designs are now deployed to tame irrational drug utilization. These mechanisms include those mentioned previously as well as tiered benefits and cost-sharing expansions such as co-insurance (Olson 2003). Moreover, development and adoption of systematic methods for preferred drug list construction is becoming normalized (Neumann 2004). All of these policies have the common goal of improving the yield of necessary medications amongst the volume of prescriptions written and to control costs in order to sustain drug coverage for plan members (Litton, Sisk, and Akins 2000; Joyce et al. 2002). In the following paragraph, we will focus on two direct approaches to improve generic usage at the point of care.

Originally motivated by concerns that prescribing expensive brand medications was leading to reduced compliance and failure to fill necessary medications (Tseng et al. 2006; Gibson, Ozminkowski, and Goetzel 2005), commercial payers have piloted direct means of improving generic utilization at the patient office visit via two mechanisms: generic sample dispensing kiosks and generic medicine vouchers. These have the asset of immediacy as the utilization control mechanism takes place at the point of care. Generic sample kiosks resemble free standing ATMs in provider's office that dispense a 30 day supply of chronic care generic formulary medicines after the clinician enters into the machine appropriate information for the patient . The Blue Shield plan that piloted the program found an increase in generic utilization for the provider's using the kiosks versus those that were not. They similarly found reductions in prescription costs for providers using the kiosks. Continued reductions in prescription costs were anticipated for the patient as the generic medication co-pays were reduced versus branded

medications. Based on an average patient savings of $15 per generic prescription versus brand the initiation on a sample generic medication would amount to an estimated $180 saved per patient annually. After subtracting installation and maintenance expenses of the kiosks the authors estimated savings of $453,545 in 2006 (Scott, Culley, and O'Donnell 2007). Based on these findings and other investigations on the influence of samples on prescribing behavior (Adair and Holmgren 2005; Brewer 1998; Boltri, Gordon, and Vogel 2002), a recent NIH supported randomized controlled trial is now underway to ascertain the impact of a generic samples program on proportion of generic prescriptions filled commonly referred to as the generic dispensing ratio (GDR), patient adherence, physician compliance with established guidelines, and prescription costs for treatment of hypertension and hyperlipidemia. One limitation inherent to the generic kiosk is the absence of pharmacist medication review and patient counseling on dispensation. Although, clinical pharmacists were available to detail the providers intermittently during the study period, the lack of review and availability of counseling could pose risks (Kaboli et al. 2006; Schnipper et al. 2006).

Generic voucher programs provide a first-fill of a generic drug usually of 30 day supply to the patient at no cost. Voucher programs require less infrastructure and storage space for distribution than a samples program. Voucher systems also avoid the regulatory and drug safety issues related to the dispensing of medications without a pharmacist present inherent to samples programs (Reiss and Hall 2000). Provision of medications vouchers still requires a trip to the pharmacy, but requires no copay when the voucher is given to the pharmacy. One study that examined the impact of vouchers in a large physician hospital organization found a small, but statistically significant improvements in GDR for patients involved in the voucher program versus those that did not (Bhargava, Greg, and Shields 2010). This was likely an underestimate

of the voucher impact as those that received the vouchers were targeted based on prior low GDR levels.

Inter-state variability of the Medicaid system is a reality since its establishment as a joint federal and state program. This provides for each state to establish its own eligibility standards, benefits package, payment rates and program administration under broad federal guidelines. This results in wide discrepancies in spending and coverage. These discrepancies result in an uneven distribution of consumption with half the states consuming more than 90% of total spending in the 1980s. The amount spent per Medicaid client is widely divergent as well with Oklahoma spending less than $1,000 per client to an upper bound of $4,800 per client in Connecticut (Holahan and Cohen 1986). These authors also delineated a relationship between state income and Medicaid spending with higher income states spending more than low income states. The federal Medicaid matching program was inversely designed such that lower income states would receive greater matching incentives and this is credited with reducing potentially even larger variance in spending. As a result, there are essentially 56 different Medicaid programs - one for each state, territory and the District of Columbia.

Wide differences are demonstrated in spending along several different metrics when states are compared. Payments for acute care, long term care, and payment for disproportionate share hospitals that bear the largest burden in caring for the indigent varies widely with Southern states traditionally paying the least and Eastern and Mid-Atlantic states typically paying the most. This geographic tendency is consisted in terms of proportion of low-income residents covered by Medicaid, Medicaid spending per beneficiary, and state Medicaid spending (Holahan and Liska 1997). These dramatic differences in spending per low income individual have discernible impact on all facets of care and benefits package provision. Review of the variations

makes it evident that each state presents its own unique program of indigent care under the auspices of the Medicaid program. This has been bourne out in terms of Medicaid drug benefit as well with states opting for closed, positive, or negative preferred drug lists (PDLs) for Medicaid drug coverage. Analyses have also underscored the wide heterogeneity exhibited when state Medicaid PDLs are compared to each other with restrictive PDL states much more likely to have fewer of the 200 most commonly prescribed drugs available on their list. The discrepancies in preferred drugs occurred despite fairly consistent information available to Pharmacy and Therapeutics Committee (P&T Committee) Members that develop the PDL. The authors concede, however, that lack of consistent guidance on what deems a drug worthy of inclusion presents a major hurdle. The dearth of concensus driven criteria for drug inclusion on a PDL also poses a significant barrier in establishing a national Medicaid P&T Committee (Moore and Newman 1993). The heterogeneity in drug benefit management from state-to-state challenges implementation policy when successful approaches in one state are emulated by another state.

The Obama administration attempted to reduce the inter-state heterogeneity in Medicaid eligibility, enrollment, and renewal processes via provisions in the Affordable Care Act. The stated goal was to apply the policies of successful states to all state Medicaid programs. The objectives were originally 5-fold: 1) to impose a federal minimum of eligibility of 133% of the Federal Poverty Level ; 2) collapse eligibility categories and reduce the possible primary covered groups to children, pregnant women, parents, and create an adult group; 3) implement an electronic data driven eligibility verification system; 4) delineate a streamlined income eligibility process for new applications and renewals; 5) ensure coordination across the Medicaid, Childrens Health Insurance Program and the Health Exchanges (Medicaid Program; Eligibility

Changes Under the Affordable Care Act of 2010 2012). The recent Supreme Court Ruling struck down the portion of the Accountable Care Act that sought to enforce penalties on states that did not expand and standardize eligibility (National Federation of Independent Business et al. v. Sebelius, Secretary of Health and Human Services, et al. 2012). This has galvanized some states to begin reducing eligibility further with Maine, Wisconsin, and Alabama evaluating adoption of new stipulations that would remove tens of thousands of current Medicaid clients (Weaver and Radnofsky 2012). This clarifies the intensity of current budget constraints as these states are willing to turn down significant federal matching dollars in order to reduce the state expenditures.

The Washington State Experience

In June 2003, The Washington State Legislature, in an effort to expressly control state prescription drug costs without reducing quality of care, developed the Prescription Drug Program (PDP) in Senate Bill 6088 (SB 6088). The PDP was designated as a joint effort of three state agencies: the Health Care Authority (HCA), the Department of Social and Health Services (DSHS) that administers the state Medicaid plan, and the Department of Labor and Industries (L&I). Since 2003, DSHS and HCA have merged into one entity. Hereafter, these state programs will be referred to as "the agencies".

One of the major components of SB6088 was development of an Evidence-Based Preferred Drug List (PDL) and a drug Therapeutic Interchange Program (TIP) to accelerate implementation of the PDL. To increase the uptake of the preferred drugs, SB 6088 instituted a mechanism for prescribers to affirm clinical support for the drug list via endorsement of the PDL to the HCA. These "endorsing practitioners" have authorized pharmacists to automatically

substitute a preferred agent for a non-preferred drug prescribed unless the prescriber has indicated 'dispense as written' (DAW) or it is for refill of an antipsychotic, antidepressant, chemotherapy, antiretroviral, immunosuppressive drug, or for the refill of a immunomodulator/antiviral treatment for hepatitis C in which case the pharmacist shall dispense the prescribed nonpreferred drug. The stated rationale for these exceptions was to mitigate risk of compromising health status for patients already stabilized on medications with narrow therapeutic windows of effect. The providers were incentivized to endorse the list in order to have the availability to indicate DAW rather than having to submit a request for formal prior authorization from the HCA in order to prescribe a non-preferred medication. The PDL originally consisted of 12 drug classes with additional drug classes added over the years for a total of 29 drug classes currently(Washington Preferred Drug List 2011).

Drugs for the PDL were chosen based upon recommendations from The Washington State Pharmacy and Therapeutics Committee (P&T Committee). The P&T Committee was created in 2003 as an independent body of pharmacists and prescribers meeting at least quarterly to review disseminating findings on efficacy and safety from the Drug Effectiveness Review Project at The Oregon Health and Sciences University. The P&T Committee reviews and recommends which medications belong within designated drug classes and which should be available on the PDL as well as which are similar in efficacy. The agencies then select a preferred drug, or drugs, for each therapeutic class based on analysis of net cost to the state.

Clinic level generic use feedback reports implemented

As described above, usage of non-preferred brand medications was still an option for endorsing providers via DAW. In 2004, the Uniform Medical Plan (UMP), the Washington state

health plan for public employees administered by the HCA, began exploring means of further reducing unnecessary non-preferred medication use at the clinic level. Applying pay for performance models used by health systems, UMP developed a reward system to incentivize preferred use along several parameters:

1. Endorsement of the PDL
2. Generic utilization above 80%
3. DAW use less than 25%

The program met with early success with 9 clinics demonstrating improvement in generic utilization and PDL compliance (Uniform Medical Plan 2005). Based on these improvements, the program was renewed for a total of 2 years (Sullivan 2012). This provided early evidence to the agencies that active monitoring of prescribing habits could result in improvements and cost reductions. The findings would be important information for Medicaid administrators when more intense budget constraints surfaced shortly later (Washington State Department of Social and Health Services 2009).

Prescriber level feedback reports initiated

The global recession ravaged state budgets and Washington state was no exception. The deficit lead to increased scrutiny and substantial reductions in public expenditures for all state services. Human services costs in Washington state exceeded $12 billion in the fiscal 2009 budget and represented the largest proportion (35.1%) of the total budget (Washington State Senate Ways and Means Committee 2009). Washington state Health and Recovery Services

Administration spent $413 million on prescription medications in 2008. Eighty-percent of total drug spend was devoted to brand name medications representing more than $330 million spent on branded drugs. In one report, DSHS found that the amount spent on brand medications alone was more than the Basic Health Program spent to insure 100,000 people. Overall, DSHS estimated $4 million in annual savings if generic use could be escalated by 1% (Washington State Department of Social and Health Services 2009).

As a consequence of these financial pressures, DSHS wished to implement a generic feedback program at the provider level similar to the UMP clinical level program to improve prescribing in Medicaid. The chief medical officer Dr. Jeffery Thompson in collaboration with UMP pharmacy director Dr. Donna Sullivan identified key therapeutic areas where significant improvement in cost effective prescribing could be made based on ample availability of first-line generic medications. DSHS estimated potential savings using an idealized 100% generic substitution rate. In total, this equated to $46.1 million in annuals savings for six categories: proton pump inhibitors for acid reflux disease, statins for cholesterol control, long-acting opioids for pain, non-steroidal anti-inflammatory drugs for pain, stimulants for attention deficit and hyperactivity disorder, and antidepressants for depression). The developers expressly stated that patients on psychiatric medications should not be switched if they are currently stabilized on these medications. Prescribers were instead encouraged to initiate a generic medication as the initial agent or to attempt a generic medication if the patient had problems adhering to a current non-preferred agent.

The program was initially deployed to focus on prescribers with historically low generic utilization relative to their peers. Providers that possessed a GDR of less than 80% or DAW use of greater than 25% were flagged. These providers were sent a letter informing them of their

current use as well as comparison to peer providers and best in class providers. They were encouraged to improve use and were informed that quarterly reports would henceforth be sent to them. If they failed to improve their prescribing trends, they would need to justify their prescribing record via discussion with DSHS or face possible loss of DAW use privileges.

Positive initial policy results and expansion

Early findings of the program have been encouraging. DSHS performed a business case analysis of utilization after two-quarters of policy implementation for the 824 prescribers who received the feedback report. For at least one therapeutic area, 29% improved both GDR and utilization of DAW usage. Fifty-four percent improved GDR only and 45% improved DAW usage only. Eighteen percent were found to have no change (Washington State Department of Social and Health Services 2010).

With 2 year of data now available, we will commence with robust econometric estimation of cost savings later this year. We will examine the statistical impact of the program on generic and DAW utilization rates, prescription costs, and patient adherence to therapy. It will be important to quantify the effects both for forecasting within the Washington state DSHS system and for prediction of effect in other Medicaid systems that can apply findings from Washington state.

DSHS is looking to expand the program to other therapeutic areas and to improve the availability of the data for providers and administration. These metrics will empower providers to actively improve their prescribing by continually informing them of their utilization. These efforts also serve to acclimate prescribers to an environment where performance will be continuously reviewed. This is not solely to address individual prescribing, but also to observe

system wide trends for targeted improvements. This program aligns with health care modernization goals of enhanced continuity of pharmaceutical care and improved data driven decision support for prescribers and health care decision makers.

Generic utilization policies are a necessary component for preservation of the Medicaid system and the 60 million lives that rely on safety net health care to lead productive lives. The Washington State experience with the provider feedback report policy has begun to demonstrate that generic use policies not only reduce cost, but also promote evidence-based practice. Given the tenuous fiscal climate and the wealth of first-line generic agents now marketed, reckless spending on branded drugs is unconscionable.

Chapter 2: Evaluation of Drug Coverage in the Private Health Insurance Market

Chapter 2 abstract

Context

Prescription drug therapy is a standard component of medical care. However, many individuals cannot obtain outpatient medications due to lack of drug coverage. Little research has been conducted to evaluate the association of drug coverage and health outcomes at a national level.

Objectives

To quantify the association between possession of prescription drug coverage and likelihood of experiencing an emergency room [ER] visit and hospitalization in the adult United States population with private health insurance.

Design and Setting

Age-, gender-, race-, income-, marital status-, census region-, education-, and year-adjusted analysis of the nationally representative Medical Expenditure Panel Survey [MEPS] from 1999 to 2008 using propensity score matched conditional logistic regression. Sensitivity analyses applied conventional multiple logistic regression.

Main Outcome Measures

We compared the likelihood of possessing drug coverage for respondents with an event versus those without for each of two outcomes separately: experiencing one or more emergency room [ER] visits and one or more in-patient hospitalizations.

Results

During the 10 year period, among individuals with private health insurance, 105 604 respondents possessed drug coverage while 9 964 did not, representing an average 118.3 million and 10.2 million people in the US annually. Propensity score matching generated 16 972 matched respondents for the primary analysis. For the outcomes of ER visits and hospitalizations, the ORs were 1.05 (95% confidence interval [CI], 0.95 to 1.15) and 1.07 (95% CI, 0.95-1.22) respectively. Indicating a non-significant increase in odds of the outcomes of ER visit and hospitalization for patients possessing drug coverage . Multiple logistic regression produced similar findings. For the outcomes of ER visit and hospitalization, the adjusted ORs were 1.03 (0.96-1.12) and 1.01 (0.91-1.21) respectively.

Conclusions

Prescription drug coverage in the United States was not associated with a reduction in likelihood of ER visit or hospitalization in this assessment pooling ten years of cross-sectional data. Failure to observe a significant reduction in likelihood of negative outcome was found regardless of methodologic approach or year.

Introduction

Prescription drug therapy is considered essential for the management of treatable chronic medical illnesses[1] which are responsible for 70% of all deaths in the United States each year,[2, 3] Prescription drug treatments prevent the acute sequelae of diseases that result in emergency and inpatient care.[4, 5] Yet many patients cannot pay for some or all of their prescribed medications, leading to impaired medication adherence and persistence.[6] Poor adherence to medication regimens translates into suboptimal management of chronic illnesses[7] and is associated with higher utilization of health care.[8-11] It is known that medication utilization is mediated by drug use need and facilitated by prescription drug coverage,[12-14] but the relationship between prescription drug coverage and use of other health services is largely unknown.

We estimated the probability of health services utilization for persons with prescription drug coverage amongst respondents with private drug coverage using a nationally representative survey sample of the United States. Specifically, we quantified the association between drug coverage and likelihood of an emergency room [ER] visit and in-patient hospitalization.

The Medical Expenditure Panel Survey [MEPS] is an extensive source of data designed for estimation and evaluation of health service use in the United States developed by the Agency for Healthcare Research and Quality and the National Center for Health Statistics. MEPS is produced and released annually reflecting the demographic attributes and health service consumption of the US population on a yearly basis.[15-17]

We sought to make our evaluation reflective of the last decade of the US population by pooling the most recent 10 years of MEPS data. Our goal was to elucidate the association between drug coverage and likelihood of ER visit and hospitalization age, gender, race, marital

status, census region, income, education level, year. We were also interested in evaluating the relationship on an individual year basis from 1999 to 2008 for the study outcomes.

Methods

Sample

We analyzed respondent data from the most recent 10 years (1999-2008) of released data from the MEPS Household Component [HC] files. MEPS is designed to provide a national reflection of family and individual demographic characteristics and health services use.[15] The HC files are data from a sample of families and individuals in selected communities across the United States, drawn from a nationally representative subsample of households that participated in the National Health Interview Survey from the prior year with oversampling of minorities and the poverty stricken. Via household interviews, MEPS collects detailed information for each person in the household including demographic characteristics, use of medical services, source of payments, access to care, health insurance coverage, pharmacy benefit coverage, and income with 3 rounds of interviews taking place each calendar year.

The panel design of the survey, involving several rounds of interviewing covering two full calendar years for each respondent, affords the delineation of how changes in respondents' possession of insurance coverage, income, marital status, and payment for care are related to their use of health services and health status. MEPS data is compiled annually from surveys of over 30,000 persons in greater than 10,000 households assessed during periodic in-person interviews and reconciled with records from pharmacists, health care providers and journal entries. Detailed information regarding survey respondents' medical conditions, prescriptions, health status, and health care usage is collected in MEPS. In addition to health information, the

MEPS database includes variables which depict the complex survey design of MEPS, including clustering, stratification, and probability weighting. This data enables the construction of unbiased national estimates of health costs and utilization.[15-19]

We adjusted for age, gender, race, income, marital status, census region, and year using propensity score matching methods.[20] To optimize the matching algorithm, categories for these adjustment variables were defined if not pre-defined by MEPS. Respondents were excluded from the analysis if they were younger than age 18 or older than age 64. Race was collapsed to categories of "white", "black", and "other". Education was coded as "high school education or below" and "more than high school education". Based on pre-defined MEPS categories, income was collapsed to categories of "low income" and "greater than low income". MEPS defines low income status as receiving an adjusted income of less than 200% of the federal poverty level.

We evaluated the association of possession of any level of drug coverage (ie. at least 1 round of drug coverage during the calendar year) and experiencing at least one ER visit and at least one in-patient hospitalization in the year of coverage for the respondent. Exposure variables were designed to answer our specific scientific questions. "Drug coverage" referred to possession of private drug coverage during at least 1 round of MEPS surveys that year. MEPS includes questions asking type of health services use including ER visits and hospitalizations. These responses were used to generate 'yes' or 'no' outcomes for the variables of experiencing an ER visit or hospitalization.

Statistical Analysis

Our goal was to perform estimation of the effect of drug coverage using real-world, nationally representative survey data. In order for valid estimates to be attained patient characteristics that could jointly influence the likelihood of exposure and outcome must be balanced between those with and those without drug coverage.[21] Propensity score matching was developed for the purpose of balancing influential characteristics between exposure groups in large, observational data sets to reduce bias. In this procedure, a summary score is produced representing the likelihood that an individual has drug coverage given his/her observed characteristics. Exposed and non-exposed, respondents with drug coverage and those without drug coverage, are then matched based on propensity score creating balanced frequency distributions of possible confounding characteristics between the two groups (ie. exposed are only compared to non-exposed with comparable characteristics).[20, 22, 23] To extend balance between treatment groups, we included 28 interaction terms to account for all pair-wise interactions between adjustment variables in the propensity score regression model.

We applied a greedy propensity score matching algorithm in which exposed and non-exposed individuals are randomly sorted and then matched. One-by-one, exposed individuals are matched to a non-exposed individual based on the 7 digit propensity score.[24, 25] The algorithm is termed 'greedy' as once a match is made, it is not reconsidered.[25] Those without drug coverage were then compared to those with drug coverage for association to the outcomes of ER visit and hospitalization. Conditional logistic regression that accounts for the matched nature of the propensity score sample was implemented.[26] Conditional logistic regression provides unbiased

estimates of treatment effect in non-independent samples where matching occurred after exposure.[27]

To evaluate covariate balance after propensity score matching, we compared the baseline variables of those without drug coverage to those with drug coverage using the standardized difference (d) recommended by Austin.[27] The standardized difference is defined by :

$$d = \frac{100 \times |\bar{x}_{\text{treatment}} - \bar{x}_{\text{control}}|}{\sqrt{\frac{s^2_{\text{treatment}} + s^2_{\text{control}}}{2}}}$$

Where $s^2_{treatment}$ and $s^2_{control}$ are the covariate value standard deviations for the treated and untreated patients, respectively. The standardized difference is not reliant on the unit of measurement and is a reflection of the sample itself without influence from sample size. This presents advantages over balance assessment using hypothesis testing which is affected by sample size.[28] Using density plots, we also compared the propensity score distributions of the two exposure groups in the non-matched and matched samples. Descriptive statistics were used for the non-matched sample including T-tests for continuous variables and chi squared tests for categorical variables. All analyses were undertaken using SAS 9.3 (Cary, NC) with $\alpha = .05$.

Sensitivity Analysis

One feature of matching techniques is the removal of non-matched individuals from the analysis.[29] This assures a highly balanced comparison,[20] but it amounts to a reduction in respondent data used for inference. An alternative means for estimation of the association of interest that uses the entire available 10 year respondent sample is conventional multiple logistic

regression. We proceeded to evaluate our primary aims using multiple logistic regression adjusted for the same characteristics used to construct propensity scores.

Results

Prevalence of exposure and outcome

During the 10 year period 115 568 respondents were included in the analysis. After survey weighting was applied this represents an annual average of 128.5 million individuals ages 18 to 64 from 1999 to 2008 with private insurance. 105 604 respondents possessed drug coverage while 9 964 did not, representing an average 118.3 million and 10.2 million people in the US (TABLE 1). Among study respondents, 11.6% (13 419) reported one or more emergency room visits and 6.4% (7 423) reported at least one hospitalization (TABLE 2).

Comparison of respondents with drug coverage and those without

Those without drug coverage were a mean age of 40.4 years old compared to 40.7 years old for those with drug coverage (P =0.03). Those without drug coverage compared to those with drug coverage were more likely to be low income (29.6% to 17.5%), have a high school education or less (70.9% to 62.9%), and of black race (16.9% to 13.5%). Respondents without drug coverage were slightly more likely to be male (49.8% to 47.6%) and less likely to be married (53.2% to 64.6%). Those without drug coverage were significantly different from those with drug coverage in terms of all adjustment variables included. (TABLE 2).

After propensity score matching of respondents with drug coverage matched to respondents without drug coverage, 8 486 matched pairs were analyzed. Propensity score matching achieved a high degree of balance for the distribution of measured baseline variables with a standardized difference that never exceeded 2% for any characteristic (TABLE 4). This was a dramatic improvement over the non-matched sample where the standardized difference between exposure groups was a minimum of 2.3% for the age variable and a maximum of 30.8% for the low income variable (TABLE 1). Standardized differences were overall much smaller for the propensity score matched sample with an average $d < 0.5$ per variable versus an average $d = 11.3$ per variable for the non-matched sample (TABLE 4). Since the standardized difference uses the summed variance, we wished to confirm separately that the differences in variable variance for the two exposure categories were reduced by propensity score matching. The variance differences were reduced from an average variance difference per variable of 3.33 to 0.001 after matching was performed (TABLE 4). In the non-matched sample, there was considerable differences in the propensity score distributions for those with drug coverage versus those without drug coverage (FIGURE 1). After propensity score matching, there was complete overlap of the two distributions demonstrating achievement of precise matching of individuals with similar characteristics including pair-wise interaction between these characteristics (FIGURE 2).

Likelihood of, emergency room visit and hospitalization

The respondents with drug coverage were associated with a non-significant increase for the ER visit and hospitalization outcomes during the ten year analysis period of 1999-2008. Respondents with drug coverage compared to those without drug coverage had an odds ratio of

1.05 (95% CI, 0.95 to 1.15) of experiencing at least one ER visit. For hospitalizations, those with drug coverage demonstrated an odds ratio of 1.07 (95% CI, 0.95 to 1.22) (TABLE 5).

Individual Year Analyses

Individual propensity score matched analysis revealed inconsistent associations of drug coverage to the study outcomes from year to year. Drug coverage was not associated with a statistically significant reduction in likelihood of ER visit in any individual year (TABLE 7).

For the outcome of hospitalization, drug coverage in general demonstrated similar associations as exhibited with the ER visits outcome with a few exceptions. Drug coverage was associated with a statistically significant reduction in odds of hospitalization in ORs for the years 2001 and 2006 with ORs of 0.78 (95% CI, 0.69-0.88) and 0.71 (95% CI, 0.62-0.81), respectively (TABLE 7).

Sensitivity Analysis: Multiple Logistic Regression

Using the non-matched 10 year data set 115 168 respondents were included in the analysis. Similar to the propensity score matched analysis, Individuals with drug coverage were more likely to have an ER visit (OR 1.03; 95% CI 0.96-1.12) and a hospitalization (OR 1.01; 95% CI, 0.91-1.21) although neither were statistically significant. In contrast to the propensity score matched analysis where drug coverage had the higher OR for hospitalization versus ER visit (OR 1.01 versus OR 1.05), in the non-matched analysis the OR for the ER visit outcome was higher than for hospitalization (OR 1.03 versus OR 1.01) (TABLE 8).

Comment

Pooled analysis of 10 years of nationally representative population-based survey data found that possessing prescription drug coverage was not significantly associated with reductions in the likelihood of emergency room visit and hospitalization amongst respondents in the United State with private health insurance. Unbiased estimates were achieved via implementation of propensity score matching that balanced characteristics proposed *a priori* as confounders as well as all pair-wise interaction terms between confounders for predilection of drug coverage. By including only those with private health insurance, we attempted to isolate the influence of drug coverage amongst individuals that shared general features associated with health resource use and to remove the influence of health insurance on outcomes.

The individual year analyses for the ER visit and hospitalization outcomes did not provide consistent associations from year to year. The two estimates exhibiting statistically significant ORs, both favored drug coverage for a reduction in odds of hospitalization in the years 2001 (OR, 0.78; 95% CI, 0.69-0.88) and 2006 (OR, 0.71; 95% CI, 0.62-0.81). However, the frequent change in OR direction makes it difficult to rule out regression to the mean.

The application of multiple logistic regression to the entire unmatched pooled dataset produced similar results to the matched propensity score analysis. The adjusted OR estimates from multiple regression approximated the propensity score matched ORs closely and were within confidence intervals for both outcomes. Although the multiple regression included nearly seven times the number of respondents as the matched analysis, the proximity of the OR estimates indicated these findings are robust to the statistical method executed.

Strengths and Limitations

Limitations exist in this analysis**.** Although, we were able to pool multiple years of nationally representative data, each individual year of MEPS data provides only a cross-sectional assessment as the panels change each year. It is possible that a study following a cohort with drug coverage and a cohort without drug coverage for multiple years would have detected a reduction in outcomes that can only be quantified temporally. The type and extent of private drug coverage is not captured in MEPS data for all respondents with drug coverage. It would have been informative to understand if drug coverage was delivered by a large pharmacy benefit manager or via a limited formulary plan. It is contended that restrictive formularies are associated with worse outcomes than open formularies[30], therefore, it would have been helpful to possess this information for adjustment. MEPS contains more specific drug coverage information for respondents reporting to have received medications during the year. However, this variable was not incorporated into all years of MEPS. In future analyses, using only the years that asked this question, we will consider restricting the analysis to those that have received medications or stratifying using this variable. There also exists the possibility for adverse selection to be influencing the study findings. Sicker patients may be incentivized to secure drug coverage as they are at elevated risk of requiring medications for their care (ie. moral hazard). These patients are more likely to require use of the ER or a hospitalization. Unfortunately, the cross-sectional structure of MEPS makes it difficult to ascertain if health decline contributed to a respondent seeking drug coverage. Moreover, health status instruments such as SF12 were not included in all years of MEPS. In our primary analysis, we used propensity score matching to minimize confounding, but the possibility that not all confounders were included could create biased estimates. The recent practice of discounting generic prescription medications by large pharmacy chains may result in an underestimate of the drug benefit effect, where patients

without drug coverage obtain their drugs through these discounted programs. Alternately, benefits of branded prescription medications may be amplified when drug coverage includes these medications but pharmacy discount programs do not.

Strengths of this study include use of a generalizeable study population via implementation of a nationally representative dataset using 10 recent years of available data. We also verified our study findings using a secondary regression approach incorporating the non-matched data.

Conclusion

Prescription drug coverage enables patients to secure the medication regimens designed to treat their chronic illnesses. Over time, patients may have fewer trips to the emergency room and fewer inpatient hospitalizations. However, at any one time it does not appear that patients with drug coverage are less associated with experiencing emergent health outcomes.

Table 2. Characteristics of Respondents With and Without Drug Coverage Prior to Propensity Score Matching, MEPS 1999-2008

Characteristic	Respondents with Drug Coverage	Respondents without drug coverage	Standardized difference, %	P-value of difference between those with drug coverage and without
Number of respondents	105 604	9 964		
Annual Weighted US population represented, millions	118.3	10.2		
Age	40.7	40.4	2.3	0.03
Male,%	47.6	49.8	4	<.001
Race, %			8.3	<.001
White	79.3	75.3		
Black	13.5	16.9		
Other	7.2	7.8		
Married, %	64.6	53.2	24.5	<.001

Low Income, %	17.5	29.6	30.8	<.001
High School Education or Less, %	62.9	70.9	14.6	<.001
Region, %			4	<.001
Northeast	16.2	15.3		
Midwest	23.0	20.1		
South	36.2	40.9		
West	24.6	23.6		

Table 3. Frequency of ER visits and hospitalizations in adults ages 18-64 with private insurance (1999-2008 pooled analysis set)

Outcome	Frequency	Proportion of Study Sample	Survey Weighted Annual Average Frequency (millions)
ER visit	13,419	11.6%	14.55
Hospitalization	7,423	6.4%	7.98

Table 4. Characteristics of Respondents With and Without Drug Coverage after Propensity Score Matching, MEPS 1999-2008

Characteristic	Respondents with Drug Coverage	Respondents without drug coverage	Standardized difference in %	P-value of difference between those with drug coverage and without
Number of respondents	8 486	8 486		
Mean age	40.1	40.1	0	0.77
Male,%	49.4	49.6	2	0.82
Race, %			2	0.62
White	82.7	82.9		
Black	12.9	12.9		
Other	4.35	4.2		
Married, %	56.7	56.7	0	0.89
Low Income, %	22.6	22.7	< 0.1	0.97
High School Education or Less, %	80.2	80.3	< 0.1	0.96
Region, %				0.93
Northeast	13.6	13.7	< 0.1	
Midwest	19.9	19.8		

South	43.1	43.2		
West	23.4	23.3		

Table 5. Standardized difference and difference in variance before and after propensity score matching

Variable	Standardized difference before matching	Standardized difference after matching	Difference in variance before matching	Difference in variance after matching
Age	2.3	0	26.4	0
Race	8.3	2	0.02	0.01
Male gender	4	2	0	0
Low income	30.8	< 0.1	0.07	0
Married	24.5	< 0.1	0.02	0
Region	4	0	0.04	0
High School Degree or less	14.6	0	0.19	0
Year	1.8	0	0.44	0
Average standardized difference per variable	11.3	<0.5	N/A	N/A

Table 6. Propensity score matched odds ratios for emergency room visit and hospitalization outcomes

Outcome	OR (95% CI)	P Value	Number of Matched Respondents
Emergency Room Visit	1.05 (0.95-1.15)	0.35	16 972
Hospitalization	1.07 (0.95-1.22)	0.28	

Table 7. Odds Ratios by Individual Years for Emergency Room Visit and Hospitalization, MEPS 1999-2008

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Number of Matched Respondents	1 800	1 830	2 030	2 214	1 654	1 714	1 646	1 680	1 626	1 898
Odds Ratio of Emergency Room Visit (95% CI)	1.24 (0.91-1.70)	1.13 (0.84-1.51)	0.806 (0.732-0.889)	0.99 (0.77-1.28)	0.90 (0.66-1.24)	1.08 (0.81-1.46)	0.88 (0.67-1.16)	1.05 (0.78-1.40)	1.00 (0.74-1.36)	1.23 (0.92-1.65)
Odds Ratio of Hospitalization (95% CI)	1.21 (0.81-1.83)	1.19 (0.81-1.74)	0.778 (0.688-0.878)	0.90 (0.65-1.24)	1.10 (0.72-1.66)	0.79 (0.54-1.17)	0.79 (0.52-1.21)	0.710 (0.62-0.81)	1.60 (0.97-2.64)	1.04 (0.71-1.51)

Table 8. Non-Matched Multiple Regression Odds Ratios for Emergency Room Visit and Hospitalization

Outcome	OR (95% CI)	P Value	Number of Non-Matched Respondents
Emergency Room Visit	1.03 (0.96-1.12)	0.42	115 123
Hospitalization	1.01 (0.91-1.21)	0.88	

Figure 1. Propensity Score Density Plot Before Matching

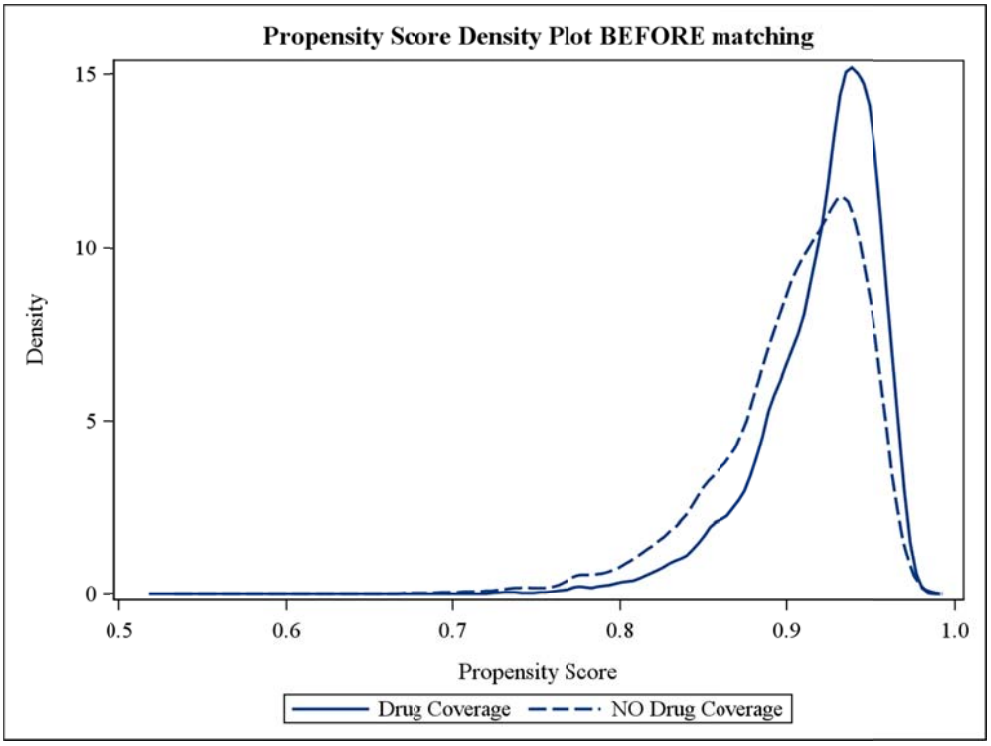
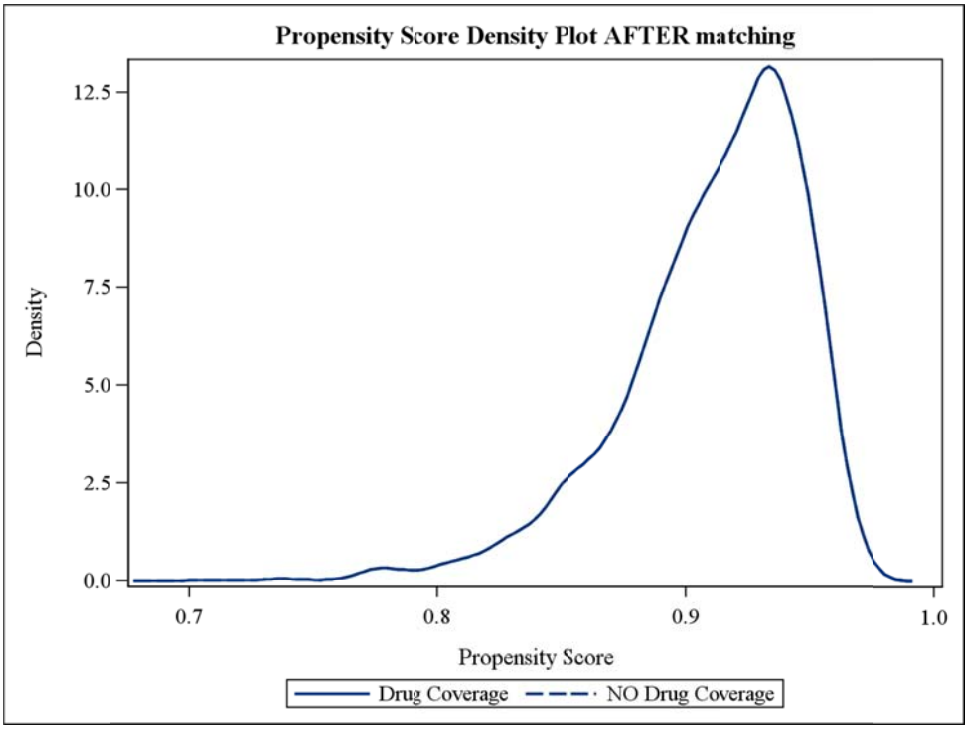


Figure 2. Propensity Score Density Plot After Matching



Chapter 3: Impact of Increasing Copayments on Chronic Medication Adherence

Chapter 3 abstract

Context

Copays for prescription medications are rising as health plans attempt to rein in mounting costs and to shunt drug utilization towards preferred agents. However, patients may respond to the increased price by reducing use of necessary medications.

Objectives

To estimate the reduction in adherence and medication supplied for patients that experience increases in average monthly copay over time for three therapeutically distinct drugs for chronic syndrome management.

Design and Setting

Age-, gender-, health plan type-, plan category-, geographic location-, comorbidity-, and year- adjusted analysis of the nationally representative MarketScan Commercial Claims Database years 2007 to 2010 using generalized estimating equations for correlated data. This database captures nearly 40 million covered lives in all geographic regions of the United States with claims from self-insured employers and health plans. Included subjects were US adults ages 18 to 64 with continuous enrollment in a health plan for at least two years. Users of simvastatin, esomeprazole, or insulin glargine with a minimum of 30 days supplied and at least two medication fills annually for a minimum of two consecutive years were analyzed as separate groups.

Main Outcome Measures

Medication Possession Ratio; Days supplied per year.

Results

A total of 1 240 885 patients were included in the analyses of the 3 drugs in the 4 years under observation. This was distributed as 735 590 simvastatin users, 375 118 esomeprazole users, and 132 177 insulin glargine users. Increase in $5 or more for average monthly copay was associated with a statistically significant reduction in MPR for all three drugs. Simvastatin experienced a change in MPR of -0.024 (95% CI, -0.026, -0.022). Assuming 365 days of use, this represents a reduction of 8.8 medication days supplied per year. Esomeprazole demonstrated a change in MPR of -0.034 (95% CI, -0.036, -0.033) or 12.4 medications days supplied yearly. Insulin glargine experienced a change in MPR of -0.05 (95% CI, -0.053, -0.047) for this exposure equivalent 18.3 fewer days supplied. Increase in $10 or more for average monthly copay was similarly associated with a statistically significant reduction in MPR

for all three drugs with a larger reduction in MPR for each compared to the $5 or more increase exposure. Simvastatin experienced a change in MPR of -0.034 (95% CI, -0.038, -0.030) representing a reduction of 14.6 medication days supplied per year. Esomeprazole showed a change in MPR of -0.044 (95% CI, -0.046, -0.042) equating to a loss of 16.0 medications days supplied per year. The change for insulin glargine MPR was -0.063 (95% CI, -0.067, -0.060). This represents a reduction in 23.0 medication days supplied per year.

Conclusions

Copay increases are associated with significant reductions in adherence of chronic medications necessary for optimal disease control. This is particularly true for higher copay branded medications. Benefit managers should factor in the possible reduction in necessary consumption when proposing increases in copay structures.

Introduction

Burdened with increasing pressure to reduce costs, health plans have increasingly applied stringent prescription copay structures to reduce excess consumption of expensive medications.[1] Prescription utilization controls typified by copay changes have been rightfully credited with billions of dollars in savings as usage of high cost brand medications can be efficiently transferred to lower cost generic equivalents.[2] The achievement of a 90% generic use rate of simvastatin by the fourth calendar quarter following patent expiration of the $2.3 billion medication Zocor represents a well documented case study in the ability of utilization controls such as copay increases to steer consumption.[3] The Zocor patent expiration was just one of many 'blockbuster' drugs to face generic competition constituting a pallet of lower cost generic medications for pharmacy benefit managers to focus use.[4]

Although the evidence is clear that copay increases can alter consumption to reduce system drug spend, this approach may be double-edged if a patient fails to take her essential medications because the copay increase is considered too onerous. Examinations of generic substitution policies have yielded disconcerting evidence that delayed initiation or early discontinuation of necessary medications may result when copays escalate.[5, 6] Given the growing number of studies associating small drops in medication adherence to catastrophic outcomes and health system costs,[7-10] delineation of the causal influence of increasing patient cost sharing and adherence is a research priority.

Reductions in adherence in response to increased copays could be theorized to differ in severity depending on perception of the necessity of the medication. Medication adherence to control silent syndromes such as hypertension and hyperlipidemia have historically suffered due

to the absence of symptoms and dearth of patient physiologic perception of therapeutic benefit[11]. Medications that rapidly ameliorate patient limiting exacerbations have been consistently tied to elevated consumption particularly for rapid onset, severely limiting exacerbations.[12, 13] It could be proposed that the drugs for diseases that are symptom dense or require frequent measurement of control markers such as blood glucose monitoring, would display more inelastic consumption properties than syndromes devoid of these physiologic reminders. This potential phenomenon has not been well described. The two goals of this investigation were to 1) Assess the influence of copay increases on adherence loss. 2) Characterize differences in adherence impact with equal changes in medication copay for representative drugs treating syndromes with varying levels of patient symptom perception.

Our investigation sheds light on the impact of copay increases on 3 different medications commonly used for different chronic disease states in the United States: simvastatin for treatment of hyperlipidemia, esomeprazole for treatment of gastroesophageal reflux disorder, and basal insulin glargine used for diabetes. Previous studies have typically performed before-and-after or difference-in-differences analyses of copay impact. Our study will make use of 4 years of available data allowing for application of rigorous repeated measurement statistics that can account for subject specific correlations in response to the copay increase.

Methods

Data Source

We executed a retrospective, longitudinal analysis using the Thompson Healthcare MarketScan commercial claims database commonly referred to as Medstat. Medstat captures nearly 40 million covered lives in all geographic regions of the United States.[14] The data includes claims from payers and health plan. The sizeable representation of large self-insured employers allows for tracking of patients over many years even as their health plans shift with approximately 200 national and local carriers and 20 regional health plans contained in the dataset. Medstat captures medical and pharmacy claims information as well as eligibility status, plan type, age, and regional information. Medstat is recognized as a robust health care claims data set amenable to rigorous research investigations with in excess of 50 peer reviewed publications in 2010 alone.[15]

Study Design

We used the most recent 4 years of Medstat (2007 through 2010) to identify patients that were users of the study medications separately. The analysis of impact of copay increase for users for the 3 drugs were conducted as 3 distinct analyses. Patients were required to be users of the study medication for at least 2 years. During their entire study period included patients had continuous enrollment. Analyses were restricted to patients 18 to 64 years of age. All patients were required to have at lease two claims for the study medication for each year they were included in the analysis data set with a minimum of 30 days supplied per year.

Primary exposure of interest was an increase in average monthly copayment of $10 or more from the previous year. Secondary exposure of interest was an increase in average monthly copay of $5 or more from previous year. Average monthly copays were determined by

determining copay per 30 day supply for each claim during the year. These copay per 30 day supply for each claim were then averaged for all claims during the year to provide an annual average monthly copay. Average monthly copay difference was determined by subtracting the succeeding year average monthly copay from the average monthly copay from the previous year. Those with a $10 or greater difference in the succeeding year are designated as exposed.

The outcome of interest for the primary and secondary exposure was the Medication Possession Ratio (MPR). MPR is a standard adherence metric adopted by researchers and clinicians as a meaningful assessment of patient compliance particularly when days supply of medications is included on the claim.[10] It is calculated by counting the days between the first and last claim during an observation period forming the denominator of the MPR value[7]. The days supply of medications dispensed in between the first and last claim is summed to form the numerator for the MPR value with 1.0 representing 100% days supplied for days requiring medication. For ease in clinical discussion, we have also converted the change in MPR to a change in annual days supply of medications assuming the patient should use the medication for the entire year as would be expected for chronic syndromes.

Statistical Methods

Descriptive statistics were used to compare patients that experienced the primary exposure of $10 or more increase in average copay to those that did not. Descriptive statistics were also applied to describe changes in number of users throughout the 4 year study period.

For the primary and secondary analyses for each study drug, we used generalized estimating equations (GEE) to assess the change in the continuous response variable MPR. Developed by Liang and Zeger,[16, 17] the GEE regression model is an extension of quasi-likelihood methods[18, 19] allowing for adjustment for possible confounding characteristics while

accounting for the correlation in responses expected with repeated measurements of the same individual over time. As a quasi-likelihood model, GEE does not require specification of the distribution of the response variable and provides valid estimates even when the correlation structure is misspecified. These features are useful in health care administrative assessments as attributes of the response distribution may not be well characterized.[20-22] We adjusted for age, gender, health plan type, plan category, geographic location, and year. To adjust for differences in baseline health status among study subjects we used a modified Charlson Comorbidity index score[23, 24] developed by Quan et al[25] that optimizes the ICD-9 code-based Charlson score proposed by Deyo et al[26] for use with administrative health records. The Quan score incorporates ICD-9 diagnosis codes present in the baseline outpatient visit for study subjects and reflects the comorbidity profile of the patient at study onset with increasing score indicating worsening health status.

GEE models provide consistent and valid estimators even when correlation structure is misspecified however they lose efficiency when correlation structure is selected incorrectly. To assess correlation structure for improved model selection the Quasi-likelihood Information Criterion (QIC) was developed by Pan.[22] The QIC functions similar to the Akaike Information Criterion (AIC) for maximum likelihood based models, but is functional in the quasi-likelihood environment of GEE.[21] Similar to AIC diagnostics, the model and associated correlation structure that produces the lowest QIC is selected.[27] For all GEE models, we specified a normal distribution to characterize the mean-variance relationship of the response.[28] Link function was assessed via QIC. All analyses were conducted using SAS 9.3 (Cary, NC). Statistical significance was set at $P < .05$.

Results

Descriptive statistics

A total of 1 240 885 patients were included in the analyses of the 3 drugs in the 4 years under observation. This was distributed as 735 590 simvastatin users, 375 118 esomeprazole users, and 132 177 insulin glargine users. These categories are not mutually exclusive as subjects could be multiple year users of more than 1 study drug.

The mean age in years ± standard deviation (SD) for simvastatin, esomeprazole, and insulin glargine was 53.0 ± 7.3, 50.4 ± 9.2, 50.3 ± 10.2. The mean copayment per month ± standard deviation (SD) for simvastatin, esomeprazole, and insulin glargine was $5.92 ± $4.92, $19.97 ± 17.43, and $20.85 ± $25.02, respectively. The mean MPR ± SD for simvastatin, esomeprazole, and insulin glargine was 0.90 ± 0.17, 0.87 ± 0.22, and 0.71 ± 0.29, respectively. The mean Quan score ± SD for simvastatin, esomeprazole, and insulin glargine was 0.18 ± 0.47, 0.13 ± 0.45, and 0.63 ± 0.69, respectively.

Simvastatin users that experienced an increase of $5 or more in copay per month compared to those that did not were slightly older at 53.7 years old compared to $52.9 years old ($P < .01$) for those that never experienced a $5 or more increase in copay per month. Their baseline copay per month was significantly different between those that experienced a $5 or more increase versus those that did not at $3.90 versus $6.02 ($P < 0.001$). MPR for simvastatin users was greater than 0.90 for both exposure groups, but was slightly higher for those that had a $5 increase in copay per month with MPR = 0.91 for subjects that had a $5 increase compared to 0.90 for subjects that did not ($P < 0.001$). Quan comorbidity score was 0.19 for those that experienced a $5 copay increase and 0.18 for those that did not ($P < .001$. Comparing

simvastatin users that experienced a $5 copay increase to those that did not, a smaller proportion possessed an health maintenance organization (HMO) plan category and a larger proportion had a preferred provider organization (PPO) plan. (Table 9).

Esomeprazole users that experienced an increase of $5 or more in copay per month were slightly younger at 49.8 years old compared to 50.6 years old for those that did not (P < .001). The baseline copay per month was higher for those that would experience a $5 or more increase in copay at $23.71 compared to $19.21 for those that did not (P <.001). Baseline MPR was slightly lower at 0.86 for those that would experience a $5 or more increase in copay compared to 0.87 for those that did not (P <.001). Quan comorbidity score was worse in those that experienced a $5 or more increase in copay at 0.122 compared to 0.132 for subjects that did not have a $5 increase (P < 0.001). Those that experienced a $5 copay increase were more likely to have an HMO plan and less likely to have a PPO. A greater percentage of esomeprazole users that experienced a $5 or more increase in copay had active, full-time employment status (57.49%) versus 44.02% that did not have the copay increase (Table 10).

Insulin glargine users that experienced a $5 or more increase in copay were similar in age to those that did not (50.2 years old versus 50.3 years old). Baseline copay per month and MPR were higher for those that did not experience a $5 or more increase in copay ($21.90 versus $20.38, P < .001). MPR was 0.723 for those that experienced a $5 increase in copay versus 0.708 (P < .001). The Quan comorbidity score was not significantly different between exposure groups 0.64 versus 0.63 (TABLE 11).

We also investigated those experiencing a $10 or more monthly copay increase. For simvastatin, 6 496 experienced a $10 or more increase and 729 094 subjects in the analysis set did not. For esomeprazole, 44 213 subjects had a $5 or more increase in copay while 328 905

did not. 25 637 users of insulin glargine experienced a $5 or more increase in copay while 106 540 users did not. By drug, demographic characteristics were similar regardless of copay per month increase threshold of $5 or more or $10 or more (TABLE 12 – 14).

All combinations of correlation structure for the normal distribution with identity link produced similar QIC values. The smallest QIC value (1 122 589.9106) was produced by specifying an unstructured correlation matrix produced the smallest QIC (1 122 589.9106). This model specification was used for the GEE analysis.

Increase in average copay of $5 or more

Increase in $5 or more for average monthly copay was associated with a statistically significant reduction in MPR for all three drugs. Simvastatin experienced a change in MPR of -0.024 (95% CI, -0.026, -0.022). Assuming 365 days of use, this represents a reduction of 8.8 medication days supplied per year. Esomeprazole demonstrated a change in MPR of -0.034 (95% CI, -0.036, -0.033) representing a reduction of 12.4 medications days supplied yearly. Insulin glargine experienced the largest change in MPR of -0.050 (95% CI, -0.053, -0.047) for this exposure. Standard error the three estimates did not exceed 0.002 (TABLE 19).

Increase in average copay of $10 or more

Increase in $10 or more for average monthly copay was similarly associated with a statistically significant reduction in MPR for all three drugs with each drug experiencing a larger reduction in MPR with the increased monthly copay escalalation. Simvastatin experienced a change in MPR of -0.034 (95% CI, -0.038, -0.030) representing a reduction of 12.4 medication days supplied per year. Esomeprazole showed a change in MPR of -0.044 (95% CI, -0.046, -0.042) equating to a loss of 16.0 medications days supplied per year. The change for insulin glargine MPR was -0.063 (95% CI, -0.067, -0.060). This was the largest single reduction in

MPR in our analysis. This represents a reduction in 23.0 medication days supplied per year. Standard error for the three estimates did not exceed 0.002 (TABLE 19).

Comment

In our nationally representative commercial claims longitudinal analysis, patients that experienced average copay increases of $5 more responded with a drop in their medication adherence. Furthermore, the declines in adherence were steeper for patients experiencing a larger escalation in copay for all drugs studied. The $10 average monthly copay was tied to an additional reduction of at least 0.1 in MPR or approximately 4 additional days of medication supply versus the $5 monthly copay increase.

Although all three drugs accompanied copay increases with adherence reductions, the magnitude was different for each. The order of medications in terms of adherence loss for an equal increase in average copay rose from simvastatin to esomeprazole to insulin glargine. *A priori*, we postulated the most elastic demand would be for simvastatin given the silent symptomatic nature of dyslipidemia. Since acid reflux presents with often painful symptoms we envisioned less elastic demand for esomeprazole in relation to simvastatin. Via blood sugar monitoring, often performed multiple times a day, diabetics are often keenly aware of their level of disease control. Given the constellation of acute sequelae associated with diabetes, the perceivable symptoms associated with hyperglycemia, and the constancy of blood sugar monitoring, we predicted consumption less elastic than simvastatin. The trend observed was reversed. The inexpensive generic medication simvastatin had the smallest reduction in days supplied with a $5 increase. The drop of 11 fewer simvastatin days supplied for a $5 average copay increase was concerning, but was a much smaller loss in medication supplied compared to

insulin glargine which experienced a drop of 25.6 days in medication supplied for the same average copay increase. Esomeprazole treats a potent array of symptoms including heartburn and acid reflux while also offering protection from painful and possibly fatal gastrointestinal erosions. This was anticipated to exhibit less price responsiveness than simvastatin. In fact, a $5 average monthly copay increase resulted in a upwards of 2 weeks of esomeprazole supplied and greater than 18 days supplied for the $10 copay increase. Our analysis adjusted for comorbidities, so the adherence reduction cannot be explained by proposing the sicker diabetic patients to be more price sensitive. One possible explanation is suggested by the differences found in baseline copays for each of the medications. The mean monthly average copay was less than $5 for simvastatin and in excess of $20 for esomeprazole and insulin glargine. There exists the possibility that copay increases are better tolerated in medications that have a lower initial copay. In the case of simvastatin, the average monthly copay would increase from $5.92 to $10.92 and $15.92 for a $5 copay and $10 copay increase, respectively. This is in contrast to Insulin glargine which would increase from $20.85 to $25.85 and $30.85 for a $5 and $10 copay, respectively. Framed differently, the patient could be responding to an overall average copay threshold with the more expensive individual copays driving down adherence to a further extent than less expensive individual copays. Since pharmacy benefit managers typically require higher copays for branded medications, this phenomenon could be particularly concerning for patients taking single-source brand medications that are dealt an increasing copay. In the case of insulin glargine, a singe-source brand medication representing the only basal insulin on the market, these copay increases could undermine disease management. The resulting health service costs from loss of disease control would rapidly erase any savings generated by the increased copays.

Although, the adherence reductions were most perpetrated for esomeprazole and insulin glargine, the drop in days supplied of simvastatin is also a concern. Several studies have demonstrated the worsening of health outcomes and increased system costs when patients are non adherent to statin therapy.[29, 30] Given the established benefit profile of statin therapy for cardiovascular health, it makes little sense to jeopardize adherence.

Strengths and Limitations

We used a nationally representative commercial claims database incorporating 4 years of health services administrative data that included in excess of 1.2 million individuals. The Medstat dataset provided information that allowed us to characterize and adjust for several elements that may be influential for medication consumption including employment and plan enrollment status, health plan payer and type, region, age, gender, and comorbidity. The GEE statistical analysis we used for inference accounts for correlated responses within subjects allowing both within and between subject comparisons not accessible with traditional difference-in-difference measurement. We also performed diagnostics to optimize efficiency of the regression model. The analysis was performed analyzing three well-characterized, extensively prescribed medications used for different chronic conditions that would be expected to elicit a distinct response when copays escalated.

Although the Medstat dataset did allow us to adjust for many influential characteristics, important patient characteristics are not available in Medstat. Race, income, education, and marital status are not included in the dataset. Although, a wealth of studies have validated the link between adherence and health outcomes, adherence remains a proxy for consumption based

on fills. Hence, it does not inform investigators if the patient physically consumed the medication.

Conclusions

Copay increases are associated with significant reductions in adherence of chronic medications necessary for optimal disease control. This is particularly true for higher copay branded medications. Benefit managers should factor in the possible reduction in necessary consumption when proposing increases in copay structures.

Table 9. Baseline Characteristics of Simvastatin Study Patients with $5 or More Copay Increase

	$5 or more increase in Copay N = 35 000	Less than $5 Increase in Copay N = 700 590	P-value
Age in years, mean (SD)	53.7 (6.8)	52.9 (7.3)	<.01
Quan et al comorbidity Score	0.19 (0.47)	0.18 (0.47)	<.001
Medication Possession Ratio	0.91 (0.17)	0.90 (0.17)	<.001
Average Copay per month supply	$3.90 (6.40)	$6.02 (4.81)	<.001
Female, %	44.8%	43.5	.04
Payer type, %			
Self-Insured Employer	61.02%	62.9%	<.001
Health Plan	38.98%	37.10%	
Plan Category			
Comprehensive	4.18%	3.95%	<.001
Exclusive Provider Organization	0.47%	1.02%	
Health Maintenance Organization	17.74%	22.56%	
Non-Capitated Point-of-Service	4.33%	9.41%	
Preferred Provider Organization	69.73%	59.29%	
Capitated or Partially-Capitated Point-of-Service	0.84%	0.69%	
Consumer-Driven Health Plan	2.06%	2.28%	
High Deductible Health Plan	0.66%	0.80%	
Region			

Northeast	19.28%	13.28%	<.001
North Central	40.69%	31.83%	
South	25.91%	35.18%	
West	13.26%	17.95%	
Unknown	0.86%	1.75%	
Employment Status			
Active Full Time	32.33%	46.78%	<.001
Active Part Time or Seasonal	0.33%	0.81%	
Early Retiree	27.44%	13.14%	
Medicare Eligible Retiree	1.68%	0.92%	
Retiree (status unknown)	0.74%	2.13%	
COBRA	0.09%	0.09%	
Long Term Disability	0.20%	0.26%	
Surviving Spouse/Dependent	1.50%	0.29%	
Other/Unknown	35.69%	35.58%	

Table 10. Baseline Characteristics of Esomeprazole Study Patients with $5 or More Copay Increase

	$5 or more increase in Copay N = 81 243	Less than $5 Increase in Copay N = 291 875	P-value
Age in years, mean (SD)	49.8 (9.1)	50.6 (9.2)	<.001
Quan et al comorbidity Score	0.122 (0.45)	0.132 (0.45)	<.001
Medication Possession Ratio	0.86 (0.22)	0.87 (0.22)	<.001
Average Copay per month supply	$22.71 (16.27)	$19.21 (17.67)	<.001
Female, %	54.93%	55.32%	0.05
Payer type, %			
Employer	72.80%	62.08%	<.001
Health Plan	27.20%	37.92%	
Plan Category			
Comprehensive	4.47%	3.66%	<.001
Exclusive Provider Organization	0.42%	0.75%	
Health Maintenance Organization	11.51%	10.94%	
Non-Capitated Point-of-Service	14.43%	10.46%	
Preferred Provider Organization	65.10%	71.36%	
Capitated or Partially-Capitated Point-of-Service	1.44%	0.74%	
Consumer-Driven Health Plan	2.30%	1.67%	
High Deductible Health Plan	0.34%	0.43%	
Region			
Northeast	11.96%	11.42%	<.001
North Central	25.31%	28.89%	

South	53.47%	47.62%	
West	8.19%	10.46%	
Unknown	1.07%	1.62%	
Employment Status			
Active Full Time	57.49%	44.02%	<.001
Active Part Time or Seasonal	0.48%	0.66%	
Early Retiree	12.25%	14.81%	
Medicare Eligible Retiree	1.00%	1.39%	
Retiree (status unknown)	1.13%	1.50%	
COBRA	0.11%	0.10%	
Long Term Disability	0.64%	0.37%	
Surviving Spouse/Dependent	0.39%	0.73%	
Other/Unknown	26.52%	36.43%	

Table 11. Baseline Characteristics of Insulin Glargine Patients with $5 or More Copay Increase

	$5 or more increase in Copay N = 40 990	Less than $5 Increase in Copay N = 91 187	P-value
Age in years, mean (SD)	50.2 (10.2)	50.3 (10.2)	0.02
Quan et al comorbidity Score	0.64 (0.69)	0.63 (0.68)	0.16
Medication Possession Ratio	0.723 (0.29)	0.708 (0.29)	<.001
Average Copay per month supply	$21.90 (21.62)	$20.38 (26.39)	<.001
Female, %	45.63%	44.52%	.001
Payer type, %			
Employer	64.98%	56.28%	<.001
Health Plan	35.02%	43.72%	
Plan Category			
Comprehensive	4.88%	3.90%	.002
Exclusive Provider Organization	0.72%	1.10%	
Health Maintenance Organization	19.67%	19.26%	
Non-Capitated Point-of-Service	9.31%	9.31%	
Preferred Provider Organization	62.17%	63.26%	
Capitated or Partially-Capitated Point-of-Service	0.79%	0.52%	
Consumer-Driven Health Plan	2.07%	2.05%	
High Deductible Health Plan	0.40%	0.60%	
Region			
Northeast	9.14%	12.09%	.006
North Central	32.97%	31.53%	
South	42.86%	37.45%	
West	13.67%	16.80%	

Unknown	1.36%	2.14%	
Employment Status			
Active Full Time	46.62%	43.59%	<.001
Active Part Time or Seasonal	0.54%	0.76%	
Early Retiree	15.61%	10.12%	
Medicare Eligible Retiree	1.24%	0.89%	
Retiree (status unknown)	0.03%	1.72%	
COBRA	0.11%	0.12%	
Long Term Disability	0.53%	0.47%	
Surviving Spouse/Dependent	0.65%	0.46%	
Other/Unknown	33.68%	41.87%	

Table 12. Baseline Characteristics of Simvastatin Study Patients with $10 or More Copay Increase

	$10 or more increase in Copay N = 6 496	Less than $10 Increase in Copay N = 729 094	P-value
Age in years, mean (SD)	52.7 (7.1)	53.0 (7.3)	0.02
Quan et al comorbidity Score	0.18 (0.48)	0.18 (0.47)	0.69
Medication Possession Ratio	0.89 (0.17)	0.90 (0.17)	<.001
Average Copay per month supply	$5.86 (9.93)	$5.92 (4.85)	0.83
Female, %	42.7%	43.6%	.15
Payer type, %			
Self-Insured Employer	54.25%	62.89%	<.001
Health Plan	45.75%	37.11%	
Plan Category			
Comprehensive	4.18%	3.96%	<.001
Exclusive Provider Organization	0.69%	1.00%	
Health Maintenance Organization	32.36%	22.24%	
Non-Capitated Point-of-Service	3.57%	9.22%	
Preferred Provider Organization	54.25%	59.84%	
Capitated or Partially-Capitated Point-of-Service	1.22%	0.69%	
Consumer-Driven Health Plan	3.17%	2.27%	
High Deductible Health Plan	0.56%	0.79%	
Region			
Northeast	28.62%	13.43%	<.001
North Central	19.97%	32.37%	

South	25.94%	34.82	
West	24.78%	17.66%	
Unknown	0.69%	1.72%	
Employment Status			
Active Full Time	43.97%	46.11%	<.001
Active Part Time or Seasonal	0.40%	0.79%	
Early Retiree	12.10%	13.83%	
Medicare Eligible Retiree	1.14%	0.95%	
Retiree (status unknown)	1.46%	2.07%	
COBRA	0.11%	0.09%	
Long Term Disability	0.18%	0.26%	
Surviving Spouse/Dependent	0.89%	0.34%	
Other/Unknown	39.75%	35.55%	

Table 13. Baseline Characteristics of Esomeprazole Patients with $10 or More Copay Increase

	$10 or more increase in Copay N = 44 213	Less than $10 Increase in Copay N = 328 905	P-value
Age in years, mean (SD)	49.7 (9.2)	50.5 (9.2)	<.001
Quan et al comorbidity Score	0.125 (0.45)	0.130 (0.45)	.04
Medication Possession Ratio	0.86 (0.22)	0.87 (0.22)	<.001
Average Copay per month supply	$23.08 (17.51)	$19.55 (17.38)	<.001
Female, %	55.22%	55.24%	0.93
Payer type, %			
Employer	75.69%	62.90%	<.001
Health Plan	24.31%	37.10%	
Plan Category			
Comprehensive	4.23%	3.78%	<.001
Exclusive Provider Organization	0.38%	0.72%	
Health Maintenance Organization	11.84%	10.96%	
Non-Capitated Point-of-Service	14.10%	10.95%	
Preferred Provider Organization	65.13%	70.66%	
Capitated or Partially-Capitated Point-of-Service	1.38%	0.82%	
Consumer-Driven Health Plan	2.54%	1.71%	
High Deductible Health Plan	0.40%	0.41%	

Region			
Northeast	11.69%	11.52%	<.001
North Central	26.26%	28.36%	
South	53.38%	48.29%	
West	7.80%	10.26%	
Unknown	0.87%	1.58%	
Employment Status			
Active Full Time	59.78%	45.22%	<.001
Active Part Time or Seasonal	0.40%	0.65%	
Early Retiree	12.58%	14.48%	
Medicare Eligible Retiree	1.08%	1.33%	
Retiree (status unknown)	1.06%	1.46%	
COBRA	0.10%	0.10%	
Long Term Disability	0.68%	0.39%	
Surviving Spouse/Dependent	0.48%	0.68%	
Other/Unknown	23.82%	35.68%	

Table 14. Baseline Characteristics of Insulin Glargine Patients with $10 or More Copay Increase

	$10 or more increase in Copay N = 25 637	Less than $10 Increase in Copay N = 106 540	P-value
Age in years, mean (SD)	50.2 (10.2)	50.3 (10.2)	0.11
Quan et al comorbidity Score	0.64 (0.68)	0.64 (0.69)	0.83
Medication Possession Ratio	0.720 (0.29)	0.711 (0.29)	<.001
Average Copay per month supply	$21.62 (22.51)	$20.67 (25.59)	<.001
Female, %	45.61%	44.47%	.001
Payer type, %			
Employer	66.74%	57.11%	<.001
Health Plan	33.26%	42.89%	
Plan Category			
Comprehensive	4.29%	4.19%	.002
Exclusive Provider Organization	0.58%	1.08%	
Health Maintenance Organization	19.34%	19.40%	
Non-Capitated Point-of-Service	8.47%	9.51%	
Preferred Provider Organization	63.98%	62.66%	
Capitated or Partially-Capitated Point-of-Service	0.73%	0.57%	
Consumer-Driven Health Plan	2.16%	2.03%	

High Deductible Health Plan	0.44%	0.56%	
Region			
Northeast	8.46%	11.83%	.006
North Central	34.01%	31.49%	
South	43.45%	38.09%	
West	12.97%	16.51%	
Unknown	1.12%	2.09%	
Employment Status			
Active Full Time	46.72%	44.00%	<.001
Active Part Time or Seasonal	0.54%	0.73%	
Early Retiree	16.74%	10.64%	
Medicare Eligible Retiree	1.49%	0.88%	
Retiree (status unknown)	0.87%	1.66%	
COBRA	0.10%	0.12%	
Long Term Disability	0.52%	0.47%	
Surviving Spouse/Dependent	0.90%	0.48%	
Other/Unknown	32.12%	41.06%	

Table 15. Frequency Experiencing Increases in Copay per Month

Drug Used	≥ $5 increase in monthly copay (%)	< $5 increase in monthly copay (%)	≥ $10 increase in monthly copay (%)	< $10 increase in monthly copay (%)
Simvastatin	35 000 (4.8)	700 590 (95.2)	6 496 (0.9)	729 094 (99.1)
Esomeprazole	81 243 (21.8)	291 875 (78.2)	44 213 (11.9)	328 905 (88.2)
Insulin glargine	40 990 (31.0)	91 187 (69.0)	25 637 (19.4)	106 540 (80.6)

Table 16. Summary Demographics ($5 or more Increase)

Drug	Age (SD)		Female %		Quan Score (SD)		MPR (SD)		Copay per Month (SD)	
	≥ $5	< $5	≥ $5	< $5	≥ $5	< $5	≥ $5	< $5	≥ $5	< $5
Simvastatin (N=735 590)	53.7 (6.8)	52.9 (7.3)	44.8%	43.5%	0.19 (0.47)	0.18 (0.47)	0.91 (0.17)	0.90 (0.17)	$3.90 (4.61)	$6.02 (4.92)
Esomeprazole (N=373 118)	48.9 (9.1)	50.6 (9.2)	54.93%	55.32%	0.122 (0.45)	0.132 (0.45)	0.86 (0.22)	0.87 (0.22)	$22.71 (16.27)	$19.21 (17.67)
Insulin glargine (N=132 177)	50.2 (10.2)	50.3 (10.2)	45.63%	44.52%	0.64 (0.69)	0.63 (0.68)	0.723 (0.29)	0.708 (0.29)	$21.90 (21.62)	$20.38 (26.39)
Total Patients = 1 240 885										

Table 17. Summary Demographics ($10 or More Increase)

Drug	Age (SD)	Female %	Quan Score (SD)	MPR (SD)	Copay per Month (SD)

	≥$10	<$10	≥$10	<$10	≥$10	<$10	≥$10	<$10	≥$10	<$10
Simvastatin (N=735 590)	52.7 (7.1)	53.0 (7.3)	42.7%	43.6%	0.18 (0.48)	0.18 (0.47)	0.89 (0.17)	0.90 (0.17)	$5.86 (9.93)	$5.92 (4.85)
Esomeprazole (N=373 118)	49.7 (9.2)	50.5 (9.2)	55.22%	55.24%	0.125 (0.45)	0.130 (0.45)	0.86 (0.22)	0.87 (0.22)	$23.08 (17.51)	$19.55 (17.38)
Insulin glargine (N=133 177)	50.2 (10.2)	50.3 (10.2)	45.61%	44.47%	0.64 (0.68)	0.64 (0.69)	0.720 (0.29)	0.711 (0.29)	$21.62 (22.51)	$20.67 (25.59)
Total Patients = 1 240 885										

Table 18. Quasi-Likelihood Information Criterion (QIC) Values

Link	Correlation	QIC
Identity	Exchangeable	1 122 590.1144
Identity	Independent	1 122 594.1198
Identity	Autoregressive	1 122 590.8279
Identity	Unstructured	1 122 590.0792

Table 19. Change in MPR & Days Supplied with $5 and $10 or More Increases in Monthly Copay

Drug	$5 or more increase in monthly copay			$10 or more increase in monthly copay		
	Change in MPR (95% CI)	Standard error the estimate	Change in days supplied assuming 365 days of use	Change in MPR (95% CI)	Standard error of the estimate	Change in days supplied assuming 365 days of use
Simvastatin	-0.024 (-0.026, -0.022)	0.001	-11.0	-0.034 (-0.038, -0.030)	0.002	-12.4
Esomeprazole	-0.034 (-0.036, -0.033)	0.001	-12.4	-0.044 (-0.046, -0.042)	0.001	-16.0
Insulin glargine	-0.050 (-0.053, -0.047)	0.002	-18.25	-0.063 (-0.067, -0.060)	0.002	-23.0

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Appendix A: Chapter 2 Propensity Score Regression Output

Model Information		
Data Set	WORK.PRACTICE	
Response Variable	anyrxcov	Any Drug Coverage
Number of Response Levels	2	
Stratum Variable	STRA9608	COMBINED VARIANCE STRATUM: 1996-2008
Number of Strata	290	
Cluster Variable	PSU9608	COMBINED VARIANCE PSU: 1996-2008
Number of Clusters	729	
Weight Variable	perwt	FINAL PERSON WEIGHT, 1999
Model	Binary Logit	
Optimization Technique	Fisher's Scoring	
Variance Adjustment	Degrees of Freedom (DF)	

Variance Estimation	
Method	Taylor Series
Variance Adjustment	Degrees of Freedom (DF)

Number of Observations Used	115123
Sum of Weights Used	1.2804E9

Response Profile			
Ordered Value	**anyrxcov**	**Total Frequency**	**Total Weight**
1	yes	105255	1179265321
2	no	9868	101174650.98

Probability modeled is anyrxcov='yes'.

Class Level Information										
Class	**Value**	**Design Variables**								
SEX	**Female**	1								
	Male	-1								
lowinc	**yes**	1								
	no	-1								
newrace2	**black**	1	0							
	other	0	1							
	white	-1	-1							
newlowed	**yes**	1								
	no	-1								
newregion	**Midwest**	1	0	0						
	Northeast	0	1	0						
	South	0	0	1						
	West	-1	-1	-1						
married	**yes**	1								
	no	-1								
yr	**1999**	1	0	0	0	0	0	0	0	0
	2000	0	1	0	0	0	0	0	0	0
	2001	0	0	1	0	0	0	0	0	0
	2002	0	0	0	1	0	0	0	0	0
	2003	0	0	0	0	1	0	0	0	0
	2004	0	0	0	0	0	1	0	0	0
	2005	0	0	0	0	0	0	1	0	0
	2006	0	0	0	0	0	0	0	1	0
	2007	0	0	0	0	0	0	0	0	1
	2008	-1	-1	-1	-1	-1	-1	-1	-1	-1

Model Convergence Status
Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	707720585	687372545
SC	707720595	687374003
-2 Log L	707720583	687372243

R-Square	1.0000	Max-rescaled R-Square	1.0000

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	20348340.5	150	<.0001
Score	22103833.6	150	<.0001
Wald	2399.4139	150	<.0001

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
SEX	1	5.1037	0.0239
newrace2	2	0.6723	0.7145
newlowed	1	16.5968	<.0001
married	1	27.0144	<.0001
newregion	3	2.2511	0.5220
lowinc	1	24.8592	<.0001
yr	9	6.9343	0.6440
age	1	50.4284	<.0001
age*SEX	1	0.6870	0.4072
age*lowinc	1	0.6408	0.4234
age*newrace2	2	1.4228	0.4909
age*newlowed	1	11.1066	0.0009
age*married	1	6.0828	0.0137
age*newregion	3	1.5299	0.6754
age*yr	9	3.3415	0.9492

Type 3 Analysis of Effects			
Effect	**DF**	**Wald Chi-Square**	**Pr > ChiSq**
lowinc*newrace2	2	10.9764	0.0041
lowinc*newlowed	1	3.3216	0.0684
lowinc*married	1	0.0018	0.9661
lowinc*newregion	3	17.0719	0.0007
lowinc*yr	9	5.3312	0.8045
SEX*lowinc	1	1.4483	0.2288
SEX*newlowed	1	6.1054	0.0135
newrace2*newlowed	2	2.3028	0.3162
newlowed*married	1	0.1953	0.6585
newlowed*newregion	3	5.0662	0.1670
newlowed*yr	9	11.6184	0.2357
SEX*married	1	42.6387	<.0001
newrace2*married	2	1.3076	0.5201
newregion*married	3	5.8386	0.1197
married*yr	9	4.6155	0.8665
SEX*yr	9	19.2742	0.0230
newrace2*yr	18	14.3412	0.7066
newregion*yr	27	39.5977	0.0558
SEX*newregion	3	5.4474	0.1418
newrace2*newregion	6	2.5150	0.8668
SEX*newrace2	2	2.6064	0.2717

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept			1	2.8681	0.1135	639.0018	<.0001
SEX	**Female**		1	0.1240	0.0549	5.1037	0.0239
newrace2	**black**		1	0.1267	0.1624	0.6093	0.4351
newrace2	**other**		1	-0.1203	0.1586	0.5757	0.4480
newlowed	**yes**		1	-0.3264	0.0801	16.5968	<.0001
married	**yes**		1	0.4108	0.0790	27.0144	<.0001
newregion	**Midwest**		1	-0.0848	0.1272	0.4439	0.5052
newregion	**Northeast**		1	-0.0788	0.1399	0.3179	0.5729
newregion	**South**		1	-0.0368	0.1188	0.0958	0.7570
lowinc	**yes**		1	-0.3250	0.0652	24.8592	<.0001
yr	**1999**		1	-0.2364	0.2146	1.2138	0.2706
yr	**2000**		1	-0.1151	0.1583	0.5290	0.4670
yr	**2001**		1	-0.0104	0.1472	0.0050	0.9436
yr	**2002**		1	0.0953	0.1420	0.4502	0.5022

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
yr	**2003**		1	0.2559	0.1489	2.9559	0.0856
yr	**2004**		1	0.0283	0.1360	0.0434	0.8349
yr	**2005**		1	-0.0959	0.1541	0.3871	0.5338
yr	**2006**		1	0.0252	0.1487	0.0287	0.8655
yr	**2007**		1	0.2123	0.1578	1.8093	0.1786
age			1	-0.0169	0.00238	50.4284	<.0001
age*SEX	**Female**		1	-0.00099	0.00120	0.6870	0.4072
age*lowinc	**yes**		1	-0.00114	0.00143	0.6408	0.4234
age*newrace2	**black**		1	-0.00155	0.00348	0.1986	0.6558
age*newrace2	**other**		1	-0.00118	0.00344	0.1182	0.7310
age*newlowed	**yes**		1	0.00605	0.00182	11.1066	0.0009
age*married	**yes**		1	-0.00396	0.00161	6.0828	0.0137
age*newregion	**Midwest**		1	0.00168	0.00287	0.3410	0.5592
age*newregion	**Northeast**		1	0.00131	0.00306	0.1821	0.6696
age*newregion	**South**		1	0.000097	0.00243	0.0016	0.9683
age*yr	**1999**		1	0.00105	0.00453	0.0543	0.8158
age*yr	**2000**		1	-0.00024	0.00319	0.0059	0.9388
age*yr	**2001**		1	0.00133	0.00318	0.1758	0.6750
age*yr	**2002**		1	0.000208	0.00282	0.0054	0.9412
age*yr	**2003**		1	-0.00365	0.00312	1.3653	0.2426
age*yr	**2004**		1	0.00104	0.00280	0.1373	0.7109
age*yr	**2005**		1	0.00154	0.00329	0.2206	0.6386
age*yr	**2006**		1	-0.00058	0.00312	0.0344	0.8529
age*yr	**2007**		1	-0.00269	0.00320	0.7063	0.4007
lowinc*newrace2	**yes**	**black**	1	0.1344	0.0406	10.9739	0.0009
lowinc*newrace2	**yes**	**other**	1	-0.1248	0.0477	6.8450	0.0089
lowinc*newlowed	**yes**	**yes**	1	0.0380	0.0209	3.3216	0.0684
lowinc*married	**yes**	**yes**	1	0.000867	0.0204	0.0018	0.9661

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
lowinc*newregion	**yes**	**Midwest**	1	-0.1436	0.0362	15.7724	<.0001
lowinc*newregion	**yes**	**Northeast**	1	0.0510	0.0381	1.7941	0.1804
lowinc*newregion	**yes**	**South**	1	0.0536	0.0275	3.8025	0.0512
lowinc*yr	**yes**	**1999**	1	-0.00536	0.0684	0.0061	0.9375
lowinc*yr	**yes**	**2000**	1	0.0527	0.0549	0.9204	0.3374
lowinc*yr	**yes**	**2001**	1	-0.0526	0.0381	1.9079	0.1672
lowinc*yr	**yes**	**2002**	1	0.0210	0.0453	0.2154	0.6425
lowinc*yr	**yes**	**2003**	1	0.0146	0.0552	0.0697	0.7918
lowinc*yr	**yes**	**2004**	1	-0.0321	0.0478	0.4507	0.5020
lowinc*yr	**yes**	**2005**	1	-0.0152	0.0499	0.0927	0.7608
lowinc*yr	**yes**	**2006**	1	-0.0231	0.0476	0.2366	0.6266
lowinc*yr	**yes**	**2007**	1	0.0560	0.0517	1.1737	0.2786
SEX*lowinc	**Female**	**yes**	1	0.0172	0.0143	1.4483	0.2288
SEX*newlowed	**Female**	**yes**	1	-0.0427	0.0173	6.1054	0.0135
newrace2*newlowed	**black**	**yes**	1	0.0740	0.0495	2.2370	0.1347
newrace2*newlowed	**other**	**yes**	1	-0.0640	0.0489	1.7075	0.1913
newlowed*married	**yes**	**yes**	1	0.00854	0.0193	0.1953	0.6585
newlowed*newregion	**yes**	**Midwest**	1	0.0512	0.0344	2.2101	0.1371
newlowed*newregion	**yes**	**Northeast**	1	0.0346	0.0380	0.8268	0.3632
newlowed*newregion	**yes**	**South**	1	-0.0362	0.0322	1.2649	0.2607
newlowed*yr	**yes**	**1999**	1	0.0170	0.0596	0.0817	0.7750
newlowed*yr	**yes**	**2000**	1	0.0246	0.0465	0.2803	0.5965
newlowed*yr	**yes**	**2001**	1	-0.0525	0.0397	1.7454	0.1865
newlowed*yr	**yes**	**2002**	1	-0.0724	0.0420	2.9751	0.0846
newlowed*yr	**yes**	**2003**	1	0.0417	0.0428	0.9509	0.3295
newlowed*yr	**yes**	**2004**	1	0.000451	0.0364	0.0002	0.9901
newlowed*yr	**yes**	**2005**	1	0.00394	0.0425	0.0086	0.9262
newlowed*yr	**yes**	**2006**	1	0.0672	0.0448	2.2450	0.1341
newlowed*yr	**yes**	**2007**	1	-0.0539	0.0435	1.5369	0.2151
SEX*married	**Female**	**yes**	1	-0.0893	0.0137	42.6387	<.0001
newrace2*married	**black**	**yes**	1	0.0514	0.0450	1.3036	0.2536
newrace2*married	**other**	**yes**	1	-0.0382	0.0476	0.6457	0.4217
newregion*married	**Midwest**	**yes**	1	-0.0267	0.0378	0.4994	0.4797
newregion*married	**Northeast**	**yes**	1	0.1092	0.0483	5.1195	0.0237
newregion*married	**South**	**yes**	1	-0.0530	0.0329	2.5907	0.1075
married*yr	**yes**	**1999**	1	-0.00990	0.0640	0.0239	0.8771
married*yr	**yes**	**2000**	1	0.0144	0.0476	0.0910	0.7629

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
married*yr	**yes**	**2001**	1	-0.0388	0.0419	0.8567	0.3547
married*yr	**yes**	**2002**	1	0.00189	0.0391	0.0023	0.9614
married*yr	**yes**	**2003**	1	0.0575	0.0400	2.0664	0.1506
married*yr	**yes**	**2004**	1	0.0126	0.0413	0.0931	0.7602
married*yr	**yes**	**2005**	1	-0.0137	0.0485	0.0799	0.7775
married*yr	**yes**	**2006**	1	-0.0515	0.0463	1.2393	0.2656
married*yr	**yes**	**2007**	1	0.0226	0.0457	0.2432	0.6219
SEX*yr	**Female**	**1999**	1	0.0567	0.0355	2.5577	0.1098
SEX*yr	**Female**	**2000**	1	0.0638	0.0331	3.7189	0.0538
SEX*yr	**Female**	**2001**	1	0.0593	0.0292	4.1122	0.0426
SEX*yr	**Female**	**2002**	1	-0.00134	0.0262	0.0026	0.9593
SEX*yr	**Female**	**2003**	1	-0.0511	0.0313	2.6730	0.1021
SEX*yr	**Female**	**2004**	1	0.00110	0.0310	0.0013	0.9717
SEX*yr	**Female**	**2005**	1	0.0168	0.0277	0.3653	0.5456
SEX*yr	**Female**	**2006**	1	-0.0298	0.0318	0.8759	0.3493
SEX*yr	**Female**	**2007**	1	-0.1112	0.0319	12.1051	0.0005
newrace2*yr	**black**	**1999**	1	0.1507	0.1610	0.8762	0.3493
newrace2*yr	**black**	**2000**	1	0.0259	0.1173	0.0488	0.8251
newrace2*yr	**black**	**2001**	1	-0.0573	0.1155	0.2457	0.6201
newrace2*yr	**black**	**2002**	1	-0.0191	0.0868	0.0482	0.8262
newrace2*yr	**black**	**2003**	1	-0.1241	0.0971	1.6309	0.2016
newrace2*yr	**black**	**2004**	1	0.1026	0.0867	1.4012	0.2365
newrace2*yr	**black**	**2005**	1	0.0814	0.0911	0.7983	0.3716
newrace2*yr	**black**	**2006**	1	-0.0573	0.0850	0.4544	0.5002
newrace2*yr	**black**	**2007**	1	-0.1038	0.0943	1.2118	0.2710
newrace2*yr	**other**	**1999**	1	-0.2741	0.2244	1.4921	0.2219
newrace2*yr	**other**	**2000**	1	-0.0725	0.1587	0.2087	0.6478
newrace2*yr	**other**	**2001**	1	0.1142	0.1361	0.7042	0.4014
newrace2*yr	**other**	**2002**	1	0.0513	0.1100	0.2174	0.6410
newrace2*yr	**other**	**2003**	1	0.1106	0.1174	0.8872	0.3462
newrace2*yr	**other**	**2004**	1	-0.0601	0.1110	0.2929	0.5884
newrace2*yr	**other**	**2005**	1	-0.1570	0.1070	2.1513	0.1424
newrace2*yr	**other**	**2006**	1	0.0177	0.1104	0.0256	0.8728
newrace2*yr	**other**	**2007**	1	0.2061	0.1139	3.2735	0.0704
newregion*yr	**Midwest**	**1999**	1	-0.1465	0.1223	1.4338	0.2311
newregion*yr	**Midwest**	**2000**	1	-0.0390	0.0817	0.2279	0.6331
newregion*yr	**Midwest**	**2001**	1	-0.1780	0.0964	3.4131	0.0647
newregion*yr	**Midwest**	**2002**	1	-0.1470	0.0877	2.8116	0.0936
newregion*yr	**Midwest**	**2003**	1	0.2017	0.0870	5.3673	0.0205

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newregion*yr	**Midwest**	**2004**	1	-0.0223	0.0947	0.0552	0.8142
newregion*yr	**Midwest**	**2005**	1	-0.1159	0.0750	2.3860	0.1224
newregion*yr	**Midwest**	**2006**	1	0.1362	0.0802	2.8869	0.0893
newregion*yr	**Midwest**	**2007**	1	0.2455	0.0918	7.1476	0.0075
newregion*yr	**Northeast**	**1999**	1	0.1196	0.1280	0.8727	0.3502
newregion*yr	**Northeast**	**2000**	1	-0.1190	0.0970	1.5043	0.2200
newregion*yr	**Northeast**	**2001**	1	0.1524	0.1051	2.1031	0.1470
newregion*yr	**Northeast**	**2002**	1	0.00508	0.0883	0.0033	0.9542
newregion*yr	**Northeast**	**2003**	1	-0.0583	0.1086	0.2883	0.5913
newregion*yr	**Northeast**	**2004**	1	0.0741	0.1166	0.4043	0.5249
newregion*yr	**Northeast**	**2005**	1	0.0599	0.0956	0.3933	0.5306
newregion*yr	**Northeast**	**2006**	1	-0.1536	0.0935	2.7023	0.1002
newregion*yr	**Northeast**	**2007**	1	-0.1423	0.1023	1.9335	0.1644
newregion*yr	**South**	**1999**	1	-0.1152	0.0889	1.6777	0.1952
newregion*yr	**South**	**2000**	1	0.0485	0.0668	0.5276	0.4676
newregion*yr	**South**	**2001**	1	0.0161	0.0709	0.0515	0.8205
newregion*yr	**South**	**2002**	1	0.0253	0.0713	0.1260	0.7226
newregion*yr	**South**	**2003**	1	-0.00410	0.0723	0.0032	0.9548
newregion*yr	**South**	**2004**	1	-0.0479	0.0751	0.4064	0.5238
newregion*yr	**South**	**2005**	1	0.0321	0.0758	0.1790	0.6723
newregion*yr	**South**	**2006**	1	0.0116	0.0691	0.0281	0.8670
newregion*yr	**South**	**2007**	1	0.0276	0.0757	0.1325	0.7158
SEX*newregion	**Female**	**Midwest**	1	0.0497	0.0218	5.1998	0.0226
SEX*newregion	**Female**	**Northeast**	1	-0.0144	0.0258	0.3116	0.5767
SEX*newregion	**Female**	**South**	1	-0.0162	0.0200	0.6534	0.4189
newrace2*newregion	**black**	**Midwest**	1	0.0395	0.0851	0.2158	0.6423
newrace2*newregion	**black**	**Northeast**	1	-0.0363	0.0794	0.2093	0.6473
newrace2*newregion	**black**	**South**	1	-0.0569	0.0650	0.7679	0.3809
newrace2*newregion	**other**	**Midwest**	1	-0.0209	0.1058	0.0390	0.8435
newrace2*newregion	**other**	**Northeast**	1	0.00831	0.1060	0.0061	0.9375
newrace2*newregion	**other**	**South**	1	0.0853	0.0857	0.9897	0.3198
SEX*newrace2	**Female**	**black**	1	0.0449	0.0286	2.4577	0.1170
SEX*newrace2	**Female**	**other**	1	-0.0481	0.0334	2.0702	0.1502

Association of Predicted Probabilities and Observed Responses			
Percent Concordant	61.7	**Somers' D**	0.251
Percent Discordant	36.6	**Gamma**	0.256
Percent Tied	1.7	**Tau-a**	0.039
Pairs	1038656340	**c**	0.626

Appendix B: Chapter 2 Matched Regression Output

Model Information		
Data Set	DRUG.MATCH4	
Response Variable	anyer	Any ER visits
Number of Response Levels	2	
Number of Strata	8486	
Model	binary logit	
Optimization Technique	Newton-Raphson ridge	

Number of Observations Read	16972
Number of Observations Used	16972

Response Profile		
Ordered Value	**anyer**	**Total Frequency**
1	1	1977
2	0	14995

Probability modeled is anyer=1.

Class Level Information		
Class	**Value**	**Design Variables**
anyrxcov	**yes**	1
	no	-1

Strata Summary				
Response Pattern	anyer 1	anyer 0	Number of Strata	Frequency
1	0	2	6629	13258
2	1	1	1737	3474
3	2	0	120	240

Newton-Raphson Ridge Optimization

Without Parameter Scaling

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics		
Criterion	Without Covariates	With Covariates
AIC	2407.993	2409.118
SC	2407.993	2416.857
-2 Log L	2407.993	2407.118

R-Square	0.0001	Max-rescaled R-Square	0.0004

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	0.8757	1	0.3494
Score	0.8756	1	0.3494
Wald	0.8755	1	0.3494

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
anyrxcov	1	0.8755	0.3494

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
anyrxcov	yes	1	0.0225	0.0240	0.8755	0.3494

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
anyrxcov yes vs no	1.046	0.952	1.149

Model Information		
Data Set	DRUG.MATCH4	
Response Variable	anyip	Any In-Patient Visits
Number of Response Levels	2	
Number of Strata	8486	
Model	binary logit	
Optimization Technique	Newton-Raphson ridge	

Number of Observations Read	16972
Number of Observations Used	16972

Response Profile		
Ordered Value	**anyip**	**Total Frequency**
1	1	1062
2	0	15910

Probability modeled is anyip=1.

Class Level Information		
Class	**Value**	**Design Variables**
anyrxcov	**yes**	1
	no	-1

Strata Summary				
Response Pattern	**anyip**		**Number of Strata**	**Frequency**
	1	**0**		
1	0	2	7468	14936
2	1	1	974	1948
3	2	0	44	88

Newton-Raphson Ridge Optimization

Without Parameter Scaling

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics		
Criterion	Without Covariates	With Covariates
AIC	1350.251	1351.064
SC	1350.251	1358.803
-2 Log L	1350.251	1349.064

R-Square	0.0001	Max-rescaled R-Square	0.0009

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	1.1871	1	0.2759
Score	1.1869	1	0.2760
Wald	1.1864	1	0.2761

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
anyrxcov	1	1.1864	0.2761

Analysis of Maximum Likelihood Estimates						
Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
anyrxcov	yes	1	0.0349	0.0321	1.1864	0.2761

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
anyrxcov yes vs no	1.072	0.946	1.216

Appendix C: Chapter 3 Multiple Regression Output

Model Information		
Data Set	WORK.PRACTICE	
Response Variable	anyer	Any ER visits
Number of Response Levels	2	

Model Information		
Stratum Variable	STRA9608	COMBINED VARIANCE STRATUM: 1996-2008
Number of Strata	290	
Cluster Variable	PSU9608	COMBINED VARIANCE PSU: 1996-2008
Number of Clusters	729	
Weight Variable	perwt	FINAL PERSON WEIGHT, 1999
Model	Binary Logit	
Optimization Technique	Fisher's Scoring	
Variance Adjustment	Degrees of Freedom (DF)	

Variance Estimation	
Method	Taylor Series
Variance Adjustment	Degrees of Freedom (DF)

Number of Observations Used	115123
Sum of Weights Used	1.2804E9

Response Profile			
Ordered Value	**anyer**	**Total Frequency**	**Total Weight**
1	1	13419	145461172.34
2	0	101704	1134978799.6

Probability modeled is anyer=1.

Class Level Information										
Class	**Value**	**Design Variables**								
anyrxcov	**yes**	1								
	no	-1								
SEX	**Female**	1								

Class Level Information										
Class	**Value**	**Design Variables**								
	Male	-1								
lowinc	**yes**	1								
	no	-1								
newrace2	**black**	1	0							
	other	0	1							
	white	-1	-1							
newlowed	**yes**	1								
	no	-1								
newregion	**Midwest**	1	0	0						
	Northeast	0	1	0						
	South	0	0	1						
	West	-1	-1	-1						
married	**yes**	1								
	no	-1								
yr	**1999**	1	0	0	0	0	0	0	0	0
	2000	0	1	0	0	0	0	0	0	0
	2001	0	0	1	0	0	0	0	0	0
	2002	0	0	0	1	0	0	0	0	0
	2003	0	0	0	0	1	0	0	0	0
	2004	0	0	0	0	0	1	0	0	0
	2005	0	0	0	0	0	0	1	0	0
	2006	0	0	0	0	0	0	0	1	0
	2007	0	0	0	0	0	0	0	0	1
	2008	-1	-1	-1	-1	-1	-1	-1	-1	-1

Model Convergence Status
Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	906504275	892784274
SC	906504285	892785742
-2 Log L	906504273	892783970

R-Square	1.0000	Max-rescaled R-Square	1.0000

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	13720302.7	151	<.0001
Score	14421076.1	151	<.0001
Wald	2509.1491	151	<.0001

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
anyrxcov	1	0.6566	0.4178
SEX	1	22.5318	<.0001
newrace2	2	18.5776	<.0001
newlowed	1	11.5858	0.0007
married	1	0.0082	0.9280
newregion	3	4.9677	0.1742
lowinc	1	23.9461	<.0001
yr	9	7.1625	0.6202
age	1	0.1094	0.7408
age*SEX	1	10.1652	0.0014
age*lowinc	1	2.4876	0.1147
age*newrace2	2	6.9494	0.0310
age*newlowed	1	0.2647	0.6069
age*married	1	6.3713	0.0116
age*newregion	3	1.5792	0.6641

Type 3 Analysis of Effects			
Effect	**DF**	**Wald Chi-Square**	**Pr > ChiSq**
age*yr	9	16.8106	0.0518
lowinc*newrace2	2	0.1403	0.9322
lowinc*newlowed	1	0.1570	0.6919
lowinc*married	1	2.5599	0.1096
lowinc*newregion	3	5.9708	0.1130
lowinc*yr	9	12.2679	0.1986
SEX*lowinc	1	0.0548	0.8149
SEX*newlowed	1	0.0171	0.8959
newrace2*newlowed	2	5.5809	0.0614
newlowed*married	1	0.3959	0.5292
newlowed*newregion	3	3.6632	0.3002
newlowed*yr	9	7.3768	0.5979
SEX*married	1	0.0011	0.9736
newrace2*married	2	0.3121	0.8555
newregion*married	3	1.4522	0.6933
married*yr	9	15.2366	0.0846
SEX*yr	9	1.6450	0.9959
newrace2*yr	18	20.1216	0.3260
newregion*yr	27	41.2086	0.0393
SEX*newregion	3	8.8541	0.0313
newrace2*newregion	6	12.1978	0.0577
SEX*newrace2	2	0.6749	0.7136

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept			1	-1.9734	0.0804	602.9435	<.0001
anyrxcov	**yes**		1	0.0161	0.0198	0.6566	0.4178
SEX	**Female**		1	0.2074	0.0437	22.5318	<.0001
newrace2	**black**		1	0.4184	0.1055	15.7438	<.0001
newrace2	**other**		1	-0.5402	0.1295	17.3930	<.0001
newlowed	**yes**		1	0.1749	0.0514	11.5858	0.0007
married	**yes**		1	0.00398	0.0441	0.0082	0.9280
newregion	**Midwest**		1	0.1420	0.0752	3.5636	0.0591
newregion	**Northeast**		1	0.0126	0.0859	0.0214	0.8837
newregion	**South**		1	-0.0316	0.0725	0.1899	0.6630
lowinc	**yes**		1	0.2367	0.0484	23.9461	<.0001
yr	**1999**		1	0.1530	0.1701	0.8090	0.3684
yr	**2000**		1	0.1338	0.1617	0.6838	0.4083

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
yr	**2001**		1	0.0774	0.1194	0.4209	0.5165
yr	**2002**		1	0.00610	0.1121	0.0030	0.9566
yr	**2003**		1	-0.0456	0.1187	0.1476	0.7009
yr	**2004**		1	0.0557	0.1077	0.2673	0.6051
yr	**2005**		1	-0.0420	0.1203	0.1221	0.7268
yr	**2006**		1	0.0778	0.1150	0.4575	0.4988
yr	**2007**		1	-0.2221	0.1236	3.2291	0.0723
age			1	-0.00063	0.00192	0.1094	0.7408
age*SEX	**Female**		1	-0.00301	0.000946	10.1652	0.0014
age*lowinc	**yes**		1	-0.00165	0.00105	2.4876	0.1147
age*newrace2	**black**		1	-0.00519	0.00235	4.8843	0.0271
age*newrace2	**other**		1	0.00832	0.00316	6.9434	0.0084
age*newlowed	**yes**		1	-0.00058	0.00113	0.2647	0.6069
age*married	**yes**		1	-0.00230	0.000911	6.3713	0.0116
age*newregion	**Midwest**		1	-0.00149	0.00169	0.7821	0.3765
age*newregion	**Northeast**		1	0.000064	0.00180	0.0013	0.9715
age*newregion	**South**		1	0.00157	0.00145	1.1705	0.2793
age*yr	**1999**		1	-0.00801	0.00314	6.5150	0.0107
age*yr	**2000**		1	-0.00395	0.00342	1.3323	0.2484
age*yr	**2001**		1	0.000456	0.00247	0.0340	0.8538
age*yr	**2002**		1	-0.00081	0.00247	0.1071	0.7434
age*yr	**2003**		1	0.00214	0.00251	0.7257	0.3943
age*yr	**2004**		1	-0.00009	0.00239	0.0013	0.9711
age*yr	**2005**		1	0.00390	0.00252	2.3924	0.1219
age*yr	**2006**		1	-0.00237	0.00257	0.8486	0.3569
age*yr	**2007**		1	0.00524	0.00276	3.6012	0.0577

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
lowinc*newrace2	**yes**	**black**	1	0.0133	0.0360	0.1372	0.7110
lowinc*newrace2	**yes**	**other**	1	-0.0140	0.0418	0.1115	0.7384
lowinc*newlowed	**yes**	**yes**	1	0.00720	0.0182	0.1570	0.6919
lowinc*married	**yes**	**yes**	1	-0.0232	0.0145	2.5599	0.1096
lowinc*newregion	**yes**	**Midwest**	1	-0.0363	0.0240	2.2986	0.1295
lowinc*newregion	**yes**	**Northeast**	1	0.0440	0.0272	2.6161	0.1058
lowinc*newregion	**yes**	**South**	1	0.0281	0.0229	1.5033	0.2202
lowinc*yr	**yes**	**1999**	1	-0.0417	0.0560	0.5546	0.4564
lowinc*yr	**yes**	**2000**	1	-0.00567	0.0491	0.0133	0.9080
lowinc*yr	**yes**	**2001**	1	-0.0883	0.0355	6.1915	0.0128
lowinc*yr	**yes**	**2002**	1	0.0372	0.0384	0.9427	0.3316
lowinc*yr	**yes**	**2003**	1	-0.0413	0.0376	1.2083	0.2717
lowinc*yr	**yes**	**2004**	1	0.0373	0.0367	1.0337	0.3093
lowinc*yr	**yes**	**2005**	1	0.0502	0.0352	2.0376	0.1534
lowinc*yr	**yes**	**2006**	1	-0.00793	0.0423	0.0351	0.8514
lowinc*yr	**yes**	**2007**	1	0.0327	0.0397	0.6763	0.4109
SEX*lowinc	**Female**	**yes**	1	0.00316	0.0135	0.0548	0.8149
SEX*newlowed	**Female**	**yes**	1	-0.00154	0.0118	0.0171	0.8959
newrace2*newlowed	**black**	**yes**	1	-0.0737	0.0314	5.5069	0.0189
newrace2*newlowed	**other**	**yes**	1	0.0785	0.0385	4.1469	0.0417
newlowed*married	**yes**	**yes**	1	0.00952	0.0151	0.3959	0.5292
newlowed*newregion	**yes**	**Midwest**	1	0.0233	0.0207	1.2716	0.2595
newlowed*newregion	**yes**	**Northeast**	1	0.00513	0.0224	0.0526	0.8187
newlowed*newregion	**yes**	**South**	1	0.0203	0.0200	1.0271	0.3109
newlowed*yr	**yes**	**1999**	1	-0.0257	0.0506	0.2583	0.6113
newlowed*yr	**yes**	**2000**	1	0.0104	0.0450	0.0535	0.8172
newlowed*yr	**yes**	**2001**	1	-0.0214	0.0308	0.4840	0.4866
newlowed*yr	**yes**	**2002**	1	0.0166	0.0299	0.3083	0.5787
newlowed*yr	**yes**	**2003**	1	0.00599	0.0329	0.0331	0.8557
newlowed*yr	**yes**	**2004**	1	0.0374	0.0340	1.2124	0.2709
newlowed*yr	**yes**	**2005**	1	0.00111	0.0333	0.0011	0.9733
newlowed*yr	**yes**	**2006**	1	-0.0636	0.0356	3.1960	0.0738
newlowed*yr	**yes**	**2007**	1	-0.00793	0.0352	0.0509	0.8216
SEX*married	**Female**	**yes**	1	-0.00042	0.0126	0.0011	0.9736
newrace2*married	**black**	**yes**	1	0.0114	0.0294	0.1508	0.6977

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newrace2*married	**other**	**yes**	1	-0.0216	0.0393	0.3013	0.5831
newregion*married	**Midwest**	**yes**	1	0.00407	0.0205	0.0394	0.8426
newregion*married	**Northeast**	**yes**	1	0.0249	0.0241	1.0696	0.3010
newregion*married	**South**	**yes**	1	-0.00564	0.0197	0.0824	0.7741
married*yr	**yes**	**1999**	1	-0.00908	0.0555	0.0268	0.8700
married*yr	**yes**	**2000**	1	0.0506	0.0427	1.4081	0.2354
married*yr	**yes**	**2001**	1	-0.0286	0.0302	0.8970	0.3436
married*yr	**yes**	**2002**	1	-0.00932	0.0308	0.0916	0.7622
married*yr	**yes**	**2003**	1	0.0170	0.0302	0.3166	0.5736
married*yr	**yes**	**2004**	1	0.0495	0.0344	2.0784	0.1494
married*yr	**yes**	**2005**	1	-0.0751	0.0286	6.9025	0.0086
married*yr	**yes**	**2006**	1	-0.0286	0.0400	0.5089	0.4756
married*yr	**yes**	**2007**	1	0.0615	0.0381	2.6076	0.1064
SEX*yr	**Female**	**1999**	1	-0.00381	0.0435	0.0077	0.9302
SEX*yr	**Female**	**2000**	1	0.0248	0.0401	0.3810	0.5371
SEX*yr	**Female**	**2001**	1	-0.0138	0.0290	0.2284	0.6327
SEX*yr	**Female**	**2002**	1	-0.00920	0.0269	0.1166	0.7327
SEX*yr	**Female**	**2003**	1	0.00112	0.0299	0.0014	0.9701
SEX*yr	**Female**	**2004**	1	-0.0127	0.0281	0.2048	0.6509
SEX*yr	**Female**	**2005**	1	-0.00595	0.0314	0.0359	0.8498
SEX*yr	**Female**	**2006**	1	0.0109	0.0317	0.1189	0.7302
SEX*yr	**Female**	**2007**	1	0.0232	0.0302	0.5932	0.4412
newrace2*yr	**black**	**1999**	1	-0.0739	0.1044	0.5001	0.4795
newrace2*yr	**black**	**2000**	1	-0.1460	0.0854	2.9257	0.0872
newrace2*yr	**black**	**2001**	1	0.00108	0.0743	0.0002	0.9884
newrace2*yr	**black**	**2002**	1	-0.0360	0.0725	0.2469	0.6192
newrace2*yr	**black**	**2003**	1	0.00882	0.0752	0.0138	0.9066
newrace2*yr	**black**	**2004**	1	0.0712	0.0676	1.1082	0.2925
newrace2*yr	**black**	**2005**	1	0.0494	0.0727	0.4620	0.4967
newrace2*yr	**black**	**2006**	1	-0.0533	0.0700	0.5795	0.4465
newrace2*yr	**black**	**2007**	1	0.0969	0.0693	1.9565	0.1619
newrace2*yr	**other**	**1999**	1	0.0370	0.1731	0.0456	0.8309
newrace2*yr	**other**	**2000**	1	0.2048	0.1303	2.4728	0.1158
newrace2*yr	**other**	**2001**	1	0.0312	0.1069	0.0854	0.7701

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newrace2*yr	**other**	**2002**	1	-0.0612	0.0889	0.4734	0.4914
newrace2*yr	**other**	**2003**	1	0.0532	0.0866	0.3770	0.5392
newrace2*yr	**other**	**2004**	1	-0.0752	0.0930	0.6534	0.4189
newrace2*yr	**other**	**2005**	1	0.0207	0.0844	0.0600	0.8065
newrace2*yr	**other**	**2006**	1	-0.00982	0.0879	0.0125	0.9110
newrace2*yr	**other**	**2007**	1	-0.0273	0.0927	0.0866	0.7685
newregion*yr	**Midwest**	**1999**	1	-0.1293	0.0862	2.2483	0.1338
newregion*yr	**Midwest**	**2000**	1	-0.0483	0.0577	0.7011	0.4024
newregion*yr	**Midwest**	**2001**	1	0.0445	0.0472	0.8894	0.3456
newregion*yr	**Midwest**	**2002**	1	-0.0176	0.0533	0.1086	0.7417
newregion*yr	**Midwest**	**2003**	1	-0.0411	0.0610	0.4533	0.5008
newregion*yr	**Midwest**	**2004**	1	-0.0220	0.0661	0.1106	0.7394
newregion*yr	**Midwest**	**2005**	1	0.1368	0.0557	6.0371	0.0140
newregion*yr	**Midwest**	**2006**	1	-0.00186	0.0544	0.0012	0.9727
newregion*yr	**Midwest**	**2007**	1	0.0840	0.0570	2.1742	0.1403
newregion*yr	**Northeast**	**1999**	1	-0.00872	0.0794	0.0121	0.9125
newregion*yr	**Northeast**	**2000**	1	0.0810	0.0639	1.6088	0.2047
newregion*yr	**Northeast**	**2001**	1	-0.0841	0.0637	1.7443	0.1866
newregion*yr	**Northeast**	**2002**	1	-0.00393	0.0544	0.0052	0.9424
newregion*yr	**Northeast**	**2003**	1	-0.0135	0.0689	0.0385	0.8445
newregion*yr	**Northeast**	**2004**	1	0.00854	0.0662	0.0166	0.8973
newregion*yr	**Northeast**	**2005**	1	-0.0494	0.0604	0.6672	0.4140
newregion*yr	**Northeast**	**2006**	1	0.0333	0.0575	0.3352	0.5626
newregion*yr	**Northeast**	**2007**	1	-0.1039	0.0604	2.9525	0.0857
newregion*yr	**South**	**1999**	1	0.2107	0.0559	14.2069	0.0002
newregion*yr	**South**	**2000**	1	-0.0746	0.0578	1.6618	0.1974
newregion*yr	**South**	**2001**	1	-0.0382	0.0421	0.8218	0.3646
newregion*yr	**South**	**2002**	1	0.0444	0.0413	1.1543	0.2826
newregion*yr	**South**	**2003**	1	0.0157	0.0521	0.0910	0.7630
newregion*yr	**South**	**2004**	1	0.0382	0.0501	0.5801	0.4463
newregion*yr	**South**	**2005**	1	-0.0525	0.0500	1.1026	0.2937
newregion*yr	**South**	**2006**	1	0.0373	0.0509	0.5363	0.4639
newregion*yr	**South**	**2007**	1	-0.0156	0.0485	0.1032	0.7480
SEX*newregion	**Female**	**Midwest**	1	0.0186	0.0226	0.6828	0.4086
SEX*newregion	**Female**	**Northeast**	1	-0.0758	0.0259	8.5734	0.0034
SEX*newregion	**Female**	**South**	1	0.0134	0.0208	0.4131	0.5204

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newrace2*newregion	**black**	**Midwest**	1	0.1267	0.0509	6.1951	0.0128
newrace2*newregion	**black**	**Northeast**	1	-0.1213	0.0600	4.0908	0.0431
newrace2*newregion	**black**	**South**	1	-0.0187	0.0444	0.1774	0.6736
newrace2*newregion	**other**	**Midwest**	1	-0.1251	0.0623	4.0357	0.0445
newrace2*newregion	**other**	**Northeast**	1	0.0574	0.0789	0.5296	0.4668
newrace2*newregion	**other**	**South**	1	0.0292	0.0612	0.2284	0.6327
SEX*newrace2	**Female**	**black**	1	-0.00151	0.0251	0.0036	0.9521
SEX*newrace2	**Female**	**other**	1	0.0177	0.0327	0.2931	0.5883

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
anyrxcov yes vs no	1.033	0.955	1.116

Association of Predicted Probabilities and Observed Responses			
Percent Concordant	57.9	**Somers' D**	0.176
Percent Discordant	40.3	**Gamma**	0.179
Percent Tied	1.7	**Tau-a**	0.036
Pairs	1364765976	**c**	0.588

Model Information		
Data Set	WORK.PRACTICE	
Response Variable	anyip	Any In-Patient Visits
Number of Response Levels	2	
Stratum Variable	STRA9608	COMBINED VARIANCE STRATUM: 1996-2008
Number of Strata	290	
Cluster Variable	PSU9608	COMBINED VARIANCE PSU: 1996-2008
Number of Clusters	729	
Weight Variable	perwt	FINAL PERSON WEIGHT, 1999
Model	Binary Logit	
Optimization Technique	Fisher's Scoring	
Variance Adjustment	Degrees of Freedom (DF)	

Variance Estimation	
Method	Taylor Series
Variance Adjustment	Degrees of Freedom (DF)

Number of Observations Used	115123
Sum of Weights Used	1.2804E9

Response Profile			
Ordered Value	**anyip**	**Total Frequency**	**Total Weight**
1	1	7423	79782171.788
2	0	107700	1200657800.2

Probability modeled is anyip=1.

Class Level Information										
Class	**Value**	**Design Variables**								
anyrxcov	**yes**	1								
	no	-1								
SEX	**Female**	1								
	Male	-1								
lowinc	**yes**	1								
	no	-1								
newrace2	**black**	1	0							
	other	0	1							
	white	-1	-1							
newlowed	**yes**	1								
	no	-1								
newregion	**Midwest**	1	0	0						
	Northeast	0	1	0						
	South	0	0	1						
	West	-1	-1	-1						
married	**yes**	1								
	no	-1								
yr	**1999**	1	0	0	0	0	0	0	0	0
	2000	0	1	0	0	0	0	0	0	0
	2001	0	0	1	0	0	0	0	0	0
	2002	0	0	0	1	0	0	0	0	0
	2003	0	0	0	0	1	0	0	0	0
	2004	0	0	0	0	0	1	0	0	0
	2005	0	0	0	0	0	0	1	0	0
	2006	0	0	0	0	0	0	0	1	0
	2007	0	0	0	0	0	0	0	0	1
	2008	-1	-1	-1	-1	-1	-1	-1	-1	-1

Model Convergence Status
Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	597382856	563582724
SC	597382866	563584192
-2 Log L	597382854	563582420

R-Square	1.0000	Max-rescaled R-Square	1.0000

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	33800434.0	151	<.0001
Score	32446795.6	151	<.0001
Wald	4503.2484	151	<.0001

Type 3 Analysis of Effects			
Effect	DF	Wald Chi-Square	Pr > ChiSq
anyrxcov	1	0.0230	0.8795
SEX	1	545.4919	<.0001
newrace2	2	1.3426	0.5110
newlowed	1	1.5513	0.2129
married	1	200.4384	<.0001
newregion	3	5.1159	0.1635
lowinc	1	45.2196	<.0001
yr	9	10.9160	0.2815
age	1	27.8513	<.0001
age*SEX	1	446.0046	<.0001
age*lowinc	1	11.9825	0.0005

Type 3 Analysis of Effects			
Effect	**DF**	**Wald Chi-Square**	**Pr > ChiSq**
age*newrace2	2	3.6537	0.1609
age*newlowed	1	8.6067	0.0033
age*married	1	199.2099	<.0001
age*newregion	3	4.0456	0.2566
age*yr	9	14.6311	0.1016
lowinc*newrace2	2	0.3693	0.8314
lowinc*newlowed	1	2.6600	0.1029
lowinc*married	1	10.4352	0.0012
lowinc*newregion	3	4.8569	0.1826
lowinc*yr	9	6.6794	0.6705
SEX*lowinc	1	0.1886	0.6641
SEX*newlowed	1	9.9930	0.0016
newrace2*newlowed	2	0.2603	0.8780
newlowed*married	1	4.1916	0.0406
newlowed*newregion	3	5.5878	0.1335
newlowed*yr	9	7.0145	0.6356
SEX*married	1	65.5686	<.0001
newrace2*married	2	3.5204	0.1720
newregion*married	3	2.5687	0.4630
married*yr	9	7.3309	0.6027
SEX*yr	9	5.1270	0.8231
newrace2*yr	18	31.0191	0.0286
newregion*yr	27	26.6872	0.4808
SEX*newregion	3	14.8721	0.0019
newrace2*newregion	6	2.8560	0.8267
SEX*newrace2	2	3.5756	0.1673

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept			1	-3.3737	0.1072	989.8249	<.0001
anyrxcov	**yes**		1	0.00380	0.0251	0.0230	0.8795
SEX	**Female**		1	1.7654	0.0756	545.4919	<.0001
newrace2	**black**		1	-0.0194	0.1269	0.0234	0.8784
newrace2	**other**		1	0.1217	0.1482	0.6744	0.4115
newlowed	**yes**		1	-0.0836	0.0671	1.5513	0.2129
married	**yes**		1	0.9674	0.0683	200.4384	<.0001
newregion	**Midwest**		1	0.0448	0.1048	0.1826	0.6691
newregion	**Northeast**		1	0.2185	0.1130	3.7402	0.0531

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newregion	**South**		1	-0.0326	0.0921	0.1256	0.7230
lowinc	**yes**		1	0.4808	0.0715	45.2196	<.0001
yr	**1999**		1	0.00182	0.2405	0.0001	0.9940
yr	**2000**		1	0.1750	0.2115	0.6850	0.4079
yr	**2001**		1	-0.0221	0.1567	0.0199	0.8877
yr	**2002**		1	-0.2084	0.1477	1.9900	0.1583
yr	**2003**		1	-0.0734	0.1619	0.2054	0.6504
yr	**2004**		1	-0.1030	0.1609	0.4096	0.5222
yr	**2005**		1	0.1567	0.1627	0.9275	0.3355
yr	**2006**		1	0.3212	0.1726	3.4643	0.0627
yr	**2007**		1	-0.3134	0.1713	3.3480	0.0673
age			1	0.0133	0.00253	27.8513	<.0001
age*SEX	**Female**		1	-0.0329	0.00156	446.0046	<.0001
age*lowinc	**yes**		1	-0.00542	0.00157	11.9825	0.0005
age*newrace2	**black**		1	0.00277	0.00283	0.9576	0.3278
age*newrace2	**other**		1	-0.00640	0.00361	3.1372	0.0765
age*newlowed	**yes**		1	0.00457	0.00156	8.6067	0.0033
age*married	**yes**		1	-0.0201	0.00143	199.2099	<.0001
age*newregion	**Midwest**		1	0.000261	0.00220	0.0140	0.9058
age*newregion	**Northeast**		1	-0.00465	0.00250	3.4634	0.0627
age*newregion	**South**		1	0.00192	0.00185	1.0770	0.2994
age*yr	**1999**		1	-0.00705	0.00551	1.6372	0.2007
age*yr	**2000**		1	-0.00218	0.00480	0.2059	0.6500
age*yr	**2001**		1	0.00136	0.00354	0.1477	0.7007
age*yr	**2002**		1	0.00525	0.00328	2.5598	0.1096
age*yr	**2003**		1	0.000902	0.00348	0.0672	0.7954
age*yr	**2004**		1	0.00147	0.00342	0.1839	0.6680
age*yr	**2005**		1	-0.00005	0.00360	0.0002	0.9886
age*yr	**2006**		1	-0.00502	0.00372	1.8215	0.1771
age*yr	**2007**		1	0.0102	0.00374	7.4931	0.0062

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
lowinc*newrace2	**yes**	**black**	1	-0.00687	0.0434	0.0251	0.8741
lowinc*newrace2	**yes**	**other**	1	0.0264	0.0544	0.2359	0.6272
lowinc*newlowed	**yes**	**yes**	1	0.0350	0.0215	2.6600	0.1029
lowinc*married	**yes**	**yes**	1	-0.0538	0.0167	10.4352	0.0012
lowinc*newregion	**yes**	**Midwest**	1	-0.0283	0.0322	0.7768	0.3781
lowinc*newregion	**yes**	**Northeast**	1	0.0783	0.0371	4.4503	0.0349
lowinc*newregion	**yes**	**South**	1	-0.0329	0.0296	1.2374	0.2660
lowinc*yr	**yes**	**1999**	1	-0.0814	0.0785	1.0773	0.2993
lowinc*yr	**yes**	**2000**	1	0.0484	0.0555	0.7626	0.3825
lowinc*yr	**yes**	**2001**	1	0.0282	0.0461	0.3747	0.5405
lowinc*yr	**yes**	**2002**	1	-0.00613	0.0497	0.0152	0.9018
lowinc*yr	**yes**	**2003**	1	-0.0630	0.0457	1.8994	0.1681
lowinc*yr	**yes**	**2004**	1	0.0263	0.0540	0.2375	0.6260
lowinc*yr	**yes**	**2005**	1	-0.00007	0.0520	0.0000	0.9989
lowinc*yr	**yes**	**2006**	1	0.00669	0.0565	0.0140	0.9058
lowinc*yr	**yes**	**2007**	1	0.0832	0.0534	2.4242	0.1195
SEX*lowinc	**Female**	**yes**	1	0.00952	0.0219	0.1886	0.6641
SEX*newlowed	**Female**	**yes**	1	-0.0526	0.0166	9.9930	0.0016
newrace2*newlowed	**black**	**yes**	1	-0.0201	0.0396	0.2578	0.6116
newrace2*newlowed	**other**	**yes**	1	0.0219	0.0504	0.1885	0.6642
newlowed*married	**yes**	**yes**	1	-0.0395	0.0193	4.1916	0.0406
newlowed*newregion	**yes**	**Midwest**	1	0.0179	0.0242	0.5445	0.4606
newlowed*newregion	**yes**	**Northeast**	1	-0.0133	0.0271	0.2394	0.6246
newlowed*newregion	**yes**	**South**	1	0.0388	0.0239	2.6217	0.1054
newlowed*yr	**yes**	**1999**	1	0.1253	0.0654	3.6774	0.0552
newlowed*yr	**yes**	**2000**	1	-0.0107	0.0490	0.0481	0.8265
newlowed*yr	**yes**	**2001**	1	0.0159	0.0374	0.1815	0.6701
newlowed*yr	**yes**	**2002**	1	0.00831	0.0421	0.0390	0.8435
newlowed*yr	**yes**	**2003**	1	0.00405	0.0434	0.0087	0.9257
newlowed*yr	**yes**	**2004**	1	0.00900	0.0404	0.0497	0.8235
newlowed*yr	**yes**	**2005**	1	-0.0534	0.0406	1.7275	0.1887
newlowed*yr	**yes**	**2006**	1	-0.0274	0.0456	0.3611	0.5479
newlowed*yr	**yes**	**2007**	1	-0.0158	0.0505	0.0976	0.7547
SEX*married	**Female**	**yes**	1	0.1464	0.0181	65.5686	<.0001
newrace2*married	**black**	**yes**	1	-0.0719	0.0385	3.4763	0.0623
newrace2*married	**other**	**yes**	1	0.0714	0.0511	1.9505	0.1625
newregion*married	**Midwest**	**yes**	1	-0.0264	0.0286	0.8502	0.3565

Analysis of Maximum Likelihood Estimates							
Parameter			**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
newregion*married	**Northeast**	**yes**	1	0.0504	0.0381	1.7521	0.1856
newregion*married	**South**	**yes**	1	0.0120	0.0308	0.1521	0.6966
married*yr	**yes**	**1999**	1	0.000694	0.0723	0.0001	0.9923
married*yr	**yes**	**2000**	1	0.0828	0.0571	2.1041	0.1469
married*yr	**yes**	**2001**	1	-0.0861	0.0462	3.4644	0.0627
married*yr	**yes**	**2002**	1	0.0190	0.0433	0.1934	0.6601
married*yr	**yes**	**2003**	1	0.00689	0.0450	0.0235	0.8782
married*yr	**yes**	**2004**	1	-0.00802	0.0428	0.0351	0.8514
married*yr	**yes**	**2005**	1	-0.0564	0.0441	1.6357	0.2009
married*yr	**yes**	**2006**	1	0.00292	0.0487	0.0036	0.9521
married*yr	**yes**	**2007**	1	-0.00253	0.0487	0.0027	0.9586
SEX*yr	**Female**	**1999**	1	-0.00241	0.0637	0.0014	0.9698
SEX*yr	**Female**	**2000**	1	-0.0658	0.0549	1.4329	0.2313
SEX*yr	**Female**	**2001**	1	-0.0252	0.0410	0.3762	0.5397
SEX*yr	**Female**	**2002**	1	0.00857	0.0427	0.0404	0.8407
SEX*yr	**Female**	**2003**	1	-0.00174	0.0468	0.0014	0.9704
SEX*yr	**Female**	**2004**	1	0.0603	0.0451	1.7866	0.1813
SEX*yr	**Female**	**2005**	1	-0.0404	0.0436	0.8588	0.3541
SEX*yr	**Female**	**2006**	1	0.0297	0.0514	0.3353	0.5626
SEX*yr	**Female**	**2007**	1	0.0486	0.0475	1.0449	0.3067
newrace2*yr	**black**	**1999**	1	-0.1197	0.1772	0.4566	0.4992
newrace2*yr	**black**	**2000**	1	0.0414	0.1024	0.1636	0.6858
newrace2*yr	**black**	**2001**	1	0.0434	0.0990	0.1923	0.6610
newrace2*yr	**black**	**2002**	1	0.1394	0.0821	2.8781	0.0898
newrace2*yr	**black**	**2003**	1	0.0595	0.1042	0.3256	0.5683
newrace2*yr	**black**	**2004**	1	-0.0587	0.1050	0.3123	0.5763
newrace2*yr	**black**	**2005**	1	0.0661	0.0975	0.4596	0.4978
newrace2*yr	**black**	**2006**	1	-0.1376	0.0923	2.2255	0.1357
newrace2*yr	**black**	**2007**	1	-0.1714	0.1106	2.3999	0.1213
newrace2*yr	**other**	**1999**	1	0.0300	0.2141	0.0196	0.8887
newrace2*yr	**other**	**2000**	1	-0.0156	0.1559	0.0100	0.9204
newrace2*yr	**other**	**2001**	1	-0.1590	0.1454	1.1954	0.2742
newrace2*yr	**other**	**2002**	1	-0.1205	0.1026	1.3797	0.2402
newrace2*yr	**other**	**2003**	1	-0.0142	0.1243	0.0131	0.9088
newrace2*yr	**other**	**2004**	1	-0.0583	0.1374	0.1803	0.6711

Analysis of Maximum Likelihood Estimates							
Parameter			DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
newrace2*yr	other	2005	1	-0.0525	0.1193	0.1940	0.6596
newrace2*yr	other	2006	1	0.2608	0.0982	7.0595	0.0079
newrace2*yr	other	2007	1	0.3252	0.1254	6.7209	0.0095
newregion*yr	Midwest	1999	1	0.00204	0.1034	0.0004	0.9843
newregion*yr	Midwest	2000	1	-0.1231	0.0822	2.2433	0.1342
newregion*yr	Midwest	2001	1	0.0480	0.0651	0.5440	0.4608
newregion*yr	Midwest	2002	1	-0.0264	0.0769	0.1183	0.7308
newregion*yr	Midwest	2003	1	-0.0721	0.0705	1.0453	0.3066
newregion*yr	Midwest	2004	1	0.0133	0.0745	0.0319	0.8582
newregion*yr	Midwest	2005	1	0.00967	0.0707	0.0187	0.8912
newregion*yr	Midwest	2006	1	-0.0483	0.0729	0.4392	0.5075
newregion*yr	Midwest	2007	1	0.00479	0.0820	0.0034	0.9534
newregion*yr	Northeast	1999	1	-0.1128	0.1140	0.9803	0.3221
newregion*yr	Northeast	2000	1	-0.0697	0.0826	0.7126	0.3986
newregion*yr	Northeast	2001	1	0.0898	0.1008	0.7926	0.3733
newregion*yr	Northeast	2002	1	-0.0244	0.0747	0.1065	0.7442
newregion*yr	Northeast	2003	1	-0.0192	0.0797	0.0581	0.8096
newregion*yr	Northeast	2004	1	0.0717	0.0749	0.9151	0.3388
newregion*yr	Northeast	2005	1	0.0355	0.0730	0.2363	0.6269
newregion*yr	Northeast	2006	1	0.0528	0.0798	0.4377	0.5082
newregion*yr	Northeast	2007	1	0.0108	0.0809	0.0179	0.8937
newregion*yr	South	1999	1	0.1281	0.0953	1.8073	0.1788
newregion*yr	South	2000	1	0.0558	0.0668	0.6976	0.4036
newregion*yr	South	2001	1	0.0348	0.0661	0.2781	0.5980
newregion*yr	South	2002	1	-0.0335	0.0544	0.3793	0.5380
newregion*yr	South	2003	1	0.0752	0.0623	1.4586	0.2272
newregion*yr	South	2004	1	-0.0632	0.0675	0.8768	0.3491
newregion*yr	South	2005	1	-0.1415	0.0631	5.0312	0.0249
newregion*yr	South	2006	1	0.0214	0.0626	0.1167	0.7327
newregion*yr	South	2007	1	0.0425	0.0655	0.4202	0.5168
SEX*newregion	Female	Midwest	1	0.0364	0.0255	2.0374	0.1535
SEX*newregion	Female	Northeast	1	-0.0850	0.0342	6.1821	0.0129
SEX*newregion	Female	South	1	-0.0510	0.0253	4.0607	0.0439
newrace2*newregion	black	Midwest	1	0.00364	0.0616	0.0035	0.9529
newrace2*newregion	black	Northeast	1	0.0476	0.0748	0.4057	0.5241
newrace2*newregion	black	South	1	-0.0380	0.0521	0.5316	0.4659
newrace2*newregion	other	Midwest	1	0.0118	0.0741	0.0254	0.8734
newrace2*newregion	other	Northeast	1	-0.0413	0.0833	0.2456	0.6202
newrace2*newregion	other	South	1	-0.0109	0.0661	0.0270	0.8694

Analysis of Maximum Likelihood Estimates							
Parameter			DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
SEX*newrace2	Female	black	1	0.0644	0.0376	2.9284	0.0870
SEX*newrace2	Female	other	1	-0.0386	0.0459	0.7062	0.4007

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
anyrxcov yes vs no	1.008	0.913	1.112

Association of Predicted Probabilities and Observed Responses			
Percent Concordant	67.3	Somers' D	0.360
Percent Discordant	31.4	Gamma	0.364
Percent Tied	1.3	Tau-a	0.043
Pairs	799457100	c	0.680

Appendix D: Chapter 3 Generalized Estimating Equations Output

Model Information		
Data Set	SIM.SIM_TESTQUAN2	Simvastatin Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	Levels	Values
ENROLID	438463	59001 121603 153401 155801 189501 196903 211901 230502 284601 286302 297002 306801 363102 379402 388302 391001 391002 417401 421001 421901 430202 436402 464801 501401 534801 551701 551702 558201 573101 573102 582602 593904 622701 624202 627401 636201 ...
up	2	1 0
YEAR	4	2007 2008 2009 2010

Class Level Information		
Class	**Levels**	**Values**
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	up	1						
Prm3	up	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		
Prm14	EESTATU					2		
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (735590 levels)
Number of Clusters	735590
Correlation Matrix Dimension	4
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	1122590.0792
QICu	1122572.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.7199	0.0027	0.7147	0.7252	270.34	<.0001
up	1	-0.0241	0.0010	-0.0259	-0.0222	-25.21	<.0001
up	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	0.0056	0.0005	0.0046	0.0066	11.27	<.0001
YEAR	2008	-0.0015	0.0004	-0.0022	-0.0007	-3.83	0.0001
YEAR	2009	0.0019	0.0003	0.0012	0.0025	5.71	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0041	0.0004	0.0033	0.0049	9.93	<.0001
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0031	0.0000	0.0030	0.0031	97.53	<.0001
HLTHPLAN	0	0.0191	0.0021	0.0151	0.0231	9.30	<.0001
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.
EESTATU	1	-0.0019	0.0020	-0.0058	0.0020	-0.96	0.3375
EESTATU	2	-0.0145	0.0027	-0.0197	-0.0093	-5.49	<.0001
EESTATU	3	0.0144	0.0020	0.0104	0.0184	7.08	<.0001
EESTATU	4	0.0147	0.0024	0.0099	0.0194	6.03	<.0001
EESTATU	5	0.0130	0.0038	0.0055	0.0205	3.40	0.0007

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
EESTATU	6	0.0068	0.0038	-0.0008	0.0143	1.76	0.0784
EESTATU	7	0.0057	0.0034	-0.0010	0.0123	1.67	0.0940
EESTATU	8	0.0035	0.0032	-0.0027	0.0096	1.10	0.2729
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	0.0129	0.0015	0.0099	0.0159	8.45	<.0001
REGION	2	0.0101	0.0015	0.0072	0.0130	6.81	<.0001
REGION	3	0.0016	0.0015	-0.0013	0.0046	1.07	0.2861
REGION	4	0.0038	0.0016	0.0007	0.0068	2.42	0.0155
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.
PLANTYP	2	0.0080	0.0017	0.0047	0.0112	4.82	<.0001
PLANTYP	3	0.0042	0.0020	0.0002	0.0081	2.06	0.0397
PLANTYP	4	-0.0088	0.0015	-0.0118	-0.0058	-5.72	<.0001
PLANTYP	5	-0.0026	0.0016	-0.0057	0.0005	-1.67	0.0950
PLANTYP	6	-0.0003	0.0015	-0.0032	0.0026	-0.18	0.8578
PLANTYP	7	-0.0018	0.0025	-0.0068	0.0032	-0.71	0.4770

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	8	-0.0031	0.0017	-0.0065	0.0002	-1.85	0.0647
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		-0.0011	0.0004	-0.0019	-0.0002	-2.37	0.0178

Model Information		
Data Set	NEX.NEX_TESTQUAN2	Esomeprazole Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	**Levels**	**Values**
ENROLID	226328	88702 155801 292201 318402 347603 485702 704701 760701 833902 937501 1157601 1225101 1248002 1267702 1464601 1509201 1531402 1582602 1628806 1705906 1954201 2057203 2405804 2637802 2917202 2996501 3053603 3092101 3131701 3181405 8946602 8950901 8965302 ...
up	2	1 0
YEAR	4	2007 2008 2009 2010
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	up	1						
Prm3	up	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		
Prm14	EESTATU					2		

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (373118 levels)
Number of Clusters	373118
Correlation Matrix Dimension	4
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	599897.2886
QICu	599876.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.7209	0.0050	0.7110	0.7307	143.87	<.0001
up	1	-0.0344	0.0009	-0.0362	-0.0327	-39.31	<.0001
up	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	-0.0158	0.0008	-0.0174	-0.0143	-19.77	<.0001
YEAR	2008	-0.0105	0.0007	-0.0119	-0.0092	-15.04	<.0001
YEAR	2009	0.0030	0.0006	0.0018	0.0043	4.69	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0071	0.0007	0.0057	0.0086	9.76	<.0001
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0032	0.0000	0.0031	0.0033	70.06	<.0001
HLTHPLAN	0	0.0038	0.0033	-0.0027	0.0104	1.15	0.2492
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.
EESTATU	1	0.0063	0.0031	0.0002	0.0124	2.01	0.0441

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
EESTATU	2	-0.0051	0.0048	-0.0144	0.0042	-1.07	0.2836
EESTATU	3	0.0315	0.0032	0.0253	0.0378	9.86	<.0001
EESTATU	4	0.0296	0.0038	0.0221	0.0371	7.69	<.0001
EESTATU	5	0.0288	0.0062	0.0166	0.0410	4.62	<.0001
EESTATU	6	0.0321	0.0063	0.0197	0.0445	5.09	<.0001
EESTATU	7	0.0128	0.0049	0.0032	0.0224	2.62	0.0087
EESTATU	8	0.0212	0.0045	0.0123	0.0301	4.68	<.0001
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	-0.0044	0.0028	-0.0099	0.0011	-1.58	0.1131
REGION	2	0.0050	0.0027	-0.0003	0.0102	1.84	0.0657
REGION	3	-0.0111	0.0027	-0.0165	-0.0058	-4.11	<.0001
REGION	4	-0.0016	0.0029	-0.0073	0.0041	-0.55	0.5819
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.
PLANTYP	2	0.0024	0.0038	-0.0051	0.0099	0.63	0.5287
PLANTYP	3	-0.0026	0.0045	-0.0113	0.0061	-0.58	0.5628

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	4	-0.0142	0.0037	-0.0214	-0.0070	-3.87	0.0001
PLANTYP	5	-0.0066	0.0036	-0.0137	0.0005	-1.81	0.0701
PLANTYP	6	-0.0031	0.0035	-0.0101	0.0038	-0.89	0.3759
PLANTYP	7	0.0058	0.0048	-0.0036	0.0152	1.21	0.2268
PLANTYP	8	-0.0050	0.0040	-0.0129	0.0028	-1.25	0.2096
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		0.0023	0.0008	0.0007	0.0039	2.75	0.0059

Model Information		
Data Set	LAN.LAN_TESTQUAN2	Insulin glargine Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	**Levels**	**Values**
ENROLID	75326	98501 268605 421901 459301 551701 593904 642705 667302 975102 1129102 1226601 1316203 1509201 1551502 1625301 1899001 1933601 2004801 2020202 2052901 2251801 2529804 3092101 3105102 8997602 9001502 9018302 9065501 9068802 9080501 9100302 9111002 ...
up	2	1 0
YEAR	4	2007 2008 2009 2010
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	up	1						
Prm3	up	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		

Parameter Information								
Parameter	**Effect**	**up**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm14	EESTATU					2		
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (132177 levels)
Number of Clusters	132177
Correlation Matrix Dimension	4
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	195980.3963
QICu	195959.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.5680	0.0096	0.5491	0.5869	58.89	<.0001
up	1	-0.0503	0.0015	-0.0533	-0.0473	-32.95	<.0001
up	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	-0.0456	0.0018	-0.0491	-0.0420	-24.90	<.0001
YEAR	2008	-0.0311	0.0014	-0.0340	-0.0283	-21.68	<.0001
YEAR	2009	-0.0152	0.0012	-0.0176	-0.0127	-12.18	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0291	0.0017	0.0258	0.0324	17.13	<.0001
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0032	0.0001	0.0031	0.0034	37.04	<.0001
HLTHPLAN	0	0.0546	0.0064	0.0421	0.0671	8.54	<.0001
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
EESTATU	1	0.0014	0.0061	-0.0104	0.0133	0.24	0.8118
EESTATU	2	-0.0329	0.0093	-0.0511	-0.0146	-3.53	0.0004
EESTATU	3	0.0414	0.0063	0.0290	0.0539	6.54	<.0001
EESTATU	4	0.0445	0.0080	0.0289	0.0602	5.59	<.0001
EESTATU	5	0.0272	0.0172	-0.0066	0.0609	1.58	0.1149
EESTATU	6	0.0155	0.0120	-0.0081	0.0390	1.29	0.1988
EESTATU	7	-0.0023	0.0099	-0.0216	0.0170	-0.23	0.8152
EESTATU	8	0.0189	0.0102	-0.0011	0.0389	1.86	0.0635
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	0.0048	0.0057	-0.0065	0.0161	0.83	0.4047
REGION	2	0.0194	0.0054	0.0087	0.0301	3.57	0.0004
REGION	3	-0.0151	0.0055	-0.0260	-0.0042	-2.72	0.0064
REGION	4	-0.0022	0.0058	-0.0134	0.0091	-0.38	0.7060
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	2	-0.0057	0.0073	-0.0199	0.0086	-0.78	0.4370
PLANTYP	3	-0.0117	0.0085	-0.0283	0.0049	-1.38	0.1671
PLANTYP	4	-0.0461	0.0070	-0.0598	-0.0325	-6.64	<.0001
PLANTYP	5	-0.0303	0.0070	-0.0441	-0.0166	-4.32	<.0001
PLANTYP	6	-0.0247	0.0067	-0.0379	-0.0116	-3.69	0.0002
PLANTYP	7	-0.0376	0.0117	-0.0605	-0.0146	-3.21	0.0013
PLANTYP	8	-0.0326	0.0075	-0.0473	-0.0180	-4.37	<.0001
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		-0.0031	0.0013	-0.0055	-0.0006	-2.46	0.0139

Model Information		
Data Set	SIM.SIM_TESTQUAN2	Simvastatin Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	**Levels**	**Values**
ENROLID	438463	59001 121603 153401 155801 189501 196903 211901 230502 284601 286302 297002 306801 363102 379402 388302 391001 391002 417401 421001 421901 430202 436402 464801 501401 534801 551701 551702 558201 573101 573102 582602 593904 622701 624202 627401 636201 ...
ten	2	1 0
YEAR	4	2007 2008 2009 2010
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	ten	1						
Prm3	ten	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		
Prm14	EESTATU					2		

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (735590 levels)
Number of Clusters	735590
Correlation Matrix Dimension	4
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	1122589.9377
QICu	1122572.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.7188	0.0027	0.7136	0.7240	269.94	<.0001
ten	1	-0.0337	0.0021	-0.0378	-0.0296	-16.07	<.0001
ten	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	0.0068	0.0005	0.0058	0.0078	13.80	<.0001
YEAR	2008	-0.0006	0.0004	-0.0014	0.0001	-1.69	0.0907
YEAR	2009	0.0027	0.0003	0.0020	0.0033	8.06	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0040	0.0004	0.0032	0.0048	9.80	<.0001
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0031	0.0000	0.0030	0.0031	97.67	<.0001
HLTHPLAN	0	0.0196	0.0021	0.0155	0.0236	9.51	<.0001
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.
EESTATU	1	-0.0018	0.0020	-0.0058	0.0021	-0.91	0.3602

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
EESTATU	2	-0.0145	0.0027	-0.0197	-0.0093	-5.45	<.0001
EESTATU	3	0.0145	0.0020	0.0105	0.0185	7.12	<.0001
EESTATU	4	0.0140	0.0024	0.0093	0.0188	5.77	<.0001
EESTATU	5	0.0133	0.0038	0.0058	0.0208	3.49	0.0005
EESTATU	6	0.0069	0.0038	-0.0007	0.0144	1.79	0.0742
EESTATU	7	0.0062	0.0034	-0.0004	0.0129	1.84	0.0663
EESTATU	8	0.0028	0.0032	-0.0034	0.0090	0.89	0.3752
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	0.0130	0.0015	0.0100	0.0160	8.53	<.0001
REGION	2	0.0101	0.0015	0.0072	0.0130	6.82	<.0001
REGION	3	0.0017	0.0015	-0.0012	0.0047	1.13	0.2572
REGION	4	0.0039	0.0016	0.0008	0.0069	2.51	0.0122
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.
PLANTYP	2	0.0032	0.0016	-0.0000	0.0064	1.93	0.0533
PLANTYP	3	0.0040	0.0020	-0.0000	0.0079	1.95	0.0506

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	4	-0.0094	0.0015	-0.0124	-0.0063	-6.08	<.0001
PLANTYP	5	-0.0031	0.0016	-0.0062	-0.0001	-2.01	0.0444
PLANTYP	6	-0.0006	0.0015	-0.0035	0.0023	-0.39	0.6950
PLANTYP	7	-0.0024	0.0025	-0.0074	0.0025	-0.96	0.3380
PLANTYP	8	-0.0033	0.0017	-0.0066	0.0000	-1.94	0.0519
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		-0.0011	0.0004	-0.0019	-0.0002	-2.37	0.0178

Model Information		
Data Set	NEX.NEX_TESTQUAN2	Esomeprazole Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	**Levels**	**Values**
ENROLID	226328	88702 155801 292201 318402 347603 485702 704701 760701 833902 937501 1157601 1225101 1248002 1267702 1464601 1509201 1531402 1582602 1628806 1705906 1954201 2057203 2405804 2637802 2917202 2996501 3053603 3092101 3131701 3181405 8946602 8950901 8965302 ...
ten	2	1 0
YEAR	4	2007 2008 2009 2010
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	ten	1						
Prm3	ten	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		
Prm14	EESTATU					2		

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (373118 levels)
Number of Clusters	373118
Correlation Matrix Dimension	4
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	599897.3666
QICu	599876.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
Intercept		0.7208	0.0050	0.7110	0.7306	143.86	<.0001
ten	1	-0.0439	0.0012	-0.0463	-0.0415	-35.97	<.0001
ten	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	-0.0138	0.0008	-0.0154	-0.0122	-17.38	<.0001
YEAR	2008	-0.0101	0.0007	-0.0114	-0.0087	-14.38	<.0001
YEAR	2009	0.0034	0.0006	0.0022	0.0047	5.33	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0072	0.0007	0.0058	0.0086	9.83	<.0001
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0032	0.0000	0.0031	0.0033	69.98	<.0001
HLTHPLAN	0	0.0036	0.0033	-0.0030	0.0101	1.07	0.2835
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.
EESTATU	1	0.0059	0.0031	-0.0002	0.0120	1.88	0.0601

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
EESTATU	2	-0.0052	0.0048	-0.0145	0.0041	-1.09	0.2750
EESTATU	3	0.0314	0.0032	0.0251	0.0376	9.81	<.0001
EESTATU	4	0.0297	0.0038	0.0222	0.0372	7.72	<.0001
EESTATU	5	0.0275	0.0062	0.0153	0.0398	4.40	<.0001
EESTATU	6	0.0317	0.0063	0.0193	0.0440	5.01	<.0001
EESTATU	7	0.0120	0.0049	0.0025	0.0216	2.47	0.0136
EESTATU	8	0.0214	0.0045	0.0125	0.0303	4.72	<.0001
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	-0.0049	0.0028	-0.0104	0.0006	-1.75	0.0793
REGION	2	0.0046	0.0027	-0.0007	0.0099	1.70	0.0886
REGION	3	-0.0118	0.0027	-0.0171	-0.0065	-4.35	<.0001
REGION	4	-0.0020	0.0029	-0.0077	0.0038	-0.68	0.4996
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.
PLANTYP	2	0.0022	0.0038	-0.0053	0.0096	0.57	0.5684
PLANTYP	3	-0.0038	0.0044	-0.0125	0.0049	-0.86	0.3918

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	4	-0.0145	0.0037	-0.0217	-0.0073	-3.95	<.0001
PLANTYP	5	-0.0073	0.0036	-0.0144	-0.0002	-2.01	0.0448
PLANTYP	6	-0.0036	0.0035	-0.0105	0.0033	-1.01	0.3113
PLANTYP	7	0.0051	0.0048	-0.0043	0.0145	1.06	0.2888
PLANTYP	8	-0.0056	0.0040	-0.0135	0.0022	-1.40	0.1603
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		0.0023	0.0008	0.0007	0.0039	2.80	0.0051

Model Information		
Data Set	LAN.LAN_TESTQUAN2	Insulin glargine Set 18-65 yr olds Minimum 30 day supply
Distribution	Normal	
Link Function	Identity	
Dependent Variable	mpr	Day Supply divided by Days between first & last claim date

Class Level Information		
Class	**Levels**	**Values**
ENROLID	75326	98501 268605 421901 459301 551701 593904 642705 667302 975102 1129102 1226601 1316203 1509201 1551502 1625301 1899001 1933601 2004801 2020202 2052901 2251801 2529804 3092101 3105102 8997602 9001502 9018302 9065501 9068802 9080501 9100302 9111002 ...
ten	2	1 0
YEAR	4	2007 2008 2009 2010
SEX	2	1 2
AGEGRP	4	2 3 4 5
HLTHPLAN	2	0 1
EESTATU	9	1 2 3 4 5 6 7 8 9
EGEOLOC	54	01 04 05 06 07 08 09 11 12 13 16 17 18 19 20 22 23 24 25 26 27 28 31 32 33 34 35 36 37 38 39 41 42 43 44 46 47 48 49 52 53 54 55 56 57 58 59 61 62 63 64 65 97 98
INDSTRY	10	1 2 3 4 5 6 7 A C W
PLANTYP	8	2 3 4 5 6 7 8 9
REGION	5	1 2 3 4 5

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm1	Intercept							
Prm2	ten	1						
Prm3	ten	0						
Prm4	YEAR		2007					
Prm5	YEAR		2008					
Prm6	YEAR		2009					
Prm7	YEAR		2010					
Prm8	SEX			1				
Prm9	SEX			2				
Prm10	AGE							
Prm11	HLTHPLAN				0			

Parameter Information								
Parameter	**Effect**	**ten**	**YEAR**	**SEX**	**HLTHPLAN**	**EESTATU**	**PLANTYP**	**REGION**
Prm12	HLTHPLAN				1			
Prm13	EESTATU					1		
Prm14	EESTATU					2		
Prm15	EESTATU					3		
Prm16	EESTATU					4		
Prm17	EESTATU					5		
Prm18	EESTATU					6		
Prm19	EESTATU					7		
Prm20	EESTATU					8		
Prm21	EESTATU					9		
Prm22	REGION							1
Prm23	REGION							2
Prm24	REGION							3
Prm25	REGION							4
Prm26	REGION							5
Prm27	PLANTYP						2	
Prm28	PLANTYP						3	
Prm29	PLANTYP						4	
Prm30	PLANTYP						5	
Prm31	PLANTYP						6	
Prm32	PLANTYP						7	
Prm33	PLANTYP						8	
Prm34	PLANTYP						9	
Prm35	Charlson_index							

Algorithm converged.

GEE Model Information	
Correlation Structure	Unstructured
Within-Subject Effect	YEAR (4 levels)
Subject Effect	ENROLID (132177 levels)
Number of Clusters	132177
Correlation Matrix Dimension	4

GEE Model Information	
Maximum Cluster Size	4
Minimum Cluster Size	0

Algorithm converged.

GEE Fit Criteria	
QIC	195980.4137
QICu	195959.0000

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		**Estimate**	**Standard Error**	**95% Confidence Limits**		**Z**	**Pr > |Z|**
Intercept		0.5684	0.0096	0.5495	0.5873	58.98	<.0001
ten	1	-0.0634	0.0019	-0.0671	-0.0597	-33.23	<.0001
ten	0	0.0000	0.0000	0.0000	0.0000	.	.
YEAR	2007	-0.0422	0.0018	-0.0458	-0.0387	-23.41	<.0001
YEAR	2008	-0.0298	0.0014	-0.0326	-0.0270	-20.83	<.0001
YEAR	2009	-0.0149	0.0012	-0.0174	-0.0125	-11.97	<.0001
YEAR	2010	0.0000	0.0000	0.0000	0.0000	.	.
SEX	1	0.0290	0.0017	0.0257	0.0324	17.09	<.0001

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
SEX	2	0.0000	0.0000	0.0000	0.0000	.	.
AGE		0.0032	0.0001	0.0031	0.0034	36.93	<.0001
HLTHPLAN	0	0.0543	0.0064	0.0417	0.0668	8.48	<.0001
HLTHPLAN	1	0.0000	0.0000	0.0000	0.0000	.	.
EESTATU	1	0.0011	0.0061	-0.0108	0.0130	0.18	0.8550
EESTATU	2	-0.0327	0.0093	-0.0510	-0.0145	-3.52	0.0004
EESTATU	3	0.0406	0.0063	0.0281	0.0530	6.40	<.0001
EESTATU	4	0.0447	0.0080	0.0291	0.0604	5.61	<.0001
EESTATU	5	0.0271	0.0172	-0.0067	0.0608	1.57	0.1159
EESTATU	6	0.0158	0.0120	-0.0078	0.0394	1.31	0.1903
EESTATU	7	-0.0032	0.0099	-0.0226	0.0161	-0.33	0.7433
EESTATU	8	0.0196	0.0102	-0.0004	0.0396	1.93	0.0542
EESTATU	9	0.0000	0.0000	0.0000	0.0000	.	.
REGION	1	0.0040	0.0057	-0.0073	0.0153	0.70	0.4859

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
REGION	2	0.0187	0.0054	0.0081	0.0294	3.44	0.0006
REGION	3	-0.0159	0.0055	-0.0267	-0.0050	-2.87	0.0041
REGION	4	-0.0026	0.0057	-0.0139	0.0086	-0.46	0.6459
REGION	5	0.0000	0.0000	0.0000	0.0000	.	.
PLANTYP	2	-0.0039	0.0073	-0.0182	0.0104	-0.54	0.5917
PLANTYP	3	-0.0126	0.0085	-0.0292	0.0040	-1.49	0.1364
PLANTYP	4	-0.0469	0.0070	-0.0606	-0.0333	-6.75	<.0001
PLANTYP	5	-0.0318	0.0070	-0.0456	-0.0181	-4.53	<.0001
PLANTYP	6	-0.0262	0.0067	-0.0394	-0.0131	-3.91	<.0001
PLANTYP	7	-0.0390	0.0117	-0.0619	-0.0161	-3.33	0.0009
PLANTYP	8	-0.0330	0.0075	-0.0477	-0.0184	-4.42	<.0001

Analysis Of GEE Parameter Estimates							
Empirical Standard Error Estimates							
Parameter		Estimate	Standard Error	95% Confidence Limits		Z	Pr > |Z|
PLANTYP	9	0.0000	0.0000	0.0000	0.0000	.	.
Charlson_index		-0.0030	0.0012	-0.0054	-0.0005	-2.40	0.0166

VITA

Jonathan Hirohiko Watanabe was born in Omaha, NE. He was raised in Salt Lake City, UT in the Cottonwood Heights area. At the University of Washington, he earned a Bachelor of Sciences degree in Zoology with a minor in History. He completed his Doctor of Pharmacy at the University of Southern California where he served as student body president. Jonathan earned his Master of Sciences from the University of Washington Pharmaceutical Outcomes Research and Policy Program (PORPP). In 2012, Dr. Watanabe earned his Doctor of Philosophy at the University of Washington in Pharmaceutical Sciences from the Pharmaceutical Outcomes Research and Policy Program. He has accepted a position as an assistant professor at Western University College of Pharmacy in Pomona, CA.