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How Does Prescription Drug Spending Affect Medication Adherence, Acute Care Use, and Health Care Costs in Heart Failure?

By

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An abstract of
A dissertation submitted to the Faculty of the
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Abstract

Introduction: Studies show that prescription drug cost sharing adversely affects appropriate medication use in chronic disorders. Moreover, greater cost sharing has been linked to increased health care use and costs. However, these effects are poorly understood in heart failure (HF), the most common cause of hospitalization in Medicare. The aim of this study was to evaluate the association between prescription drug spending by Medicare beneficiaries with HF and (1) refill adherence, (2) hospital and emergency care use, and (3) inpatient and total health care costs.

Methods: Cross-sectional study of pooled data from the Medicare Current Beneficiary Survey, 2010-12. The sample consisted of community-dwelling participants with self-reported HF and continuous Part D drug coverage. Multivariate analysis included linear regression and generalized linear models. Sampling weights and variance estimation adjustments accounted for the complex survey design.

Results: Among patients without the low-income subsidy (LIS), percent of income spent on a β blocker was associated with the adjusted odds of non-adherence, OR=1.41, 95% CI [1.01, 1.98], p=.046, and decreased medication use, B=-3.63, SE=1.57, p=.022. No association was observed for anti-angiotensin drugs. Conditional on the effect of no Medicaid entitlement, average out-of-pocket payment per HF prescription was borderline associated with rates of HF-related hospitalization, RR=1.02, 95% CI [1.00, 1.05], p=.060, and hospitalized days, RR=1.04, 95% CI [1.00, 1.07], p=.057. Average prescription payment was not associated with the odds of HF-related hospitalization or emergency department use. Conditional on not receiving the LIS, predicted annual Medicare costs rose an average $126, 95% CI [-10, 261], p=.068, with each additional dollar spent per prescription. Average prescription spending was not associated with total or Medicare inpatient costs, or with total health care costs. Total out-of-pocket spending on HF drugs was not associated with any of the cost outcomes.

Conclusion: Among HF patients with Part D but no low-income assistance, there was a slight decline in β-blocker adherence and marginal evidence for greater hospital use and Medicare costs at higher prescription spending levels. Yet, most patients absorbed modest drug payments without dramatic spikes in related health care use and costs. This study contributes evidence to ongoing discussions about cost sharing in chronic disorders.

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Table of Contents

CHAPTER 1

Introduction

Background on Cost Sharing

Health care costs in the U.S. are rising faster than inflation (Kamal & Sawyer, 2018; U.S. Bureau of Labor Statistics, 2018), and Americans spend more per capita on health care than their peers without corresponding gains in health status (Squires & Anderson, 2015). One cost-containment strategy that public and private health insurers have employed is to shift some of the cost of care to patients. This strategy, known broadly as *cost sharing*, includes several types of point-of-care, out-of-pocket expenditures, such as deductibles, coinsurance, and copays (Geyman, 2012). Cost-sharing amount typically rises with the cost of procuring the service without regard to clinical value: the more expensive the intervention, the more the patient pays (Tang et al., 2014). In the case of prescription drugs, this approach takes shape in tiered formularies, which usually dictate higher cost-sharing liability for more expensive drugs.

The theoretical rationale for cost sharing in health care rests on a concept known as *moral hazard.* First used in the 19th century to describe the risk of careless or fraudulent behavior after purchasing fire insurance, moral hazard gained currency in health care policy in the 1960s when detailed by Pauly in a commentary on Arrow's proposal for social health insurance (Baker, 1996, pp. 248-249; Stone, 2011). In that widely cited piece, Pauly (1968) suggested that patients use an excess quantity of health services when insured, since insurance effectively lowers prices, sometimes to zero. This price distortion obscures the true cost or value of a service to patients, predisposing them to seek more care (or take more health risks) than they otherwise would. Moral hazard

from insurance coverage that is too generous results in inefficiency and collective welfare loss (Pauly, 1968). Cost sharing presents a solution to curb those excesses by making patients more sensitive to the true cost of care before they choose whether to use it (Eaddy, Cook, O'Day, Burch, & Cantrell, 2012).

The concept of moral hazard has underpinned cost sharing in health care for over 50 years and was the engine behind the consumer-driven health plans (i.e., high-deductible coverage paired with tax-sheltered health savings accounts) of the early 2000s (Geyman, 2012). In fact, the 2004 Economic Report of the President included three paragraphs describing how moral hazard operates in health care (Gladwell, 2005). Yet, this theory is open to multiple critiques. Firstly, health care providers frequently have more influence over the decision to use a health service than patients themselves (Geyman, 2012; Stone, 2011). Secondly, the vast majority of patients use health care only when they feel it necessary, and rock-bottom prices do not give rise to eager throngs of customers for liver transplants or leg amputations (Nyman, 2004; Stone, 2011). Thirdly, unlike normal markets, there is information asymmetry in health care transactions: prices are often opaque, decisions are made under stress or with urgency, search costs (for "comparison shopping") are burdensome, and evaluation of quality is impracticable for most lay persons (Frick & Chernew, 2009; Geyman, 2012).

Fourthly, and perhaps most relevant to this dissertation, is the observation that not all additional care consumed with the acquisition of health insurance is wasteful. To the extent that patients forego needed care in the absence of adequate health coverage, the care consumed at insurance prices may actually be efficient or welfare-improving (Frick & Chernew, 2009). When cost sharing deters or restricts the use of needed health

services, the result may be sicker patients who require costlier care down the road. Roemer, Hopkins, Carr, and Gartside (1975) voiced the concern that cost sharing in health insurance may be "penny wise but pound foolish" over 40 years ago, and this concern motivated the RAND Corporation's Health Insurance Experiment (HIE) of the 1970s-80s.

The HIE recruited 2750 families and randomly assigned them to one of five health insurance plans, each with a distinct cost-sharing structure (Brook et al., 2006). The banner finding from the experiment was that less generous health plans lowered health service use with minimal effects on the average health of participants (Manning et al., 1987; Newhouse, 2004). Therefore, even substantial cost-sharing amounts (up to 95%) could be justified on the basis that foregone care at higher prices was probably non-essential. Yet, this conclusion overlooked several nuances. First, low-income participants with hypertension had poorer blood pressure control and higher predicted mortality in the plans with cost sharing (Brook et al., 1983). Second, fewer low-income participants in the "free care" plan experienced serious symptoms: shortness of breath, chest pain on exertion, loss of consciousness, non-traumatic bleeding, and unintended weight loss (Shapiro, Ware, & Sherbourne, 1986). Finally, attrition was substantially higher in the cost-sharing plans, which could account for almost all the reduction in hospital use observed in those plans (Nyman, 2007). In other words, patients in stingier plans who needed or were likely to need hospitalization may have just left the study.

Given these caveats about the RAND HIE and the growth of cost sharing in health insurance, researchers have directed renewed attention to the potentially adverse effects of cost sharing in recent years. Cost sharing for prescription drugs, in particular, has

received sustained scrutiny because of the importance of medications to secondary prevention in costly chronic diseases. To the extent that medications are effective at preventing disease progression or exacerbation, cost-sharing levels that deter their use may be suboptimal (Newhouse, 2006). Published studies of prescription drug cost sharing usually report its effects on medication adherence, health outcomes and service use, health care costs, or some combination of the three.

Evidence of Prescription Cost Sharing Effects

Medication adherence. Goldman et al. (2004) published a seminal work that showed a statistically significant association between increased copays and decreased use of chronic disease maintenance drugs in a retrospective analysis of claims data from 52 health plans across 30 employers. Using predicted values, they found that doubling copayments was associated with reductions in overall days supplied of eight therapeutic classes: lipid-lowering agents (34%), anti-ulcerants (33%), anti-asthmatics (32%), antihypertensives (26%), antidepressants (26%), and antidiabetics (25%). These drugs showed less price-sensitivity than the more symptom-based antihistamines and nonsteroidal anti-inflammatory drugs (Goldman et al., 2004). Nevertheless, the sizes of the predicted reduction in days supplied at higher copay levels were notable.

Over the last 10 years, an inverse correlation between prescription cost sharing and refill adherence in chronic diseases has been well documented. For example, in a managed care population with type 2 diabetes, the average medication possession ratio (a common proxy for adherence in pharmacy claims data) was 52% when oral antidiabetic copays were $20 or more, compared to 58% at copays under $10 (Barron, Wahl, Fisher, & Plauschinat, 2008). After adjustment for covariates, generalized linear modeling

predicted that adherence declined by 1.5% with every $10 increase in drug copay (Barron et al., 2008). Likewise, among health plan subscribers with type 2 diabetes at a large employer, the adjusted odds of adherence were 2.0 times higher in the low-copay group (<$10) compared to the high-copay group (≥$20) for subscribers under age 65 (Colombi, Yu-Isenberg, & Priest, 2008). Among those over age 65, odds of adherence were 2.6 times higher in the low-copay group (Colombi et al., 2008). And a $10 rise in the plan average for out-of-pocket diabetes drug costs was associated with 1.9% lower adherence across 35 large, self-insured employers (Thornton Snider, Seabury, Lopez, McKenzie, & Goldman, 2016).

Payers may raise cost-sharing amount to discourage use of certain medications when cheaper alternatives are available, but unintended consequences may result. After United Healthcare moved sitagliptin from the 2nd to 3rd tier across its pharmacy plans, only 44% of the patients who discontinued it switched to a preferred drug within the same class, while 30% had not replaced it at all or had stopped diabetes treatment altogether nine months later (Huang, Liu, Shankar, & Rajpathak, 2015). The introduction of a three-tier formulary for antidepressants at a managed care organization shifted some users from non-preferred to preferred agents, but it also slowed the growth in probability of antidepressant use, which declined 0.3 percentage points more in the three-tier group compared to a control group after the policy change (Hodgkin, Parks Thomas, Simoni-Wastila, Ritter, & Lee, 2008). And among long-term users of specialty medications at one health maintenance organization, the risk of non-persistence (a gap in therapy) was 2.5 times higher for anti-inflammatory injectables and three times higher for immunosuppressants when copays rose compared to no copay change (Kim et al., 2011).

Even Medicaid beneficiaries with nominal copays demonstrate price-sensitivity. After Oregon Medicaid introduced a prescription copay requirement in 2003, use of prescription drugs was 17.2% lower than what would have been predicted without the policy change (Hartung et al., 2008). This reduction was statistically significant across drug classes, including medications for respiratory disease (18.7%), cardiovascular disease (13.1%), and schizophrenia (12.4%) (Hartung et al., 2008). When Georgia Medicaid raised copays on brand-name and non-preferred drugs in 2002, the number of prescription days per person fell by 127 and 150 relative to two control states among adults with cancer (Subramanian, 2011). Similarly, a 30-day copay increase from $2 to $7 for lipid-lowering agents at the Philadelphia Veterans Affairs Medical Center was associated with 39% lower adjusted odds of adherence and twice the rate of non-persistence compared to veterans exempt from copays (Doshi, Zhu, Lee, Kimmel, & Volpp, 2009).

The advent of Medicare Part D prescription drug coverage and the growing popularity of bundled Medicare Advantage plans have prompted scrutiny of cost sharing among older adults, especially considering their higher chronic disease burden. Among fee-for-service Medicare beneficiaries with a standalone Part D plan, odds of non-adherence were higher by 60% for antihypertensives and 59% for lipid-lowering drugs in the absence of supplemental coverage for the Part D coverage gap (or “doughnut hole”) compared to receipt of the Low-Income Subsidy (LIS) for cost-sharing assistance (Li, McElligott, Bergquist, Schwartz, & Doshi, 2012). Among Medicare Advantage enrollees without prior drug coverage, the medication possession ratio improved by 13.4, 17.9, and 13.5 percentage points for lipidemia, diabetes, and hypertension drugs, respectively, net

of the changes observed in the group with no coverage change (Zhang et al., 2010). The adjusted odds of adherence increased by 67% for lipidemia, 236% for diabetes, and 209% for hypertension after the start of Part D coverage compared to no change, and these effects were only slightly smaller when LIS recipients were excluded (Zhang et al., 2010).

Health outcomes and service use. Given that prescription drug cost sharing appears to negatively affect treatment adherence, and that lower adherence is associated with poorer outcomes across chronic disorders, a cost sharing effect on health outcomes would be logical. There is some empirical support for this hypothesis. Of the 25 studies on cost sharing and outcomes included in a 2012 literature review, 76% showed evidence of a negative effect on one or more of the following: self-reported health status, symptoms, adverse events, emergency care use, office visits, hospitalizations, nursing home admissions, or medical costs (Eaddy et al., 2012). Of the six remaining studies, five also failed to demonstrate a cost sharing effect on adherence, which would have been expected if adherence mediates the effect of drug cost sharing on outcomes (Eaddy et al., 2012).

Some studies report the effect of adherence on outcomes independent of the effect of cost sharing on adherence. For example, Barron et al. (2008) observed an average 0.12-point decrease in glycosylated hemoglobin (HbA_{1c}) per 10% increase in medication possession ratio in the same sample that experienced slightly lower adherence when mean oral antidiabetic copay rose $10. Yet, they did not report a direct link between copay and HbA_{1c}. Likewise, Goldman, Joyce, and Karaca-Mandic (2006) predicted that full adherence to lipid-lowering drugs would be associated with 357 fewer

hospital admissions annually per 1000 patients at high risk of coronary heart disease. While their modeling also predicted a decline of 6 percentage points in prevalence of full adherence when copays doubled from $10 to $20, they did not report an explicit link between drug copay and hospitalization (Goldman et al., 2006).

Other study authors have looked directly at the effect of medication copay on outcomes, with or without accounting for adherence. For example, Colombi et al. (2008) reported that risk of any-cause hospitalization was 36% lower in the low-copay group than in the high-copay group for diabetic patients over age 65 at a large employer. Health plan subscribers across 35 employers saw a predicted reduction of 0.17 in annual hospitalized days per $10 rise in the plan's average out-of-pocket cost for antidiabetics (Thornton Snider et al., 2016). Among adult Medicaid beneficiaries with cancer in Georgia, Subramanian (2011) observed that the proportion with an emergency department visit increased after copays were raised on many drugs, compared with the two control states. And among Medicare Part D enrollees on dialysis, Park et al. (2015) reported 20-27% higher risk of death in the groups with no LIS (except for the group that reached catastrophic coverage) compared to LIS recipients.

However, consistent with the main results of the RAND HIE, other studies show no evidence of association between prescription cost sharing and health outcomes or service use. For instance, two years after the start of drug copays in the Oregon Medicaid program, there was no statistically significant change in rates of office visits, emergency department encounters, or hospitalizations, despite the decline in prescription drug use (Hartung et al., 2008). And an analysis of older Canadian patients in a province-wide myocardial infarction (MI) database showed no evidence of increased readmissions,

physician encounters, emergency department use, or mortality after the introduction of 25% coinsurance for prescriptions, although this study lacked a control group (Pilote, Beck, Richard, & Eisenberg, 2002). In sum, questions of whether, when, and by how much the amount of drug cost sharing worsens health and increases service use remain largely unresolved.

Health care costs. Several studies have investigated the effect of prescription cost sharing on total and non-pharmacy medical costs, and their conclusions vary. Type 2 diabetes patients with lower average drug copays (<$10) had 22% lower total health care spending compared to patients with high copays (≥$20) after one year of follow-up, p = .012 (Colombi et al., 2008). In the authors' analysis, that difference equated to $3116 per patient per year in savings from lower copays (Colombi et al., 2008). Among adult Medicaid beneficiaries with cancer in Georgia, where drug copays rose as much as 600%, total 6-month costs were more than $2000 higher per patient than in comparison states (Subramanian, 2011). And among Part D enrollees on dialysis, Medicare hospitalization costs were significantly higher among patients who reached the doughnut hole or subsequent catastrophic coverage compared to those who received the LIS; the difference for patients in the initial coverage phase (before reaching the doughnut hole), however, was non-significant (Park et al., 2015).

Contradictory results also appear in the literature. For example, an analysis of claims for diabetes patients from 35 self-insured employers found evidence of higher inpatient costs per member when diabetes drug copays rose, and this effect was greater with comorbid heart failure: a shift from the 10^{th} to 90^{th} percentile for drug copay was associated with a predicted $1328 rise in net payer costs in the presence of heart failure

(Thornton Snider et al., 2016). Yet, an older study of commercially insured adults with heart failure (with or without diabetes) found that, despite evidence of significantly decreased adherence and greater odds of hospitalization at higher drug copays, there was no significant effect on total health care costs (Cole, Norman, Weatherby, & Walker, 2006). One approach to isolating economic impacts is to look instead at the effect of lowering, rather than raising, prescription copays, as the next section will describe.

Value-Based Insurance Design

Overview. With growing evidence of the adverse effect of prescription cost sharing on adherence, and modest evidence for elevated health care use and costs, some payers have begun experimenting with value-based insurance design (V-BID). Also known as value-based benefit design, V-BID policies typically lower or eliminate cost-sharing requirements to promote adherence to treatments that are known to be effective at reducing illness or death (Lee, Maciejewski, Raju, Shrank, & Choudhry, 2013). Under V-BID, cost-sharing amount varies by the potential of the service to improve outcomes and reduce costs for specific patients or across the whole population (Chernew, Rosen, & Fendrick, 2007). The theory behind V-BID is that it reveals the clinical value of a treatment to patients more clearly than conventional plan designs, better aligning out-of-pocket payments with expected benefits (Gibson et al., 2011; Hirth, Cliff, Gibson, McKellar, & Fendrick, 2016).

The City of Asheville in North Carolina was an early adopter of V-BID for employees, retirees, and dependents in its group health plan in the 1990s (Nair et al., 2010). More recently, the Patient Protection and Affordable Care Act (2010) embodied V-BID principles by banning cost sharing for a set of preventive health services, such as

recommended cancer screenings and immunizations, in most private health plans. It also authorized the U.S. Centers for Medicare & Medicaid Services (CMS) to experiment with a V-BID Model in select Medicare Advantage plans (CMS, 2018). In addition, several states—including Oregon, Maryland, Michigan, and Connecticut—are considering or have applied V-BID policies in their employee health plan, Medicaid program, or health insurance exchange (Hirth et al., 2016).

Cost-effectiveness analyses. A handful of formal economic evaluations have documented theoretical cost savings that would accrue from offering full coverage for select, evidence-based medications. For example, first-dollar coverage for combination pharmaco-therapy after MI, compared to standard Part D coverage, would result in greater functional life expectancy (0.35 additional quality-adjusted life years [QALY]) and less resource use (-$2500) per patient (Choudhry, Patrick, Antman, Avorn, & Shrank, 2008). From a cost-effectiveness perspective, that makes full drug coverage the dominant (i.e., cost-saving) strategy in this scenario. A follow-up study with model inputs from the MI Free Rx Event and Economic Evaluation (FREEE) trial also showed quality-adjusted survival gains (0.14 QALY) and less resource use (-$4011) per patient with full coverage for post-MI preventive medications, compared to usual drug benefits; these results were robust to alterations in the assumed reduction in risk of post-MI events (except stroke) from full coverage (Ito et al., 2015).

Theoretical cost savings have been demonstrated in other conditions. In a hypothetical cohort of postmenopausal Part D beneficiaries with hormone-receptor-positive early-stage breast cancer, full coverage for aromatase inhibitors would result in longer functional survival (0.03 QALY) and less resource use (-$275) per beneficiary,

compared to standard Part D benefits (Ito, Elkin, Blinder, Keating, & Choudhry, 2013). Also compared with conventional Part D, full coverage of angiotensin-converting enzyme (ACE) inhibitors for renal preservation in diabetes would prolong life (0.23 QALY) and save money (-$1606) for the average beneficiary (Rosen et al., 2005). Despite these notable findings, studies of real-world cohorts, especially in the working-age population, are essential to understanding the effects of V-BID.

Empirical retrospective studies. One of the first studies to address targeted copay reductions and use a comparison group found improvements in adherence to five recommended chronic disease medication categories after the launch of a large employer's V-BID program, which lowered target drug copays by 50% for brand-name products and to $0 for generics (Chernew et al., 2008). Medication possession ratio increased at the V-BID employer by 3.4 percentage points for hydroxymethylglutaryl–coenzyme A reductase inhibitors ("statins"), 4.0 for anti-diabetics, 3.0 for β blockers, and 2.6 for ACE inhibitors and angiotensin receptor blockers, all $p < .001$ (Chernew et al., 2008). The increase of 1.9 points for inhaled corticosteroids was not statistically significant. Notably, both the V-BID and comparison employers had disease management programs in place at the time of the policy change, so adherence differences were unlikely attributable to these programs (Chernew et al., 2008).

Since then, multiple quasi-experimental studies have documented improvements in adherence to recommended treatments after the adoption of V-BID. In a large, Midwestern health plan alliance that lowered copays for brand-name statins by an average 43% (compared to a control group that saw an increase of 17%), statin adherence increased 2.7 percentage points more in the year after the change relative to the control

group, $p = .03$, reducing non-adherence by 12% (Frank et al., 2012). In the year after the same alliance moved most diabetic drugs and supplies to its lowest cost-sharing tier, the odds of adherence were 1.56 times higher compared to a group of matched controls, $p = .03$ (Zeng et al., 2010). Similarly, after a large North Carolina health insurer eliminated copays for generic diabetes and cardiovascular drugs for V-BID plan members (and lowered brand-name copays for everyone), adherence improved by 1.5 percentage points for calcium-channel blockers, $p < .05$, and by 2.6 points for statins, 2.7 for β blockers, 3.1 for ACE inhibitors, and 3.8 for metformin (all $p < .001$) compared to matched controls (Maciejewski, Farley, Parker, & Wansink, 2010).

V-BID policies have a more mixed record with respect to service utilization. After all diabetes drugs and supplies were moved to the lowest-cost tier in a state government employee health plan, emergency department visits fell by 31% in year 1 and 36% in year 2, compared to baseline (Nair et al., 2010). Office visits also declined 12% in year 1, but there were no other statistically significant changes in service use, and this study had no control group (Nair et al., 2010). Lower copays for statins and clopidogrel at a large, self-insured employer led to significant reductions in physician visits (rate ratio [RR], 0.80 for statins, 0.87 for clopidogrel) and hospital and emergency department admissions (RR, 0.90 for statins, 0.89 for clopidogrel), but no change in coronary events 12 months later (Choudhry et al., 2012). Emergency department visits by V-BID participants declined 1.3 percentage points more than among controls in year 2 compared to the baseline year after chronic disease drug copays were lowered or eliminated at a state government employer, but patients in this plan were also required to obtain certain preventive and chronic care services or face a surcharge (Hirth et al., 2016).

There is some evidence that V-BID policies are cost-neutral to the payer, but the case for cost savings is much less obvious than suggested by the economic simulation models. For example, asthma-specific net payments by a large pharmaceutical employer were 2% lower per member in the third year of a V-BID program compared to baseline, and diabetes-related net payments were 37% lower (Kelly, Turner, Frech-Tamas, Doyle, & Mauceri, 2009). However, hypertension-related payments were 9% higher, though averted complications of hypertension may not be evident after only three years (Kelly et al., 2009). At a similar firm, there was a significant, gradual decline in total health care spending for a cardiovascular cohort in a V-BID plan: $2122 lower per member in year 2 and $3722 in year 3 (Gibson et al., 2011). Yet, total spending was no different from the comparison group for the asthma and diabetes cohorts (Gibson et al., 2011). And in a zero-copay program for generic drugs, there was a significantly smaller increase in employer spending on lipid-lowering agents (but not anti-diabetics): $51 per member annually compared to $143 for controls, $p < .001$ (Clark et al., 2014). The authors attribute this reduced growth in pharmacy spending to generic switching (Clark et al., 2014).

Clinical trials. To date, published results from clinical trials of V-BID interventions are limited. The MI FREEE trial randomly assigned 5855 post-infarction patients to full or usual coverage for statins, β blockers, and ACE inhibitors or angiotensin receptor blockers (Kulik et al., 2013). Although full coverage increased adherence across drug classes (all $p < .05$), the reduction in rates of major vascular events and re-vascularization procedures was non-significant (Kulik et al., 2013). There was no change in overall health spending, which can be interpreted as evidence of a cost-neutral

intervention, given the significant increase in pharmacy spending by insurers (Kulik et al., 2013). In addition to MI FREEE, a study protocol was published in 2009 for the MHealthy Focus on Diabetes trial, which prospectively evaluated adherence and medical costs in response to targeted copay relief for certain high-value services for diabetes (Spaulding et al., 2009). However, the groups were not randomized, and results are yet to be published.

Knowledge Gap in Heart Failure

Notwithstanding the body of work on prescription cost sharing in other chronic disorders, heart failure (HF) has received surprisingly little attention in this area. The evidence gap is notable, because chronic HF poses a major public health burden in the United States. Nearly one million hospital admissions each year are attributable to HF, accounting for 5% of all inpatient stays among Medicare beneficiaries—more than any other cause (Pfuntner, Wier, & Stocks, 2013). Approximately 825,000 individuals are newly diagnosed with HF each year, and direct medical costs for HF exceed $30 billion annually (Go et al., 2014; Heidenreich et al., 2011). Moreover, the crude prevalence of HF is expected to increase by 17% from 2015 to 2030, due largely to therapeutic advancements in heart disease and the aging of society (Heidenreich et al., 2011).

The effective management of HF requires strict adherence to multiple daily medications, together with challenging dietary restrictions and early recognition of exacerbation (Marti et al., 2013). Virtually all adults with systolic HF (and many with diastolic HF) should take an ACE inhibitor or angiotensin receptor blocker along with a β blocker to reduce cardiac workload (Yancy et al., 2013). Many also require a diuretic to prevent fluid volume overload and/or a cardiac glycoside to improve contractility (Yancy

et al., 2013). In addition, a combined formulation of the vasodilators hydralazine and isosorbide dinitrate is the only medication shown to improve survival in African Americans with HF (Carmody & Anderson, 2007). These regimens and other self-care demands occur in the context of impaired physical and cognitive function and diminished quality of life, which may impose additional barriers to adherence.

Two published studies have reported estimates of prescription cost sharing effects on adherence in HF. A retrospective study of United Healthcare claims from 2002 showed that a $10 increase in 30-day copay was associated with a 2.6% decrease in medication possession ratio for ACE inhibitors and a 1.8% decrease for β blockers (Cole et al., 2006). Likewise, a retrospective analysis of claims from over 30 commercial health plans showed that, among HF patients over age 50, there was a 9% decrease in medication possession ratio for β blockers in the high-copay (>$25) versus low-copay (≤$1) group, and odds of non-adherence were significantly elevated in the higher copay groups (>$20) (Patterson, Blalock, Smith, & Murray, 2011). No results for ACE inhibitors or other drug classes were reported in that study, but estimates were adjusted for spending on concurrent medications and the prior year's β-blocker adherence (Patterson et al., 2011).

Only one of these two studies examined service use and total costs. Cole et al. (2006) used predicted adherence from their first models to estimate the effect of copay-attributable non-adherence on hospitalization and costs in their second models. They found that the 2.6% decline in ACE inhibitor adherence per $10 rise in copay predicted 6.1% higher odds of HF-related hospitalization, and the 1.8% decline in β-blocker adherence per $10 rise in copay predicted 8.7% increased odds of hospitalization for HF

(Cole et al., 2006). However, they observed no significant effect on total health care costs (Cole et al., 2006). On the other hand, Thornton Snider et al. (2016) observed that the drug copay effect on net payer costs among diabetic patients was over 13 times higher in the presence of comorbid HF. With only two published studies in the past 12 years directly addressing prescription cost sharing in HF, only one of which looked at service use and cost outcomes and neither of which focused on the Medicare population, there is need for more evidence in this area.

Study Purpose and Aims

Given the evidence gap, the purpose of this dissertation was to determine whether and how cost sharing for HF medications in Medicare prescription drug plans was related to prescription refill adherence, HF-related acute care use, and total health care costs in a national Medicare sample. The specific aims of this dissertation were to:

Specific Aim 1. Examine the relationship between average out-of-pocket payment and refill adherence for three drug classes commonly prescribed for HF.

Hypothesis 1a/b: Mean out-of-pocket drug payment, as a proportion of average monthly income, will be negatively associated with medication possession ratio (MPR) and positively associated with odds of non-adherence (MPR < 80%) for β blockers.

Hypothesis 1c/d: Mean out-of-pocket drug payment, as a proportion of average monthly income, will be negatively associated with MPR and positively associated with odds of non-adherence (MPR < 80%) for ACE inhibitors.

Hypothesis 1e/f: Mean out-of-pocket drug payment, as a proportion of average monthly income, will be negatively associated with MPR and positively associated with odds of non-adherence (MPR < 80%) for angiotensin receptor blockers.

Specific Aim 2. Examine the relationship between average out-of-pocket payment per HF-indicated prescription and HF-related acute care use.

Hypothesis 2a: Mean out-of-pocket drug payment will be associated with odds of HF-related hospitalization.

Hypothesis 2b: Mean out-of-pocket drug payment will be associated with odds of HF-related emergency department (ED) visit.

Hypothesis 2c: Mean out-of-pocket drug payment will be associated with rate of HF-related hospital admissions.

Hypothesis 2d: Mean out-of-pocket drug payment will be associated with rate of HF-related inpatient days.

Specific Aim 3. Examine the association between out-of-pocket payments for HF prescriptions and both inpatient and total costs to Medicare and all payers.

Hypothesis 3a/b: Mean out-of-pocket payment per HF prescription will be associated with inpatient and total health care payments by all payers.

Hypothesis 3c/d: Mean out-of-pocket payment per HF prescription will be associated with inpatient and total health care payments by Medicare.

Hypothesis 3e/f: Total annual out-of-pocket payments for HF prescriptions will be associated with inpatient and total health care payments by all payers.

Hypothesis 3g/h: Total annual out-of-pocket payments for HF prescriptions will be associated with inpatient and total health care payments by Medicare.

Conceptual Framework

Insurers justify cost sharing with conventional moral hazard theory, which predicts that lower out-of-pocket prices lead to excess health care consumption and

collective welfare loss due to the resulting inefficiency (Geyman, 2012; Nyman, 2004; Pauly, 1968). Yet, increased use of certain high-value services, especially preventive care, may yield net welfare gains in terms of long-run cost savings for society (Chernew et al., 2007; Newhouse, 2006). Frick and Chernew (2009) describe this concept as *beneficial moral hazard*: greater consumption of high-value care may improve rather than diminish efficiency-related welfare. In their conceptual framework, beneficial moral hazard appears when: (a) the social marginal cost of a service is lower than its market price, as in the case of many prescription drugs; (b) there are positive externalities such as a benefit to other plan members (e.g., lower premiums) if a patient uses care that improves his or her health; and (c) the demand curve for services like preventive care would be more inelastic (i.e., less sensitive to price changes), if consumers were perfectly informed about the expected benefits of the service and did not undervalue future benefits (Frick & Chernew, 2009; Newhouse, 2006). To the extent that lower out-of-pocket prices promote consumption in these circumstances, they move the market closer to, not farther from, optimality.

Newhouse (2006), an investigator on the RAND HIE which initially seemed to validate the conventional moral hazard theory, more recently supported a subsidy for lower cost sharing to promote use of health services that reduce employers' labor costs. This conclusion recognizes the potential of beneficial moral hazard in the presence of externalities (Newhouse, 2006). Even Pauly, who popularized the relevance of moral hazard to health insurance, acknowledged its limits when consumers undervalue certain types of care: if patient demands fall short of informed demands, value-based cost sharing can be superior to just providing information (Pauly & Blavin, 2008). This revised view

supports the potential of beneficial moral hazard when the actual demand curve is more elastic than a perfectly informed demand curve would be.

To the extent that cost sharing dissuades consumption of medically necessary, cost-effective care, it may result in welfare loss. The purpose of this dissertation was to evaluate evidence for this loss in the context of community-dwelling HF patients with Medicare Part D. Specifically, the study hypotheses defined above reflect the third scenario of beneficial moral hazard: the ideal, "fully informed" demand curve for high-value preventive care is more inelastic than the actual, "misinformed" demand curve (Figure 1.1). Therefore, lower out-of-pocket prices theoretically move consumption toward the optimal quantity of care defined by the fully informed demand curve (Frick & Chernew, 2009). This study hypothesizes that higher prices deter use of high-value care (i.e., recommended prescription drugs for chronic HF), resulting in welfare loss in the form of increased HF-specific acute care use and higher inpatient and total medical costs.

Research Methods

Study design and data source. This dissertation was a retrospective, cross-sectional study using a data set from the Medicare Current Beneficiary Survey (MCBS). The MCBS comprises in-depth questionnaires of personal health and financial information that are matched when possible to administrative and claims data from CMS (Cubanski, Swoope, Damico, & Neuman, 2014; CMS, 2016). The stratified, cluster sample is designed to be representative of the national Medicare population, with oversampling of distinct population subgroups, e.g., under age 65 and over age 85 (Briesacher, Tjia, Doubeni, Chen, & Rao, 2012). The sample is derived from a random selection of metropolitan statistical areas and non-metropolitan county clusters, from

Conceptual framework

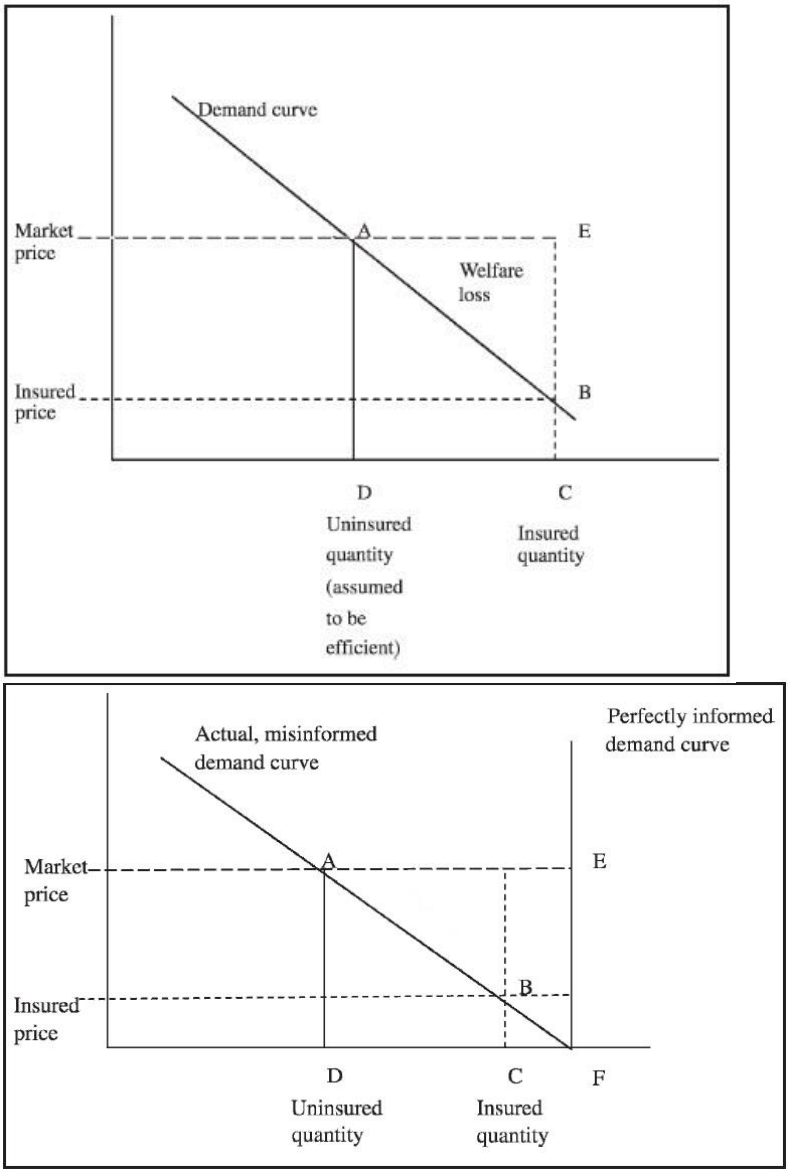

Figure 1.1. Conventional view of moral hazard in health insurance (above), and one scenario of "beneficial moral hazard" (below). Price is on the Y-axis; quantity of care used is on the X-axis. The insured quantity in the lower panel is closer to the fully informed demand curve than the uninsured quantity. Lower prices yield less under-consumption, reducing the size of the welfare loss from triangle ADF to triangle BCF. Adapted from Frick & Chernew (2009).

which a random sample of ZIP codes is drawn, within which individual Medicare beneficiaries are randomly selected for recruitment (Briesacher et al., 2012).

MCBS employs a rotating panel design: a new probability sample is recruited annually, and data from each sample are collected at three time points yearly for four years (DiMartino, Shea, Hernandez, & Curtis, 2010). Interviewers use a software program to collect questionnaire data, and they request participants to bring all billing documents and prescription containers to the interview (Lopert et al., 2012). Health care encounters reported in the survey are linked to Medicare Parts A, B, and D records through a reconciliation process (CMS, 2016). About 75% of prescriptions in the MCBS also appear in the Medicare records among participants with continuous Part D coverage during the survey year. According to an independent analysis, 11% of the remaining prescriptions were obtained outside the Medicare plan (e.g., from the Department of Veterans Affairs), and many of the rest could be matched to existing Part D records using a more sensitive algorithm (Stuart, 2013).

MCBS data are divided into two distinct but overlapping modules: Access to Care and Cost & Use. This study analyzed Cost & Use files, which contain a broad range of information about the provision of and payment for health care services. Three years of data were requested (with the initial intent to look at time trends), and the most recent years available at the time of the data request were 2010 through 2012. The average annual response rate was 62% during this period (CMS, 2016). The overall data set consisted of 32,941 person-year records. Each record has sampling weights to account for unequal probabilities of selection due to the complex sample design; the weights also adjust for non-response and post-stratification (Briesacher et al., 2012).

Sample specification. This study analyzed records for community-dwelling adults with self-reported HF and continuous Part D coverage. Participants who answered "yes" when asked "Has a doctor ever told you that you had congestive heart failure?" or "Since [12 months ago], has a doctor told you that you had congestive heart failure?" (depending on the interview round) met the definition of HF for this study. A claims-based definition was considered, but it would have required excluding Medicare Advantage (MA) subscribers—about one-third of Medicare beneficiaries overall—since MA plan sponsors do not report complete encounter data for Parts A- and B-covered services to CMS (Cubanski et al., 2014). It also would have biased the sample for Aim 2, because the outcomes were specified using the same claims records. (Participants who met the inclusion criteria would have been likelier to experience the outcome, by definition.) An interrater agreement analysis of the questionnaire item and a claims-based approach to defining a HF cohort in MCBS data (DiMartino et al., 2010) returned an unweighted kappa statistic of .40 for Part D enrollees, suggesting fair to moderate agreement between the sample selection methods (McHugh, 2012).

The analysis sample was restricted to participants with Part D coverage in every month of the survey year, because pharmacy plan cost-sharing structures could not be observed directly, so average out-of-pocket payment for prescriptions in the presence of continuous Part D coverage was assumed to approximate cost sharing. In addition, only prescriptions in the Medicare records contain complete transaction data (including days supplied, which is essential for adherence estimation), and these records were only available for Part D enrollees (Roberto & Stuart, 2014). About 60% of participants satisfied this criterion. The sample also included just the participants identified in the

survey as “community-dwelling” for the entire year, because residents of facilities may not be responsible for acquiring or taking their own medications (S. Y. Chen et al., 2014). In addition, the health status segment of the survey (including the HF question) was altered for facility-dwelling participants. Approximately 9% of Part D enrollees were excluded for living in a facility.

Variables of interest. Part D plans vary in design, which complicates operationalization of prescription cost sharing. Three in five Part D enrollees hold standalone pharmacy plans, while the rest access pharmacy benefits through a bundled MA product (Hoadley, Cubanski, & Neuman, 2016). Although the annual deductible is capped (at $360 in 2016), it varies from plan to plan, and some plans have no deductible (Hoadley et al., 2016). The so-called doughnut hole triggers a lapse in drug coverage between certain benefit amounts, after which catastrophic coverage kicks in (Eapen et al., 2013; Li et al., 2012). Medicare beneficiaries may also qualify for Medicaid or purchase supplemental coverage, and 29% of Part D enrollees receive the LIS to offset costs (Hoadley et al., 2016). This variation means that drug copay at a single point in time may not reflect the typical cost to the beneficiary. Therefore, this study used average out-of-pocket payment per prescription, standardized to a 30-day supply, as a proxy for cost-sharing liability (Cole et al., 2006; Patterson et al., 2011).

Prescriptions were considered HF-related if the First Databank generic drug name in the record corresponded to an ACE inhibitor, angiotensin-receptor blocker (ARB), β blocker, diuretic, aldosterone antagonist, or cardiac glycoside. Hydralazine and isosorbide (dinitrate or mononitrate) were also included if they were prescribed in a combination formulation or both were filled separately within the same calendar year.

Ocular β blockers were excluded. Direct renin inhibitor aliskiren was also excluded, unless combined in a single formulation with an included drug, due to unfavorable clinical trial results that may have affected prescribing behavior (McMurray, Dickstein, & Kober, 2016). First-in-class agents sacubitril and ivabradine were not yet on the market during the study period.

Adherence was approximated with the medication possession ratio (MPR), which Peterson et al. (2007) define as the total days supplied with a prescription divided by the number of days between the first and last fills during the observation period (less the days' supply from the last fill). MPR is distinct from the commonly used Proportion of Days Covered (PDC) metric in allowing the size of the denominator (i.e., the observation period) to vary, which is important when prescriptions may be discontinued by the prescriber (Peterson et al., 2007). Extreme MPR values (<20% and >120%) were discarded, to focus on stable use and maximize comparability with the prior study most similar in aims to this one (Cole et al., 2006). Other studies truncate MPR at 100%, but that approach often does not produce normally distributed values, and linear regression was anticipated for this analysis to maximize interpretability of effects (see below). For categorical analysis, MPR was dichotomized into ≥80% for adherent and <80% for non-adherent (S. Y. Chen et al., 2014; Nair et al., 2010; Patterson et al., 2011; Zhang et al., 2010).

MPR was computed independently for each of three commonly prescribed drug classes in chronic HF: β blockers, ACE inhibitors, and ARBs. According to American College of Cardiology Foundation and American Heart Association guidelines, all symptomatic HF patients with reduced ejection fraction should be prescribed a β blocker

and either an ACE inhibitor or an ARB unless contraindicated (Yancy et al., 2013). In practice, these agents are often prescribed for patients with preserved ejection fraction, too, and the prescriber is unlikely to discontinue then restart them (compared to diuretics, for example). Therefore, refill consistency is a reasonable proxy for adherence in these drug classes. Participants who switched drugs within a class were excluded for this calculation to avoid overestimating adherence from the medication supply still on hand from the terminated prescription (Cole et al., 2006; Kim et al., 2011).

HF-related hospitalizations were identified by inpatient events that contained a principal or secondary diagnosis of HF, based on International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 428.xx, 402.x1, 404.x1, or 404.x3 (DiMartino et al., 2010). Total days hospitalized was the sum of the length of all HF-related hospital stays during the year (from admission to discharge dates, inclusive). Hospital stays that straddled the calendar year were retained, because they represented <1% of admissions. HF-related ED visits were identified by outpatient events with a reported event type of "ER" and a principal or secondary diagnosis corresponding to one of the ICD-9-CM codes listed above. This method only identified ED visits not resulting in admission to the hospital, but those encounters should have been captured in the inpatient events. Diagnosis-Related Groups (DRGs) were considered instead of ICD-9 codes, but contributing conditions for DRGs are not specified in the MCBS, and HF is frequently an underlying contributor to other diagnoses such as pulmonary edema or renal failure. Therefore, ICD-9 codes were used to capture secondary diagnoses.

Cost outcomes consisted of total amount spent per participant per year: (a) on all health care services by all payers, (b) on all inpatient services by all payers, (c) on all

health care services by Medicare, and (d) on all inpatient services by Medicare. These payments from the MCBS summary files covered health services for all diagnoses, not just HF, which allowed the estimation of cost effects more broadly. For beneficiaries with incomplete survey participation, a contractor at the University of Chicago imputed missing payments for non-Medicare-covered services; payments for Medicare-covered events were available in the claims (CMS, 2016). All monetary values were converted to 2012 dollars for this study using the Consumer Price Index for All Urban Consumers to account for general price inflation.

Analysis plan. All study variables were summarized with estimates and standard errors for population-level descriptive statistics, and plots were created to visualize relationships before inferential statistical procedures were performed. Data were analyzed primarily with SAS version 9.4, using procedures that compute standard errors with Taylor-series linearization to account for stratification and clustering in the survey design (Heeringa, West, & Berglund, 2010; Lewis, 2017). However, single-cluster strata occurred in the analysis for Aim 2, in which case SAS either arbitrarily collapses strata or assigns all variance estimates for those strata to zero (X. Chen & Gorrell, n.d.). Therefore, logit models for Aim 2 were built instead with SAS-callable SUDAAN version 11, which estimates variance for single-cluster strata as the squared difference between the stratum mean and the overall mean (X. Chen & Gorrell, n.d.). Stata version 15.1 was used to build the Poisson, negative binomial, and gamma log-link models required for Aims 2 and 3 (see below), because SAS and SUDAAN cannot adjust most of these models for complex survey designs (Heeringa et al., 2010). Observations from all three years were pooled, and a weighted average of the sampling weights (i.e., the sum of

the cross-sectional weights divided by number of years in the survey) was applied (Briesacher et al., 2012). Multivariate analysis adjusted for the effects of several sociodemographic and health status characteristics, which will be described separately for each specific aim in the subsequent chapters.

Specific Aim 1. Ordinary least squares regression was used to model the relationship between mean out-of-pocket payment per prescription, as a proportion of average monthly income, and MPR for each drug class. Logistic regression was used to model the probability of non-adherence (MPR < 80%) for each drug class. In the interest of parsimony, models were built with a purposeful variable selection approach (Bursac, Gauss, Williams, & Hosmer, 2008; Heeringa et al., 2010). That approach was a main reason for scaling out-of-pocket payments by income, in case income was not retained as a covariate in the final models. The MCBS income variable included Social Security, retirement account, and pension payments to the participant and his or her spouse (CMS, 2016). In addition, since the LIS was expected to alter refill behavior, participants who received the LIS at any point during the survey year were excluded from this analysis (S. Y. Chen et al., 2014).

Specific Aim 2. Mean out-of-pocket payment per HF prescription, standardized to a 30-day supply, was calculated irrespective of drug class. Parsimony in variable selection was a lower priority, because SUDAAN and Stata handle single-cluster strata more flexibly than SAS (X. Chen & Gorrell, n.d.; UCLA: Statistical Consulting Group, n.d.), so variables with missing data were less problematic. Therefore, theory and prior research drove covariate selection, and income was included as a covariate in all the models rather than serving as a scalar for out-of-pocket spending. This analysis excluded

MA participants, because MA plan sponsors do not report complete encounter data to CMS for Parts A- and B-covered services (Cubanski et al., 2014). Since the identification of HF-related hospitalizations and ED visits depended on using those claims, the outcomes would have been underreported for over one-third of the sample.

Logistic regression modeled the effect of drug spending on odds of HF-related hospital admission and ED visit. Poisson regression modeled the effect on hospitalization rate. Due to evidence of over-dispersion (i.e., the variance of the dependent variable was significantly greater than its mean), negative binomial regression modeled the effect on rate of days hospitalized (Hayat & Higgins, 2014). A sensitivity analysis with zero-inflated versions of the Poisson and negative binomial models was carried out, because HF-specific hospitalization in the survey year was somewhat rare (Hayat & Higgins, 2014). Finally, an interaction between out-of-pocket drug spending and Medicaid eligibility was hypothesized because, in bivariate analysis, participants with very low cost sharing appeared to be distinct from the rest of the sample in terms of HF-specific inpatient use, and Medicaid eligibility was the starkest difference between these two groups. This interaction was also meaningful, because LIS recipients were retained for this analysis (in contrast to Aim 1) in the interest of maximizing effective sample size in the absence of MA plan subscribers, and all LIS recipients were also Medicaid-eligible.

Specific Aim 3. This aim required the construction of generalized linear models with a log link function and a gamma-family distribution. This type of model is common with cost outcomes, which are never negative and frequently right-skewed (Basu, Manning, & Mullahy, 2004). This analysis retained MA subscribers, because the cost variables were not diagnosis-specific and therefore did not depend on the claims records.

An interaction between prescription drug spending and LIS status was hypothesized, analogous to the Medicaid interaction for Aim 2. (LIS status was chosen instead of Medicaid *a priori* to promote consistency with prior research on prescription cost sharing in Part D, although there is substantial overlap between the two groups.) Finally, the effects of both average spending per prescription and total prescription spending for the year were modeled independently.

Protection of human subjects. CMS supplied the relevant data files and documentation under the auspices of a data use agreement for this study. The Emory University Institutional Review Board approved this study with a waiver of additional informed consent documentation. This study met federal regulations defining minimal risk: "The probability and magnitude of harm or discomfort … are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" [§46.102]. All analysis for this investigation was performed on data already collected as part of the MCBS; no additional subjects were recruited, and no prospective data were collected. MCBS data files are Limited Data Sets, which means they exclude most direct personal identifiers specified by the Health Insurance Portability and Accountability Act (CMS, 2017). In addition, no publications or presentations from this study will include cell sizes of fewer than 11 cases, in compliance with CMS policy (Mburu, 2017). Finally, all study data were stored in a password-protected folder on a secure server at the Emory University Rollins School of Public Health.

Summary

Heart failure (HF) is a leading cause of hospitalization and a costly burden on the

health care system. Treatment adherence can prevent complications and costly acute care use. Previous studies show that prescription drug cost sharing has a negative effect on adherence—and potentially adverse effects on service use and health care costs—in various chronic disorders. Yet, these effects are not well understood in HF, much less among HF patients in Medicare. This dissertation used data from the Medicare Current Beneficiary Survey to evaluate these effects, guided by Frick and Chernew's conceptual framework of beneficial moral hazard. The following chapters take the form of three scientific manuscripts, addressing the associations between (1) average out-of-pocket payment and refill adherence for three drug classes commonly prescribed for HF; (2) average out-of-pocket payment per HF-related prescription and HF-specific acute care use; and (3) out-of-pocket payments for HF prescriptions and medical costs incurred by all payers and by Medicare. The concluding chapter considers the results in light of the conceptual framework, study methods, and prior research. These results have the potential to inform ongoing discussions about optimal prescription cost sharing in HF and other chronic diseases.

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CHAPTER 2

Prescription Drug Spending and Medication Adherence in Heart Failure

Abstract

Background. Evidence suggests that cost sharing adversely affects appropriate prescription drug use for chronic disorders. However, few studies have evaluated this effect in heart failure (HF), the most common cause of hospitalization in Medicare. **Objective.** To determine whether spending on HF pharmacotherapy by community-dwelling patients with Medicare Part D was associated with prescription refill adherence. **Methods.** Cross-sectional analysis of Medicare Current Beneficiary Survey data from 2010-12. **Results.** Risk-adjusted models showed that percent of monthly income spent on a β blocker was associated with odds of non-adherence, odds ratio = 1.41, 95% CI [1.01, 1.98], $p = .046$, and inversely associated with medication possession ratio, $B = -3.63$, $SE = 1.57$, $p = .022$. No association was observed for ACE inhibitors or angiotensin receptor blockers. **Conclusions.** Price sensitivity was evident for β blockers, but not anti-angiotensin drugs, despite very low out-of-pocket costs and high adherence. This study is relevant to the growing use of costly new products in HF management.

Keywords

Heart failure, cost sharing, medication adherence, Medicare Part D

Introduction

Health insurers use deductibles, copays, and/or coinsurance to discourage inappropriate use of prescription drugs, but this practice may reduce appropriate use as well. Studies have shown that patients with chronic diseases who have high medication cost-sharing requirements are less likely to fill the prescriptions they need to manage their illness (Barron, Wahl, Fisher, & Plauschinat, 2008; Chen et al., 2014; Cole, Norman, Weatherby, & Walker, 2006; Colombi, Yu-Isenberg, & Priest, 2008; Doshi, Zhu, Lee, Kimmel, & Volpp, 2009; Goldman, Joyce, & Karaca-Mandic, 2006; Kim et al., 2011; Li, McElligott, Bergquist, Schwartz, & Doshi, 2012; Patterson, Blalock, Smith, & Murray, 2011; Thornton Snider, Seabury, Lopez, McKenzie, & Goldman, 2016). Emerging evidence also links medication cost-sharing level to downstream health care use and costs (Cole et al., 2006; Colombi et al., 2008; Goldman et al., 2006; Park et al., 2015; Subramanian, 2011; Thornton Snider et al., 2016). However, the impact of cost sharing on medication adherence has not been well characterized for patients with heart failure (HF), which afflicts an estimated 5.8 million people in the United States (American Heart Association, 2017).

HF is the most common reason for hospital admission among Medicare beneficiaries and costs society over $30 billion annually (Heidenreich et al., 2011; Pfuntner, Wier, & Stocks, 2013). Survival with HF depends on adherence to a burdensome daily regimen of multiple prescription drugs, dietary restrictions, and self-monitoring (Marti et al., 2013). Lack of adherence to prescribed medication regimens may lead to worsening symptoms, hospitalization, and poorer outcomes, whereas optimal adherence lowers the risks of hospital admission, emergency care, and death (Esposito,

Bagchi, Verdier, Bencio, & Kim, 2009; Marti et al., 2013; Wu, Lennie, Dekker, Biddle, & Moser, 2013). Therefore, factors that impede adherence should be minimized. The purpose of this study was to assess whether medication adherence was associated with cost sharing in prescription drug plans among Medicare beneficiaries with HF.

We focused on three classes of drugs commonly used in HF management: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and β blockers. These agents are recommended for routine use in most patients with reduced ejection fraction (EF) and many with preserved EF (Caboral-Stevens, 2014), so infrequent refills were likely to reflect poor adherence rather than prescriber interruption. Although β blockers and ACE inhibitors now carry low out-of-pocket costs, brand-name β blockers were more common at the time of data collection, and some ARBs had sizable copays. Therefore, this analysis is relevant to the growing use of costly new products such as sacubitril and ivabradine in HF management.

Methods

Sample selection. We conducted a secondary analysis of 2010-12 pooled data from the Medicare Current Beneficiary Survey (MCBS) Cost and Use files. The MCBS matches health questionnaire responses to Medicare claims data in a representative sample of the national Medicare population (Lopert et al., 2012; U.S. Centers for Medicare and Medicaid Services [CMS], 2016). The average response rate for 2010-12 was 62.3% (CMS, 2016). Participants were included in this study if they replied "yes" on the survey when asked, "Has a doctor (ever) told you that you had congestive heart failure?" Use of Medicare claims to identify HF cases would have underrepresented Medicare Advantage (MA) participants, because MA plan sponsors do not report

complete encounter data to the Centers for Medicare & Medicaid Services (CMS) (Cubanski, Swoope, Damico, & Neuman, 2014).

Analysis was restricted to participants with Part D coverage in every month of the survey year, because only Medicare-covered prescription drug records have complete transaction data (Roberto & Stuart, 2014) (Figure 1). In addition, only community-dwelling participants were included, because residents of facilities may be given their medications directly by staff (Chen et al., 2014). Finally, recipients of the Low-Income Subsidy (LIS) for Part D cost-sharing assistance were excluded, because LIS results in negligible out-of-pocket spending on prescriptions, which could have altered beneficiaries' refill behavior (Chen et al., 2014).

Study variables. We computed the mean out-of-pocket payment for each medication, standardized to a 30-day supply (Cole et al., 2006; Patterson et al., 2011). (MCBS does not report the specific cost sharing requirements of Part D plans.) This figure was then divided by the participant's average monthly income, which included Social Security, pension, and retirement account payments for the participant and his or her spouse. The resulting proportion was multiplied by 100 to express beneficiaries' out-of-pocket liability for each medication as a percentage of income.

Adherence was estimated by the medication possession ratio (MPR), defined as the total days supplied for all but the last refill divided by the number of days between the first and last fills in each year (Peterson et al., 2007). MPR values were expressed as percentages for ease of interpretability. Consistent with prior research, MPRs below 20% and above 120% were discarded, since our goal was to analyze stable use, not up-titrations or very infrequent use (Cole et al., 2006). Also consistent with prior studies,

MPR was dichotomized into <80% (non-adherent) and ≥80% (adherent) for categorical analysis (Chen et al., 2014; Patterson et al., 2011).

Sociodemographic covariates included sex, race, Latino ethnicity, highest degree obtained, marital status, income, Census region, urbanicity, MA plan enrollment, and age. Health-related covariates included self-rated health status compared to others the same age and compared to one year prior (with higher scores reflecting worse health), body mass index (BMI), smoking status, self-reported type 2 diabetes, difficulty walking 2-3 blocks or ¼ mile, and basis for Medicare entitlement (disability or renal disease compared to age only).

Data analysis. We tested associations between MPR and out-of-pocket spending independently for β blockers, ACE inhibitors, and ARBs. Participants who switched medications within the same drug class were excluded from the analysis of that class, because leftover supply of the discontinued drug would have inflated adherence estimates (Cole et al., 2006; Kim et al., 2011). This resulted in exclusion of 7.1% of participant-year records for β-blockers, 2.8% for ACE inhibitors, and 10.9% for ARBs. Participants who filled the prescription only once during the year of observation were also excluded, because at least two fills are necessary to compute the MPR (Peterson et al., 2007). About 6.9% of records for β-blockers, 7.0% for ACE inhibitors, and 15.2% for ARBs were excluded for this reason.

Potential covariates were screened for associations with the MPR for each class. If an association with a significance of $p < .25$ was detected, then that covariate was included in the corresponding model (Bursac, Gauss, Williams, & Hosmer, 2008; Heeringa, West, & Berglund, 2010). Logistic regression was used to model the effect of

out-of-pocket spending on dichotomized MPR, and ordinary least squares (OLS) regression was used for the effect of spending on absolute MPR value. Standard errors were estimated with Taylor-series linearization to account for the complex sample design (Heeringa et al., 2010). Linearity in the logit was tested with interactions between the continuous predictors and their logarithms, and categorical predictors were cross-tabulated to ensure adequate cell counts (Field, 2013). Log-likelihood statistics were not computed due to violation of their assumptions by the complex sample design (Lewis, 2017). OLS models were evaluated for departures from homoscedasticity and independence of the residuals. In both model types, multicollinearity was assessed with variance inflation factors.

CMS provided sampling weights for each participant record to account for unequal selection probabilities, post-stratification, and nonresponse (Briesacher, Tjia, Doubeni, Chen, & Rao, 2012). For participants with multiple years of data, we applied a weighted average of their cross-sectional sampling weights, because exclusion of multi-year participants in pooled analysis of MCBS data is not recommended (Briesacher et al., 2012). A sensitivity analysis was conducted without the participants who died during their year of observation. Data were analyzed with SAS version 9.4. The Emory University Institutional Review Board approved this study.

Results

Sample characteristics. The final sample consisted of 797 participant-year records (derived from 543 unique patients). Of these, 462 (58%) were retained for the β-blocker analysis, 360 (45%) for the ACE inhibitor analysis, and 122 (15%) for ARBs (Figure 1). The sample was about equally divided between men and women (Table 1).

Accounting for sampling weights, 12% of respondents identified a racial group other than white, and 7% identified as Hispanic or Latino. The weighted median age was 75.7 years, about five years older than the parent MCBS sample.

With respect to health status measures, 53% rated their health as fair or poor compared to others the same age, 41% said their health was worse than one year earlier, and 53% were unable to walk a quarter mile or 2-3 blocks or could do so only with "a lot" of difficulty. About 68% reported ever smoking cigarettes, cigars, or tobacco, and 30% reported having been told they have type 2 diabetes. Based on BMI, which was computed using reported height and weight, 36% of respondents were obese, and a further 33% were overweight.

Average out-of-pocket spending on the three drug classes analyzed was low, even though the sample did not include LIS recipients: median expenditure standardized to a 30-day supply was $4.00 for β blockers, $3.59 for ACE inhibitors, and $13.30 for ARBs. In most cases, these amounts were well under 1% of the participant's average monthly income, the median of which was $2,201. Adequacy of drug supply obtained was high, on average. Median MPR was 95% for β blockers and ACE inhibitors, and nearly 98% for ARBs.

Multivariate analysis. Logistic models of the adjusted odds of ACE inhibitor and ARB non-adherence (i.e., MPR < 80%) showed no significant effect from out-of-pocket spending as a share of income. In the logistic model for β blockers, on the other hand, the adjusted odds of non-adherence were significantly associated with the share of income spent on that β blocker, odds ratio = 1.41, 95% CI [1.01, 1.98], $p = .046$ (Table 2). Similarly, the OLS models for ACE inhibitors and ARBs showed no significant

association between adherence and prescription drug spending as a share of income. In the OLS model for β blockers, there was a significant inverse association between share of income spent on the β blocker and MPR, B = -3.63, SE = 1.57, p = .022 (Table 3). Exclusion of the nine respondents who died during their respective observation year did not alter the effect estimates (data not shown).

Discussion

Percent of income spent on a β-blocker prescription was associated with the odds of non-adherence and lower adherence scores among Part D enrollees with HF. This finding corroborates an earlier study in a commercially insured HF sample that found significantly increased odds of non-adherence for β-blocker copays over $20 (Patterson et al., 2011). It must be interpreted with caution, however, because most participants spent far less than 1% of monthly income on their β-blocker prescription. Assuming a linear relationship, an increase of 0.1 in percent of income spent (equivalent to a shift from the 25th to 50th percentiles in this sample) was associated with 4% increased odds of non-adherence. The same increase in spending was associated with an average decline of 0.4 in the MPR.

No association was found between out-of-pocket spending and adherence for ACE inhibitors or ARBs. It is unclear why this effect was observed for β blockers and not anti-angiotensin drugs, but adherence to the latter was slightly higher overall: three-quarters of the sample had enough drug supply to cover 85% of days observed for ACE inhibitors and 90% for ARBs, compared to 82% for β blockers. There may not have been enough variation in anti-angiotensin adherence to detect a significant effect. The only other published study of spending and adherence for ACE inhibitors in HF found that a

$10 rise in copay predicted a significantly decreased MPR, but that study was published 12 years ago (Cole et al., 2006). Most ACE inhibitors are now available off patent and appear on $4 lists at major pharmacies. Although median spending was comparable for ACE inhibitors and β blockers in this sample, β-blocker spending varied more widely, rising to a maximum of $85.00 (compared to $42.32 for ACE inhibitors).

One reason for the wider range of spending and adherence with β blockers may have been the greater use of brand-name products. Carvedilol was the agent prescribed to 35% of the β-blocker subsample. Generic carvedilol was not first labeled for chronic HF use until midway through the data collection period (Raymond, 2017), and the controlled-release formulation is still brand-name only. Therefore, this agent may have been on higher-cost tiers in some Part D plans. In addition, β blockers are often prescribed after initiation of anti-angiotensin drugs, so patients may have already spent disposable income on ACE inhibitors or ARBs. With prevalent use of multiple drugs—64% of β-blocker users also filled prescriptions for anti-angiotensin drugs, for example—spending on other drug classes could have affected β-blocker adherence.

Average out-of-pocket payment was five times higher for ARBs than for β blockers, but the smaller ARB subsample could have made any effect between spending and adherence more difficult to detect. Also, ARBs are frequently prescribed when patients cannot tolerate ACE inhibitors. If patients have fewer options, they are less likely to be price-sensitive even when the price is high. Indeed, median MPR was highest for ARBs in this sample, indicating good adherence despite greater out-of-pocket costs. Furthermore, the patient and prescriber may discuss the relative prices of ARBs and ACE inhibitors in advance. If patients who cannot afford an ARB do not get a prescription in

the first place, they would not appear in the Part D records. This form of sample selection may have affected the ARB analysis.

As with any observational study, an unobserved or omitted variable may account for the association between β-blocker spending and adherence, and the possibility of a spurious association cannot be ruled out. One possible non-economic reason for this finding is side effects. Common side effects of the β blockers indicated for chronic HF use include fatigue, weakness, and erectile dysfunction (Vallerand, Sanoski, & Deglin, 2017), which could have interfered with adherence. If these effects varied by drug price, then the models may have ignored a source of confounding. ACE inhibitor side effects, on the other hand, are likely to prompt discontinuation and substitution with an ARB, which would not have appeared as non-adherence in the analysis.

Incidental findings from this analysis warrant further investigation. When running statistical tests on a complex sample, a subpopulation variable is specified (rather than sub-setting the data) so that all subjects contribute sample design information to variance estimation (Heeringa et al., 2010). In this study, the output for the parent MCBS sample showed that percent of income spent was associated with the unadjusted odds of non-adherence for ACE inhibitors and ARBs as well as β blockers. These agents are used for multiple conditions other than HF, including hypertension and coronary heart disease. It may be that the clinical severity of HF attenuates any association between spending and adherence, but further analysis (including risk adjustment) is needed.

Implications. To our knowledge, this study is the first published attempt to address the question of cost sharing and adherence related to HF drugs in the Medicare population. It is also the first to study this issue with population-level survey data. The

MCBS is powerful, because it combines detailed interviews with verifiable events in CMS records, and it is representative of Medicare beneficiaries nationally. Therefore, our findings can be generalized to community-dwelling Medicare patients with self-reported HF and continuous Part D coverage (without the LIS). Moreover, this study demonstrates that analysis of MCBS data is a viable option for investigating cost sharing and adherence in the Medicare population generally.

If out-of-pocket spending indeed predicts non-adherence to β blockers in this population, then limits on patient liability for β blockers relative to income may increase efficiency, should costs rise. That is because adherence to HF treatment is associated with fewer hospitalizations (Esposito et al., 2009; Marti et al., 2013), longer cardiac event-free survival (Wu et al., 2013), and lower cumulative Medicare spending (Lopert et al., 2012). Moreover, copay-attributable non-adherence has been linked to increased risk of hospitalization in HF (Cole et al., 2006). In addition, the potential cost-effectiveness of full drug coverage has been demonstrated for medications in other cardiovascular disorders, especially post-infarction coronary heart disease (Choudhry, Patrick, Antman, Avorn, & Shrank, 2008; Ito et al., 2015). Similar economic analyses in the HF population are warranted.

This study is relevant to ongoing discussions about cost sharing in health care generally. The Patient Protection and Affordable Care Act (ACA) prohibited cost sharing for 18 preventive health services in adults, but not for secondary prevention such as chronic disease management drugs (ACA, 2010). The ACA also provides for cost sharing subsidies to low-income persons in some non-group plans (Rae, Claxton, & Levitt, 2017), but at the time of this writing, continued funding for those subsidies was the subject of

litigation and Senate debate (Goldstein, 2017; Pear, 2017). The future of cost sharing for pharmacotherapy in chronic diseases remains uncertain, and there is scope for further research to inform policy development.

Limitations. An important limitation of this study was its cross-sectional design. Since prescription drug spending and adherence estimates were averaged over the survey year, non-adherent behavior could have occurred before the observed out-of-pocket drug expenses. This problem of temporality limits any causal inference that can be made. Also, MPR estimates were not adjusted for observation time, so there was less opportunity to observe non-adherence in participants with shorter intervals between the first and last prescription fills.

Identification of HF cases with a single questionnaire item may have missed respondents who were unaware of or poorly understood their diagnosis. Selection bias may also have resulted from requiring at least one prescription fill to get out-of-pocket payment data and two fills of the same agent to compute the MPR, because this implies a minimum level of adherence (Patterson et al., 2011). In addition, Part D enrollees may choose health plans with higher coverage of the drugs that they already use, which would have biased results toward the null hypothesis. Exclusion of participants who switched drugs within a class during the survey year would have obscured any cost-sharing effect that contributed to the switch, but again, including them would have overestimated adherence due to leftover supply of the discontinued drug.

No clinical data on EF or HF class were available, so it was difficult to assess whether advancing illness made patients less price-sensitive. The analysis did not include comorbidities other than type 2 diabetes, because few relevant diagnoses were available

from the questionnaire (and using claims would have required excluding MA enrollees). The analysis also assumed that out-of-pocket spending on one drug class was independent of spending on another, yet there was substantial use of multiple drug classes. For instance, 64% of β-blocker users also filled anti-angiotensin prescriptions, so the β-blocker cost-sharing effect may have depended partly on ARB or ACE inhibitor spending.

Pooling data from multiple years could have underestimated standard errors due to autocorrelation, because observations from participants who contributed data in multiple years were not independent. Nonetheless, when variance estimates account for cluster sampling, it may be unnecessary to correct for additional autocorrelation from repeated observations (Briesacher et al., 2012). Finally, we excluded survey-reported prescriptions that were not matched to Medicare records. Although this may have biased spending and adherence estimates, only about 6% of unmatched prescriptions among Part D enrollees reflect true out-of-plan use for common chronic disease medications; many of the rest are likely duplicates (Roberto & Stuart, 2014).

Conclusions

Despite having Part D drug coverage, some Medicare beneficiaries may have faced a modest financial barrier to optimal HF therapy: β-blocker adherence was inversely related to out-of-pocket β-blocker spending as a percent of income in this study. Similar associations were not observed for ACE inhibitors or ARBs, possibly because of the sequence of prescribing or differences in generic availability. Yet the β-blocker finding is notable because HF is a common cause of hospitalization, for which β-blocker use reduces the risk. In addition, this finding has implications for newer products in HF

management that may carry higher out-of-pocket costs. Future research should use longitudinal data and address utilization to determine whether lower drug cost sharing encourages adherence and reduces poor outcomes in HF.

Table 2.1. *Sample characteristics, community-dwelling Part D enrollees with self-reported heart failure in the Medicare Current Beneficiary Survey, 2010-12*[a]

Variable		**Count** (unweighted)	**Percent** (weighted)	**95% CI** (design-adjusted)	
TOTAL		797	100.00	---	---
Gender					
	Male	402	50.85	45.37	56.34
	Female	395	49.15	43.66	54.63
Race					
	Non-white[b]	90	11.82	8.98	14.65
	White	705	88.18	85.35	91.02
Ethnicity					
	Latino	49	7.29	4.23	10.35
	Non-Latino	747	92.71	89.65	95.77
Education					
	None	≤10	---	---	---
	Nursery-8th grade	91	10.93	7.51	14.35
	9th-12th grade	140	16.27	12.17	20.38
	High school diploma	244	31.01	26.12	35.89
	Vocational/tech.	55	7.07	4.73	9.40
	Some college	116	15.34	11.46	19.22
	Associate's degree	29	3.91	1.96	5.87
	Bachelor's degree	73	10.46	7.26	13.66
	Post-graduate	43	4.59	2.75	6.43
Marital status					
	Married now	426	56.25	51.15	61.35
	Married previously	355	41.57	36.61	46.53
	Never married	16	2.18	1.03	3.34
Urbanicity					
	Metropolitan area	559	72.12	67.78	76.46
	Non-metro. area	238	27.88	23.54	32.22
Region					
	Northeast	115	15.35	11.63	19.06
	Midwest	204	24.50	20.82	28.18
	West	118	16.34	11.91	20.77
	South or Puerto Rico	360	43.82	38.89	48.75
Health vs. others the same age					
	Excellent	44	5.61	3.28	7.93
	Very good	134	15.30	12.11	18.50
	Good	263	33.37	29.12	37.61
	Fair	242	31.08	27.08	35.08
	Poor	108	14.64	11.35	17.93
Health now vs. one year ago					
	Much better	44	5.66	3.72	7.61
	Somewhat better	98	12.71	10.01	15.41
	About the same	367	45.74	41.82	49.66
	Somewhat worse	238	29.88	26.27	33.49
	Much worse	48	6.00	4.05	7.96

Difficulty walking ¼ mile or 2-3 blocks					
	None	181	23.80	19.32	28.27
	A little	89	11.07	8.36	13.78
	Some	95	12.23	9.81	14.65
	A lot	135	16.43	13.42	19.44
	Unable	292	36.48	31.63	41.32
Ever smoked cigars/ cigarettes/tobacco					
	Yes	553	67.82	62.96	72.68
	No	264	32.18	27.32	37.04
Ever told they had type 2 diabetes					
	Yes	229	29.92	26.10	33.74
	No	566	70.08	66.26	73.90
Medicare eligibility					
	Disability/ESRD	63	12.30	8.46	16.14
	Age only	734	87.70	83.86	91.54
Benefit type					
	Medicare Advantage	362	47.73	43.00	52.46
	Fee-for-service	435	52.27	47.54	57.00

Variable	**Median**	**Interquartile range**		**Mean**	**SE**
Age (in years)	75.70	68.84	82.18	75.80	0.54
Annual income[c]	$26,412	$18,343	$38,886	$33,427	1472.14
Body mass index	27.87	24.22	31.86	29.10	0.47
Average patient payment for a 30-day supply					
ACE inhibitors	$3.59	$1.65	$5.00	$3.82	0.21
ARBs	$13.30	$4.75	$39.83	$25.20	2.84
β blockers	$4.00	$2.14	$6.41	$5.11	0.29
Percent of income spent on a 30-day supply					
ACE inhibitors	0.15%	0.05%	0.26%	0.21%	0.02
ARBs	0.77%	0.19%	1.66%	1.31%	0.16
β blockers	0.17%	0.06%	0.29%	0.28%	0.02
Medication possession ratio					
ACE inhibitors	95.1%	85.0%	100.0%	89.3%	1.16
ARBs	97.6%	90.0%	100.7%	92.3%	1.69
β blockers	95.0%	82.4%	99.8%	89.0%	1.10

Note. Percentages are population-level estimates based on sampling weights and may not correspond to unweighted survey counts; confidence intervals for percentage estimates are adjusted for clustering and stratification in the sample design. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CI = confidence interval; ESRD = end-stage renal disease; SE = standard error of the mean.

[a] Excludes Low-Income Subsidy recipients

[b] Includes mixed-race participants

[c] Includes Social Security, retirement account, and pension payments for participant and spouse

Table 2.2. *Logistic regression of non-adherence, community-dwelling Medicare Part D enrollees with self-reported heart failure, 2010-12*[a]

Effect	**β blockers** *n* = 456		**ACE inhibitors** *n* = 359		**ARBs** *n* = 119	
	Adjusted OR	95% CI	Adjusted OR	95% CI	Adjusted OR	95% CI
Percent of monthly income[b] spent on 30-day supply	**1.41**[d]	1.01, 1.98	0.40	0.13, 1.29	0.90	0.35, 2.36
Age (in years)	0.99	0.96, 1.03	0.98	0.95, 1.01	---	
Body mass index	1.03	0.98, 1.09	---		---	
Income ('000s)	---		0.99[e]	0.97,1.00	0.98	0.96, 1.01
Education level	---		---		0.48[d]	0.28, 0.83
Health vs. others same age[c]	---		---		1.29	0.54, 3.08
Health now vs. a year ago[c]	---		---		2.86[d]	1.17, 7.00
Race						
Non-white or mixed race	2.00[e]	0.93, 4.29	2.80[d]	1.09, 7.21	12.95[d]	2.57, 65.32
White	*reference*		*reference*		*reference*	
Census region						
South (or PR)	1.36	0.82, 2.24	---		1.26	0.32, 4.93
Other	*reference*				*reference*	
Type 2 diabetes						
Yes	1.38	0.77, 2.47	---		4.59[e]	0.98, 21.50
No	*reference*				*reference*	
Medicare Advantage						
Yes	1.24	0.77, 2.01	---		---	
No	*reference*					
Ethnicity						
Latino	---		2.91	0.64, 13.17	---	
Non-Latino			*reference*			
Marital status						
Married	---		0.57[e]	0.30, 1.06	---	
Unmarried			*reference*			
Sex						
Male	---		---		3.82[e]	0.88, 16.58
Female					*reference*	

Note. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CI = confidence interval; OR = odds ratio; PR = Puerto Rico.

[a] Excludes Low-Income Subsidy recipients

[b] Includes Social Security, retirement account, and pension payments for participant and spouse

[c] 5-point scale; higher score reflects worse health

[d] Significant at the $p < .05$ level

[e] Significant at the $p < .10$ level

Table 2.3. *Linear regression of medication possession ratio, community-dwelling Medicare Part D enrollees with self-reported heart failure, 2010-12*[a]

Effect	**β blockers** *n* = 438		**ACE inhibitors** *n* = 343		**ARBs** *n* = 114	
	B (*SE*)	*t*	*B* (*SE*)	*t*	*B* (*SE*)	*t*
Percent of monthly income[b] spent on 30-day supply	**-3.63** (1.57)	-2.30[d]	-0.35 (1.57)	-0.22	-1.10 (1.32)	-0.84
Income ('000s)	0.02 (0.03)	0.70	0.03 (0.02)	2.08[d]	---	
Education level	0.29 (0.48)	0.60	---		1.86 (0.86)	2.16[d]
Age (in years)	0.06 (0.14)	0.45	---		---	
Health vs. others same age[c]	-0.81 (0.80)	-1.01	---		-1.63 (2.11)	-0.77
Health now vs. a year ago[c]	-0.87 (1.10)	-0.79	-1.57 (1.30)	-1.20	-1.84 (2.09)	-0.88
Race						
Non-white or mixed race	-10.13 (4.76)	-2.13[d]	-10.11 (5.17)	-1.96[e]	-11.89 (6.84)	-1.74[e]
White	*reference*		*reference*		*reference*	
Medicare entitlement						
Disability or ESRD	-3.79 (4.35)	-0.87	---		---	
Age	*reference*					
Medicare Advantage						
Yes	-1.28 (1.85)	-0.69	---		---	
No	*reference*					
Ethnicity						
Latino	---		-12.40 (6.95)	-1.78[e]	3.87 (5.35)	0.72
Non-Latino			*reference*			
Marital status						
Married	---		1.75 (2.14)	0.82	---	
Unmarried			*reference*			
Sex						
Male	---		---		-8.70 (4.22)	-2.06[d]
Female					*reference*	
Ever smoked						
Yes	---		---		-2.45 (3.11)	-0.79
No					*reference*	
Adjusted R^2	.073		.070		.187	

Note. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ESRD = end-stage renal disease; SE = standard error.

[a] Excludes Low-Income Subsidy recipients

[b] Includes Social Security, retirement account, and pension payments for participant and spouse

[c] 5-point scale; higher score reflects worse health

[d] Significant at the $p < .05$ level

[e] Significant at the $p < .10$ level

Sample selection procedure

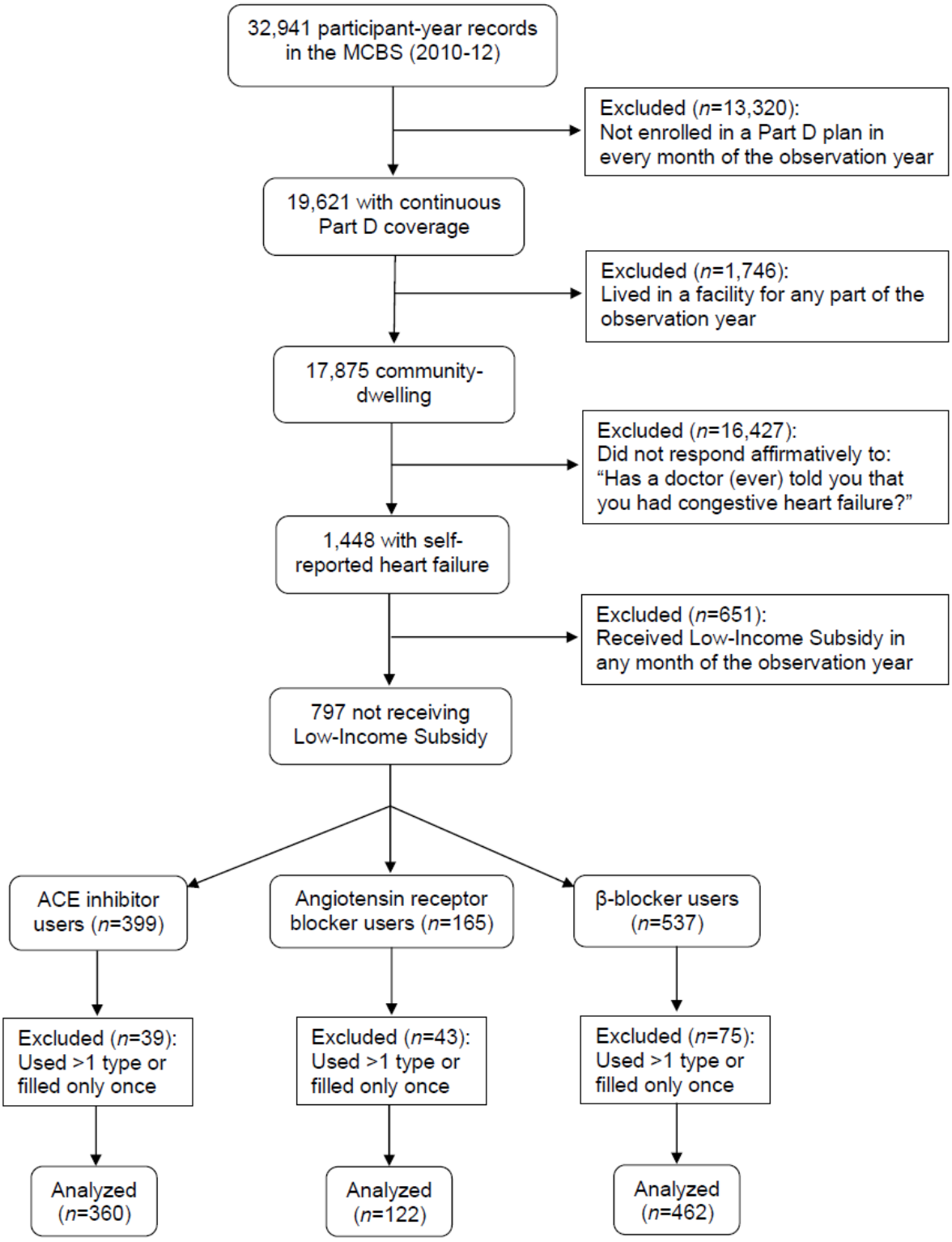

Figure 2.1. ACE = angiotensin-converting enzyme; MCBS = Medicare Current Beneficiary Survey.

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CHAPTER 3

Prescription Drug Spending and Acute Care Use in Heart Failure

Abstract

Background. Heart failure (HF) is the most common cause of hospitalization in Medicare. High medication adherence reduces the risk of hospitalization and emergency department (ED) use in HF patients. Studies show that adherence is adversely affected by medication cost sharing in chronic disorders, but the effects on downstream health care use are not well understood, especially in HF. **Objective.** To test for associations between out-of-pocket drug spending and acute care use among Medicare Part D enrollees with self-reported HF. **Methods.** Cross-sectional analysis of pooled 2010-12 data from the Medicare Current Beneficiary Survey. Analysis was limited to community-dwelling beneficiaries with fee-for-service Medicare and continuous Part D coverage. The predictor of interest was average out-of-pocket payment per HF-related prescription, normalized to a 30-day supply. Main outcomes were odds of hospitalization or ED use with a principal or secondary diagnosis of HF; frequency of such hospitalizations; and number of HF-related inpatient days during year of observation. Logistic, Poisson, and negative binomial models, respectively, were built and included an interaction of prescription drug spending with Medicaid eligibility. **Results.** Conditional on the effect of no Medicaid entitlement, average out-of-pocket expenditure per HF prescription was not significantly associated with odds of HF-related hospitalization, odds ratio (OR) = 1.01, 95% CI [0.98, 1.05], p = .401, or ED use, OR = 1.02, 95% CI [0.97, 1.08], p = .419. Average expenditure per prescription was borderline significantly associated with rates of HF-related hospital admission, rate ratio (RR) = 1.02, 95% CI [1.00, 1.05], p = .060, and

hospitalized days, RR = 1.04, 95% CI [1.00, 1.07], p = .057. These effects were not significant in zero-inflated versions of the models. **Conclusions.** Fee-for-service Medicare patients with a Part D plan and self-reported HF may absorb modest prescription cost sharing without dramatic spikes in related hospital and emergency care use. Among patients without a Medicaid entitlement, however, out-of-pocket drug spending may modestly increase hospitalization rates, so cost sharing should be imposed with caution. This study contributes useful information to ongoing discussions about appropriate cost-sharing levels in chronic disorders.

Introduction

Heart failure (HF) is the most common reason for inpatient claims in the Medicare program and is the second leading cause of hospital admission for adults aged 65-84 in the United States (Pfuntner, Wier, & Stocks, 2013). HF places a substantial burden on the U.S. health care system, accounting for an estimated $30 billion in direct medical costs annually (Heidenreich et al., 2011). High adherence to prescription drug regimens reduces the risk of poor outcomes in HF patients, including hospitalization, emergency care use, and mortality (Esposito, Bagchi, Verdier, Bencio, & Kim, 2009; Marti et al., 2013; Wu, Lennie, Dekker, Biddle, & Moser, 2013). Yet adherence to HF treatment may be reduced by out-of-pocket drug expenses, such as deductibles and copays (Cole, Norman, Weatherby, & Walker, 2006; Patterson, Blalock, Smith, & Murray, 2011).

Health insurers, including Medicare Part D plan sponsors, use patient cost-sharing strategies to curb excess benefit use. However, studies in patients with a chronic disease have shown an inverse relationship between prescription drug cost-sharing level and medication adherence: as out-of-pocket expenses rise, adherence often declines (Barron, Wahl, Fisher, & Plauschinat, 2008; Chen et al., 2014; Cole et al., 2006; Colombi, Yu-Isenberg, & Priest, 2008; Doshi, Zhu, Lee, Kimmel, & Volpp, 2009; Goldman, Joyce, & Karaca-Mandic, 2006; Kim et al., 2011; Li, McElligott, Bergquist, Schwartz, & Doshi, 2012; Patterson et al., 2011; Thornton Snider, Seabury, Lopez, McKenzie, & Goldman, 2016). But whether and when this copay-linked nonadherence contributes to adverse health outcomes remains unclear. The RAND Health Insurance Experiment of the 1970s-80s demonstrated negligible impact of less generous insurance

plans on average health outcomes (except among low-income participants with hypertension) (Geyman, 2012; Newhouse, 2004). Yet this finding has been questioned due to unequal attrition across experimental conditions (Nyman, 2007). Study results since then have been mixed, though 76% of papers included in a 2012 review showed an adverse effect of cost sharing on health outcomes (Eaddy, Cook, O'Day, Burch, & Cantrell, 2012).

Furthermore, only one published study in the last 12 years has reported the effect of prescription drug copays on health care use in HF, despite the significance of HF as a cause of hospitalization and related expenses, especially in the Medicare program (Cole et al., 2006). Therefore, we designed this study to test for associations between out-of-pocket drug spending and acute care use among Medicare beneficiaries with self-reported HF. Specifically, this study investigated the association between average out-of-pocket spending per HF prescription and (1) the odds of a HF-related hospital admission, (2) the odds of emergency department (ED) use for HF, and (3) the number and cumulative length of HF-related hospital stays.

Methods

Sample selection. This was a cross-sectional study of 2010-12 pooled data from the Medicare Current Beneficiary Survey (MCBS) Cost and Use files. The design of the MCBS has been described extensively elsewhere (Briesacher, Tjia, Doubeni, Chen, & Rao, 2012; Cubanski, Swoope, Damico, & Neuman, 2014; Lopert et al., 2012; U.S. Centers for Medicare and Medicaid Services [CMS], 2016). Briefly, it is a rotating panel survey of Medicare beneficiaries that enrolls about 12,000 new participants every year and follows them for four years. Extensive health and financial questionnaire data are

matched (when possible) to events in the Medicare claims records. Cost and use data are available for three calendar years for each panel, and the sample is designed to be representative of the ever-enrolled Medicare population in each year. The average response rate for 2010-12 was 62.3% (CMS, 2016).

To address the study aims, we selected a subsample of MCBS participants. A participant was included if he or she (1) replied "yes" when asked, "Has a doctor (ever) told you that you had congestive heart failure?" on the survey, (2) had continuous Part D coverage in the year of observation, (3) did not live in a facility for any part of the observation year, and (4) was not enrolled in a Medicare Advantage (MA) plan during the observation year. MA participants were excluded due to incomplete reporting of encounter data by plan sponsors (Cubanski et al., 2014). Facility-dwelling respondents were excluded, because health care workers may directly administer their medications (Chen et al., 2014). The requirement of continuous Part D coverage minimizes the number of prescriptions with incomplete or imputed transaction data (Roberto & Stuart, 2014), and it aligns with the study purpose of addressing cost sharing in prescription drug plans.

Study variables. MCBS does not report the cost-sharing requirements of specific pharmacy plans. Out-of-pocket drug payments were assumed to represent cost sharing, because only prescription drug events from Part D records were analyzed. We identified out-of-pocket payment for each HF-related prescription and normalized it to a 30-day supply (Cole et al., 2006; Patterson et al., 2011). For example, a $12 copay for a 90-day supply was treated as three $4 payments. We then averaged these payments across the year of observation and adjusted the result to 2012 dollars using the Consumer Price

Index for All Urban Consumers. A payment was included in this calculation if the generic drug name corresponded to an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin receptor blocker, a β blocker (if not ocular), a cardiac glycoside, a diuretic, an aldosterone antagonist, or a direct vasodilator (hydralazine or isosorbide, if both filled in the same year). Direct renin inhibitors were not included unless combined with another relevant agent in a single formulation.

HF-related hospitalization was identified by any inpatient Medicare claim with a principal or secondary diagnosis of HF, based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 428.xx, 402.x1, 404.x1, or 404.x3 (DiMartino, Shea, Hernandez, & Curtis, 2010). HF-related ED visit was identified by any outpatient Medicare claim with a principal or secondary diagnosis corresponding to one of the same ICD-9-CM codes and when the event type was specified as "ER." This method captured only ED visits not resulting in hospital admission. Cumulative inpatient days was defined by computing the length of each HF-related hospital stay from admission through discharge dates, then summing all the lengths of stay during the observation year. Hospital stays that straddled the calendar year were retained, since they represented less than 1% of admissions.

Covariate selection was based primarily on prior studies of HF medication adherence and acute care use (Cole et al., 2006; Lopert et al., 2012). Sociodemographic covariates included sex, race/ethnicity, marital status, annual income, educational attainment, Census region, urbanicity, Medicaid eligibility, and age. Health-related covariates included self-rated health status (compared to others the same age and compared to one year prior), body mass index (BMI), Charlson Comorbidity Index

(modified to exclude HF), difficulty walking 2-3 blocks or ¼ mile, and basis for Medicare entitlement (disability or age). Sex, race/ethnicity, marital status, urbanicity, Medicaid eligibility, and disability were dichotomized. Education levels between high school diploma and bachelor's degree were collapsed, and education was treated as continuous. Self-rated health status and difficulty walking were reported on Likert-type scales, with higher scores reflecting worse health.

We included a flag for death or lost to follow-up, to adjust for censoring, and year of participation as a proxy for time effects (Lopert et al., 2012). We also included a count of HF-related drug classes used in the observation year as a proxy for disease severity (Lopert et al., 2012). Finally, we included an interaction term to determine if the effects of prescription drug spending were moderated by Medicaid eligibility. Visualization of data showed that hospitalization frequency declined above an average drug payment of about $1, then began to slope gradually upward (Figure 1). Participants who spent $1 or less on the average 30-day HF prescription were far likelier to be entitled to Medicaid, so we hypothesized that the adjusted effect of drug spending on hospitalization depended on factors related to Medicaid eligibility.

Analysis plan. We used logistic regression to model the effect of average spending per HF prescription on the odds of HF-related hospital admission and ED use. We built a Poisson model for the effect of drug spending on number of hospitalizations and, due to evidence of over-dispersion, a negative binomial model for the effect on total inpatient days (Hayat & Higgins, 2014). Since hospitalization for HF during the observation year was somewhat uncommon (17% of participant-year records), we also built zero-inflated versions of the count models and compared the results (Hayat &

Higgins, 2014). All count models included an offset for number of days the participant was entitled to Medicare that year. Standard errors were computed by Taylor-series linearization to account for the design effect of stratified, cluster sampling (Heeringa, West, & Berglund, 2010). After reviewing the initial models, we removed participant age due to evidence of collinearity and because the MCBS sample design already stratifies by age.

The first author had full data access under a data use agreement with the Centers for Medicare & Medicaid Services (CMS). CMS provided sampling weights for each participant record to account for unequal probabilities of selection, post-stratification and nonresponse (Briesacher et al., 2012). For participants with multiple years of data, a weighted average of their cross-sectional sampling weights was applied, because exclusion of multi-year participants in pooled analysis of MCBS data is not recommended (Briesacher et al., 2012). Logistic regression was performed in SAS-callable SUDAAN version 11, and the Poisson and negative binomial models were fitted in Stata version 15. The Emory University Institutional Review Board approved this study.

Results

Sample characteristics. The final sample consisted of 911 participant-year records, of which 819 (90%) contained at least one purchase of a HF-related prescription in the year of observation. The 911 records were derived from 608 individuals. Accounting for sampling weights, the majority (58%) were female, and 25% were non-white, multiracial, and/or Latino. Only about 10% had completed a four-year degree or higher, and 64% were unmarried at the time of survey. The mean annual income was

about $23,500 (in 2012 dollars). Over half (58%) rated their health as fair or poor compared to others the same age, 26% had a Medicare-qualifying disability or disease, mean BMI was 30, and mean Charlson Comorbidity Index value (excluding HF) was 3.6.

In terms of out-of-pocket spending, $4.21 was the average patient expenditure for a 30-day HF prescription, and 43% were entitled to Medicaid benefits. Fifteen percent of the subpopulation was hospitalized for HF during the year of observation, and 2% had a HF-related ED visit not resulting in admission. The mean number of HF-related hospital admissions was 0.2, and the mean cumulative days hospitalized was 1.3. Patients used an average of two drug classes for HF treatment, and 8% were lost to follow-up or died during the year of observation (Table 1).

Multivariate analysis. In most of the risk-adjusted models, the interaction of average payment per prescription with Medicaid eligibility approached or attained statistical significance. Therefore, the interaction term was retained in all models, and drug spending effect estimates are conditional on Medicaid status. For the Medicaid non-eligible group, average expenditure per HF prescription was not significantly associated with odds of HF-related hospitalization, odds ratio (OR) = 1.01, 95% CI [0.98, 1.05], p = .401 (Table 2). Likewise, there was no significant association between spending per prescription and odds of HF-related ED use, OR = 1.02, 95% CI [0.97, 1.08], p = .419.

In the conventional Poisson model, the estimated conditional effect of average spending per prescription on frequency of HF-related hospitalization was small, rate ratio (RR) = 1.02, 95% CI [1.00, 1.05], and approached but did not reach statistical significance, p = .060 (Table 2). In the conventional negative binomial model, the estimated conditional effect of spending per prescription on total days hospitalized for HF

was similar, RR = 1.04, 95% CI [1.00, 1.07], and again approached significance, p = .057. Figure 2 displays the predicted marginal effects of average drug expenditure on total inpatient days by Medicaid status based on this model. These effects were smaller and non-significant in the zero-adjusted models (data not shown).

Discussion

In this sample of community-dwelling, fee-for-service Medicare beneficiaries with Part D coverage and self-reported HF, there was no evidence of an association between average out-of-pocket payment per HF prescription and odds of HF-related hospitalization or ED use. On the other hand, there was some evidence that out-of-pocket spending per prescription was mildly associated with rates of HF-related hospital use. Conditional on not qualifying for Medicaid, each additional dollar spent per prescription was associated with a 2% rise in hospital admissions and a 4% rise in days hospitalized due to HF. However, these effects only approached statistical significance (p = .060 and p = .057, respectively), and they were clearly non-significant in the more conservative zero-inflated models, which accounted for the probability of being hospitalized in the first place.

One possible explanation for the lack of significant findings is the relative immediacy and severity of HF complications due to non-adherence. Compared to other chronic diseases in which medication cost sharing has been studied, HF is a severe condition with a poor prognosis, and low adherence is likely to precipitate exacerbation requiring costly acute care (Esposito et al., 2009; Lopert et al., 2012; Marti et al., 2013; Wu et al., 2013). As a result, HF patients may be largely insensitive to the price of prescription drugs that prevent exacerbations. In fact, a previous analysis of select drug

classes in these data showed that median adherence was high: 95-98% for β blockers and anti-angiotensin drugs (McGee, Phillips, Higgins, & Butler, 2017). In addition, average out-of-pocket drug spending was very low in this study, with an adjusted mean of $4.21 per 30-day supply. With low costs and high adherence, it is unlikely that drug prices would have substantially affected acute care use.

The only other published study to investigate HF drug copays and hospital outcomes found that risk of HF-related hospitalization rose with copay-attributable declines in medication adherence: odds of hospital admission increased by a predicted 6% with each $10 rise in ACE inhibitor copay, and by 9% per $10 rise in β-blocker copay (Cole et al., 2006). However, that study was conducted in a commercially insured population, which may have been younger and healthier on average, and therefore more price-sensitive, compared to Medicare beneficiaries. In addition, $10 is more than double the average out-of-pocket payment per prescription in our sample, limiting comparability between the two studies.

Notably, the number of HF-indicated drug classes used was a significantly positive predictor of hospitalization across the models. This finding could result from the burden of polypharmacy on adherence, it could reflect patients in worse health (though the models adjusted for multiple health status variables), or it could be the outcome of total drug spending. This study analyzed the effect of average out-of-pocket expenditure for a 30-day supply per prescription, rather than total out-of-pocket expenditure on all HF drugs, to avoid inflating the cost sharing estimate for patients who were prescribed more drugs. Number of drug classes used was included in the models to adjust for disease

severity, but its significant effect on hospitalization may also be a function of total drug spending burden.

We did not examine the effect of adherence on outcomes because of difficulties estimating adherence across multiple drug classes from claims data. Our previous analysis of these data showed that out-of-pocket spending on β blockers as a proportion of monthly income was inversely associated with adherence (McGee et al., 2017). Yet the effect size was small, and that analysis excluded recipients of the Part D low-income subsidy (LIS), for whom out-of-pocket spending is negligible. It may be that inclusion of LIS recipients in this study affected the results by driving down average costs, although effect estimates were conditional on Medicaid eligibility, and all LIS recipients in this sample were Medicaid-eligible. Previous studies have reported lower adherence at higher drug spending levels in HF, but the effect was only significant at copays of $10 or $20 (Cole et al., 2006; Patterson et al., 2011).

There was no evidence that out-of-pocket drug expenditure affected the odds of emergency care for HF in this study. However, the ED outcome was rare: only 19 participant-year records contained such an encounter. This number would have been larger if ED encounters resulting in hospital admission were identified in the data. The large standard errors in the logit model were probably due to the low prevalence of the outcome and the inclusion of multiple categorical predictors (Field, 2013). The Cox and Snell R^2 for this model was just .02 (compared to .18 for the hospitalization logit model), suggesting low predictive ability (Bewick, Cheek, & Ball, 2005). This analysis should be repeated in a larger sample and with data that identify ED visits resulting in admission, not just discharge.

As with most studies of retrospective databases, measurement error was a concern. Since we could not observe the cost-sharing structure of beneficiaries' Part D plans, we estimated cost sharing by computing average out-of-pocket payments. That approach is not sensitive to the dynamic nature of Part D plans, which often include deductibles and coverage gaps (Hoadley, Cubanski, & Neuman, 2016). If measurement error was random, it probably biased our results toward the null hypothesis. In addition, the reason for more frequent hospitalization among Medicaid-eligible participants at lower drug prices is unclear (Figure 2). It is possible that non-Medicaid patients received better medical management or bore a greater share of hospitalization costs. The latter would dissuade hospital use but cannot be assessed without observing the benefit structure.

Furthermore, some prescriptions and outcomes may have been misclassified. A prescription was defined as HF-related if it matched a pre-determined list of drug names, but some drugs could be used for other conditions. Effects of non-HF drug prices may also be important. In a recent study of type 2 diabetes medications, moving from the 10^{th} to 90^{th} cost-sharing percentile raised hospitalization costs by a predicted $1328 per patient in the presence of co-morbid HF (Thornton Snider et al., 2016). In addition, an outcome would have been misclassified if HF was listed as the secondary diagnosis for a completely unrelated encounter. However, using only the principal diagnosis would have excluded patients treated for conditions to which HF can be a major contributor, such as pulmonary edema or renal failure. Since the claims records did not specify contributing conditions for Diagnosis-Related Groups, we relied on principal and secondary ICD-9

codes, an approach modeled on a prior study of patients with HF admissions in the MCBS (DiMartino et al., 2010).

Despite the largely non-significant results, our study still found marginal evidence of a modest copay effect in non-Medicaid patients: a 2% rise in hospitalizations and a 4% rise in days hospitalized due to HF with each additional dollar spent on the average HF prescription. These near-significant effects were observed despite very low out-of-pocket costs, infrequent hospital use, and adjustment for many covariates. Additionally, Medicaid status moderated the association between drug spending and number of hospitalizations and inpatient days, where the association between drug spending and hospital use was flat to weakly positive for patients without Medicaid but significantly negative for Medicaid-eligible patients. Future research should attempt to clarify the relationship between drug spending and hospital use in HF with more current data and complete benefit design information, especially given the growing use of costly new agents in HF management.

Limitations. An important limitation of this study was its cross-sectional design. Since prescription drug spending was averaged over the year of observation, the outcomes analyzed could have occurred before some of the out-of-pocket drug payments. This problem of temporality limits any causal inference that can be made. Relying on a questionnaire response to identify HF cases may have resulted in misclassification, because some patients may not understand or remember their diagnosis. Beneficiaries may also have chosen Part D plans with better coverage of the drugs that they already were using, which could have biased the spending effects downward. In addition, no

disease-specific clinical data (e.g., HF class or ejection fraction) were available, so it was difficult to assess whether patients with more advanced illness were less price-sensitive.

Pooling data from multiple survey years could have underestimated standard errors due to autocorrelation, since observations from multi-year participants are not truly independent. But according to Sarndal and Swensson, the necessity of correcting for this additional clustering is unclear as long as the primary sampling unit is specified correctly (Briesacher et al., 2012). Exclusion of survey-reported prescriptions that did not match a Medicare record may have biased spending estimates. However, only about 6% of unmatched survey prescriptions reflect true out-of-plan use for Part D enrollees with common chronic diseases in MCBS data; many of the rest could be matched with a more sensitive algorithm (Roberto & Stuart, 2014). And as with any analysis of administrative data, findings may be spurious because of omitted variables or sampling error.

Conclusions

This study offers support for the notion that fee-for-service Medicare patients with self-reported HF can absorb modest prescription drug copays without raising the risks of hospital and emergency care use. Among patients with no Medicaid entitlement (i.e., greater average out-of-pocket exposure), prescription drug spending may modestly increase hospitalization frequency and total inpatient days, so medication copays should be levied with caution. These findings apply only to community-dwelling beneficiaries with continuous Part D coverage. Nonetheless, they contribute useful information to ongoing discussions about appropriate cost-sharing levels in chronic disorders.

Table 3.1. *Sample characteristics*

Variable		Count (unweighted)	Percent (weighted)	95% CI (design-adjusted)	
TOTAL		911	100.00	---	---
Gender					
	Male	389	42.4%	37.3%	47.5%
	Female	522	57.6%	52.5%	62.7%
Race/ethnicity					
	Non-white[a] or Latino	227	24.8%	19.7%	29.9%
	White, non-Latino	683	75.2%	70.1%	80.3%
Marital status					
	Married	309	36.3%	31.9%	40.7%
	Unmarried	601	63.7%	59.3%	68.1%
Education					
	No schooling	17	1.6%	0.2%	3.0%
	Nursery-8th grade	154	16.2%	13.0%	19.4%
	9th-12th grade	186	20.4%	17.2%	23.7%
	High school diploma	263	27.9%	24.1%	31.8%
	Vocational/technical, some college or associate's	202	24.1%	20.2%	28.0%
	Bachelor's degree	54	6.3%	3.8%	8.8%
	Post-graduate	33	3.5%	1.4%	5.5%
Medicaid coverage					
	Eligible	397	43.3%	38.6%	47.9%
	Ineligible	514	56.7%	52.1%	61.4%
Urbanicity					
	Metropolitan area	545	61.9%	56.4%	67.4%
	Non-metro. area	366	38.1%	32.6%	43.6%
Region					
	Northeast	112	13.9%	11.1%	16.6%
	Midwest	231	25.4%	20.3%	30.5%
	West	112	12.2%	6.7%	17.7%
	South or Puerto Rico	456	48.6%	42.6%	54.5%
Health vs. others the same age					
	Excellent	29	3.0%	1.8%	4.3%
	Very good	117	11.5%	9.0%	14.1%
	Good	260	27.2%	23.5%	30.8%
	Fair	300	34.4%	30.9%	37.9%
	Poor	200	23.9%	20.5%	27.3%
Health now vs. one year ago					
	Much better	52	5.8%	3.8%	7.8%
	Somewhat better	118	13.5%	10.5%	16.5%
	About the same	382	40.4%	36.1%	44.6%
	Somewhat worse	292	32.9%	29.4%	36.5%
	Much worse	64	7.4%	5.1%	9.7%
Difficulty walking ¼ mile or 2-3 blocks					
	None	137	16.4%	12.8%	20.0%
	A little	83	8.9%	6.9%	10.8%

	Some	94	9.9%	7.9%	11.9%
	A lot	164	18.1%	15.1%	21.2%
	Unable	428	46.6%	42.3%	50.9%
Medicare entitlement					
	Disability/ESRD	198	25.7%	20.8%	30.6%
	Age only	712	74.3%	69.4%	79.2%
Censoring					
	Died or LTFU	56	8.1%	5.2%	10.9%
	Alive, retained	855	91.9%	89.1%	94.8%
Year of observation					
	2010	314	33.4%	30.3%	36.6%
	2011	309	34.3%	31.8%	36.8%
	2012	288	32.3%	29.3%	35.2%
HF-related hospitalization					
	Yes	139	15.0%	12.3%	17.8%
	No	772	85.0%	82.2%	87.7%
HF-related ED use					
	Yes	19	2.0%	1.2%	2.8%
	No	892	98.0%	97.2%	98.8%

Variable	**Median** (unweighted)	**Interquartile range** (unweighted)		**Mean** (weighted)	**SE** (design-adjusted)
Age (in years)	76.0	68.0	83.0	72.4	0.58
Annual income ('000s)[b]	$16.7	$10.8	$28.4	$23.5	1.13
Body mass index	28.2	24.7	32.7	30.0	0.36
Charlson Comorbidity Index[c]	3.0	1.0	5.0	3.6	0.13
HF-related drug classes used	2.0	1.0	3.0	2.1	0.06
Mean out-of-pocket expenditure per HF Rx[d]	$2.30	$0.92	$5.00	$4.21	0.31
HF-related hospitalizations	0.0	0.0	0.0	0.2	0.02
HF-related inpatient days	0.0	0.0	0.0	1.3	0.16

Note. CI = confidence interval; ED = emergency department; ESRD = end-stage renal disease; HF = heart failure; LTFU = lost to follow-up; Rx = prescription; SE = standard error of the mean.
[a] Includes multiracial participants
[b] Converted to 2012 dollars; includes Social Security, pension, and retirement account payments for participant and spouse
[c] Modified to exclude heart failure
[d] Normalized to a 30-day supply

Table 3.2. *Effect of average out-of-pocket payment per HF prescription on acute care use, community-dwelling HF patients with traditional Medicare and Part D, 2010-12*

Effect	HF-related hospitalization		HF-related ED visit[a]		No. of HF hospitalizations		No. of HF inpatient days	
	OR	95% CI	OR	95% CI	RR	95% CI	RR	95% CI
Mean out-of-pocket payment per Rx[b]	1.01	0.98-1.05	1.02	0.97-1.08	1.02[d]	1.00-1.05	1.04[d]	1.00-1.07
Eligible for Medicaid								
Yes	2.94[e]	1.33-6.50	0.77	0.16-3.72	2.34[e]	1.20-4.57	2.98[e]	1.33-6.71
No		*reference*		*reference*		*reference*		*reference*
Interaction of Rx payment with Medicaid status	0.68[d]	0.46-1.01	0.86	0.47-1.57	0.68[e]	0.51-0.90	0.68[e]	0.48-0.95
Health vs. others the same age[c]	1.42[e]	1.11-1.81	1.50	0.85-2.67	1.21[e]	1.01-1.46	1.64[e]	1.24-2.17
Health now vs. a year ago[c]	1.10	0.82-1.47	0.75	0.40-1.41	1.05	0.81-1.35	1.01	0.76-1.34
Body mass index	0.96[e]	0.93-0.98	1.03	0.96-1.10	0.96[e]	0.94-0.98	0.95[e]	0.91-0.99
Difficulty walking 1/4 mile or 2-3 blocks[c]	1.10	0.91-1.32	1.40	0.86-2.29	1.19[e]	1.03-1.38	1.09	0.88-1.34
Medicare eligibility								
Disability/ESRD	0.42[e]	0.23-0.76	0.87	0.22-3.39	0.65	0.37-1.15	0.35[e]	0.19-0.65
Age only		*reference*		*reference*		*reference*		*reference*
Modified Charlson Comorbidity Index	1.31[e]	1.17-1.46	1.06	0.91-1.24	1.22[e]	1.16-1.29	1.35[e]	1.23-1.49
Gender								
Male	1.23	0.72-2.12	0.37	0.11-1.27	1.00	0.68-1.49	1.74[d]	0.99-3.03
Female		*reference*		*reference*		*reference*		*reference*
Race/ethnicity								
Non-white/Latino	0.46[e]	0.21-0.98	0.86	0.19-4.00	0.61	0.32-1.17	0.47[e]	0.25-0.91
White, non-Latino		*reference*		*reference*		*reference*		*reference*
Presently married								
Yes	0.57	0.28-1.15	0.84	0.23-3.08	0.44[e]	0.27-0.71	0.53[d]	0.28-1.03
No		*reference*		*reference*		*reference*		*reference*
Education level	1.22[e]	1.03-1.44	1.04	0.67-1.62	1.18[e]	1.03-1.35	1.30[e]	1.08-1.57
Census region								
Northeast	1.52	0.84-2.75	1.74	0.55-5.48	1.51[e]	1.06-2.15	1.34	0.65-2.76
Midwest	1.28	0.77-2.11	0.97	0.28-3.28	1.43[e]	1.02-2.02	1.20	0.72-2.00
West	0.81	0.33-1.95	1.87	0.65-5.38	0.74	0.41-1.36	0.33[e]	0.15-0.70
Southeast or PR		*reference*		*reference*		*reference*		*reference*
Urbanicity								
Metro. area	1.27	0.88-1.82	0.50[d]	0.22-1.14	0.97	0.73-1.27	2.01[e]	1.36-2.96
Non-metro. area		*reference*		*reference*		*reference*		*reference*
Annual income ('000s)	1.00	0.99-1.01	1.00	0.98-1.01	1.00	1.00-1.01	1.00	0.99-1.00

Censoring								
Died or LTFU	0.74	0.27-2.04	0.75	0.08-7.32	0.92	0.47-1.80	0.73	0.23-2.30
Alive and retained		*reference*		*reference*		*reference*		*reference*
Year of observation								
2010	1.10	0.74-1.66	0.90	0.27-2.99	1.28	0.93-1.77	1.80[e]	1.12-2.89
2011	0.75	0.44-1.27	1.39	0.44-4.41	0.95	0.63-1.44	1.17	0.69-1.97
2012		*reference*		*reference*		*reference*		*reference*
No. of HF drug classes used	2.12[e]	1.58-2.84	1.72[d]	0.93-3.16	1.80[e]	1.48-2.18	1.97[e]	1.57-2.47

Note. CI = confidence interval; ED = emergency department; ESRD = end-stage renal disease; HF = heart failure; LTFU = lost to follow-up; OR = odds ratio; PR = Puerto Rico; RR = rate ratio; Rx = prescription.

[a] Not resulting in admission

[b] Normalized to a 30-day supply

[c] 5-point scale; higher score reflects worse health or function

[d] Significant at the $p < .10$ level

[e] Significant at the $p < .05$ level

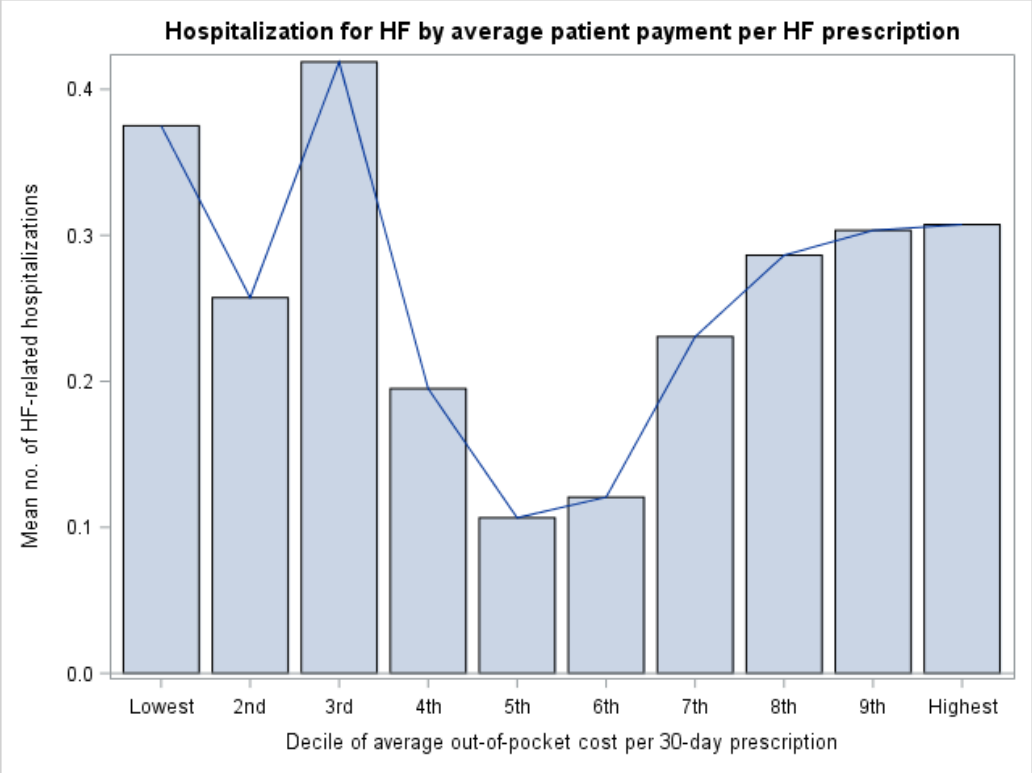

Figure 3.1. HF = heart failure.

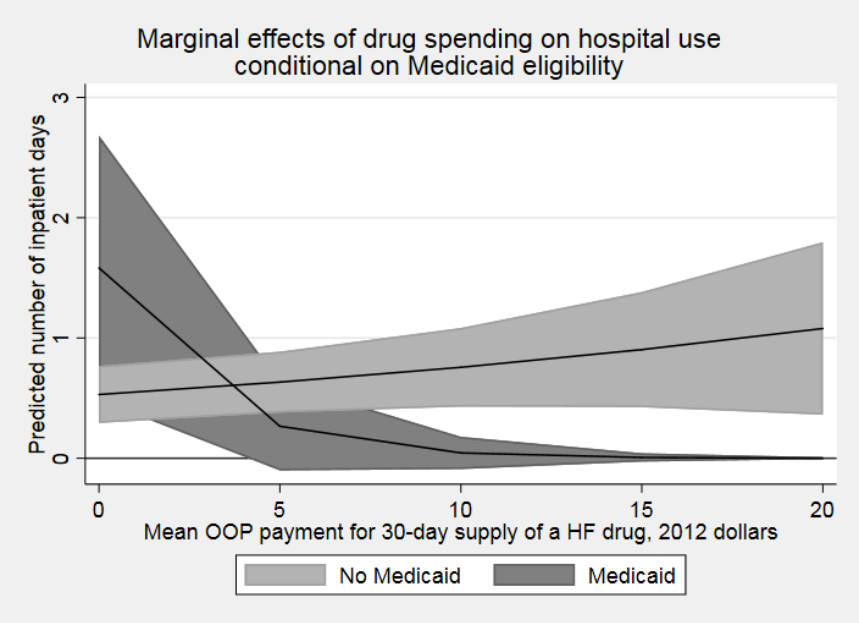

Figure 3.2. OOP = out-of-pocket.

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CHAPTER 4

Prescription Drug Spending and Health Care Costs in Heart Failure

Abstract

Background. Heart failure (HF) is the most common cause of hospitalization in Medicare. High medication adherence has been linked to lower hospitalization and expenditure in HF patients. Studies also show that adherence is adversely affected by prescription drug cost sharing in various chronic disorders, but the effects of drug cost sharing on overall health care costs are poorly understood, especially in HF. **Objective.** To model the association between out-of-pocket drug spending and costs for inpatient and total health care services among Medicare Part D enrollees with self-reported HF. **Methods.** Cross-sectional analysis of pooled 2010-12 data from the Medicare Current Beneficiary Survey. Analysis was limited to community-dwelling beneficiaries with continuous Part D coverage. The predictors of interest were average out-of-pocket payment per HF-related prescription, normalized to a 30-day supply, and total out-of-pocket payments for HF drugs in the year of observation. The outcomes were total and Medicare-specific payments for inpatient and all health care services during the observation year. Gamma regression models with a log link were constructed and included an interaction of prescription drug spending with Low-Income Subsidy (LIS) status. **Results.** Conditional on not receiving the LIS, predicted Medicare costs per patient rose $126, 95% CI [-10, 261], $p = .068$, for each additional $1 spent per prescription, on average. This equates to a 1.2% increase in median annual Medicare costs. Average payment per prescription was not significantly associated with Medicare inpatient costs, total inpatient costs, or total health care costs. Annual out-of-pocket

spending on all HF drugs was not significantly related to any of the cost outcomes.

Conclusions. Community-dwelling Medicare patients with Part D coverage and self-reported HF may absorb modest prescription drug cost sharing without dramatic spikes in inpatient or total health care costs. Among patients without the LIS, however, out-of-pocket drug spending may modestly increase total Medicare costs, so cost sharing should be imposed with caution.

Introduction

In recent years, a growing body of research has documented the potential and limits of value-based insurance design (V-BID) in improving health outcomes and controlling costs (Chang, Liberman, Coulen, Berger, & Brennan, 2010; Chernew et al., 2008; Choudhry et al., 2012; Frank et al., 2012; Gibson et al., 2011; Hirth, Cliff, Gibson, McKellar, & Fendrick, 2016; Kelly, Turner, Frech-Tamas, Doyle, & Mauceri, 2009; Maciejewski, Farley, Parker, & Wansink, 2010; Nair et al., 2010; Zeng et al., 2010). Also known as value-based benefit design or evidence-based plan design, V-BID usually entails the reduction or elimination of patient cost sharing (e.g., copayments and deductibles) to promote adherence to treatments that are shown to reduce illness or death (Lee, Maciejewski, Raju, Shrank, & Choudhry, 2013). Under a V-BID policy, the amount of cost sharing for a given service varies as a function of its clinical value and potential to reduce net costs for specific patients (Chernew, Rosen, & Fendrick, 2007).

Simulation models have demonstrated the theoretical cost-effectiveness of full coverage for certain secondary prevention therapies, such as angiotensin-converting enzyme (ACE) inhibitors for renal preservation in diabetes mellitus (Rosen et al., 2005), aromatase inhibitors in early breast cancer (Ito, Elkin, Blinder, Keating, & Choudhry, 2013), and combination pharmacotherapy after myocardial infarction (Choudhry, Patrick, Antman, Avorn, & Shrank, 2008; Ito et al., 2015). Results from empirical studies are more mixed. A 2013 systematic review found that V-BID policies were not associated with significant changes in overall health care spending after the first year (Lee et al., 2013). However, two of the included studies showed a significant reduction in hospital

admissions and emergency department use with V-BID policies (Choudhry et al., 2012; Nair et al., 2010).

To date, the research on V-BID and the economic effects of cost sharing has focused largely on vascular disease, asthma, and diabetes. Yet, heart failure (HF) is the most common cause of hospitalization among Medicare beneficiaries in the U.S. and accounts for an estimated $34 billion in direct medical costs annually (Heidenreich et al., 2011; Pfuntner, Wier, & Stocks, 2013). Prescription drug spending by HF patients with Medicare Part D varies, and little is known about the effect of medication cost sharing on downstream health care costs in this population. Therefore, this study was designed to investigate the effect of out-of-pocket drug spending on total and inpatient costs for Medicare Part D enrollees with HF.

Methods

Data and study sample. The Medicare Current Beneficiary Survey (MCBS) is a national panel survey that enrolls about 12,000 new participants annually (DiMartino, Shea, Hernandez, & Curtis, 2010; U.S. Centers for Medicare and Medicaid Services [CMS], 2016). It consists of detailed face-to-face interviews three times yearly, and health care use and payment data are collected for three calendar years (Briesacher, Tjia, Doubeni, Chen, & Rao, 2012; Lopert et al., 2012). Health care encounters reported on the survey are matched to Medicare claims when possible (Cubanski, Swoope, Damico, & Neuman, 2014; Lopert et al., 2012). The annual Cost and Use files are designed to be representative of the ever-enrolled Medicare population in that year (CMS, 2016). For this study, data were pooled from 2010-12, the three most recent years of Cost and Use files available when the data use agreement was executed.

The subsample for this study consisted of participants who responded affirmatively to the survey question, “Has a doctor (ever) told you that you had congestive heart failure?” Respondents were required to have held Part D coverage in all 12 months of the year of observation, because the purpose of the study was to understand the impact of prescription cost sharing in health plans with drug coverage. Furthermore, spending data is less likely to be imputed for prescriptions in the Part D records (Roberto & Stuart, 2014). In addition, participants who lived in a facility during all or part of the year of observation were excluded, because facility residents may be given their medications directly by staff (Chen et al., 2014).

Measures. The key independent variables were average and total out-of-pocket (OOP) expenditure on HF-related prescriptions. A prescription record was included in the calculation of OOP spending if its generic drug name could be identified as an ACE inhibitor, an angiotensin receptor blocker, a β blocker, a diuretic, an aldosterone antagonist, or a cardiac glycoside. (Ocular β blockers were excluded.) In addition, isosorbide and hydralazine were included if both were filled during the same year (Carmody & Anderson, 2007). Direct renin inhibitors were excluded unless they were formulated in combination with a drug from one of the other classes. First-in-class agents sacubitril and ivabradine were not yet available at the time of data collection.

MCBS does not include data on benefit structure, such as copayment amounts. Therefore, medication cost sharing was approximated by computing average and total OOP payments for HF prescriptions in the Part D records. Total cost was simply the sum of all OOP payments for HF drugs in the observation year. To obtain average cost, payments were normalized to a 30-day supply by dividing 30 by the actual days supplied

and multiplying the payment by the result (Cole, Norman, Weatherby, & Walker, 2006; Patterson, Blalock, Smith, & Murray, 2011). For example, a $12 payment for a 90-day supply would be converted to $4. An average of 30-day payments was then computed, such that a payment for 30 days counted once, and a 30-day-normalized payment for 90 days counted three times.

The outcome variables were total and inpatient payments by Medicare and by all payers during the observation year. These cost estimates were derived from the MCBS person- and service-summary files and were not diagnosis-specific, which permitted assessment of the impact on medical costs broadly. For participants with incomplete participation during the observation year, payments for non-Medicare-covered services were imputed by the MCBS team (CMS, 2016). (Payments for Medicare-covered services were available in the claims.) Costs were standardized to 2012 dollars using the Consumer Price Index for All Urban Consumers (U.S. Bureau of Labor Statistics, 2018).

Multivariate analysis adjusted for sex, race/ethnicity, marital status, annual income (in 2012 dollars), educational attainment, Census region, urbanicity, Medicare Advantage (MA) enrollment, and receipt of the Low-Income Subsidy (LIS) for Part D cost assistance. Sex, race/ethnicity, marital status, urbanicity, MA enrollment, and LIS receipt were dichotomized. Census region was also dichotomized into Southeast (including Puerto Rico) or other. Educational attainment was quasi-normally distributed and treated as continuous after the categories between high school diploma and four-year degree were collapsed. Age was not included in the models due to collinearity with other predictors, and because the MCBS sample was already stratified by age (CMS, 2016).

In addition, the analysis adjusted for several health status variables: Likert-type scales of self-rated health (compared to one year ago and to others the same age) and difficulty walking 2-3 blocks or ¼ mile; body mass index (BMI) derived from reported height and weight; basis for Medicare entitlement (disability or age); and number of HF drug classes used during the year (1, 2, or ≥3). A comorbidity index was not computed, because relevant claims data are incomplete for MA enrollees (Cubanski et al., 2014). Nonetheless, the analysis adjusted for self-reported type 2 diabetes and depression, due to their clinical relevance for HF outcomes (Cavender et al., 2015; Wu, Lennie, Dekker, Biddle, & Moser, 2013). Models also included an interaction between drug spending and LIS status, because receipt of the LIS was expected to modify any effect of prescription cost sharing. Finally, all models contained indicators of death or attrition and year of observation as proxies for censoring and time effects, respectively (Lopert et al., 2012).

Statistical analysis. Because cost variables are non-negative and right-skewed, generalized linear models were built using a log-link function and gamma distribution (Basu, Manning, & Mullahy, 2004). MCBS sampling weights were applied to account for unequal probabilities of selection, post-stratification, and nonresponse; for multi-year participants, a weighted average of cross-sectional sampling weights was used (Briesacher et al., 2012). Standard errors were computed with Taylor-series linearization to adjust to clustering and stratification in the sample design (Heeringa, West, & Berglund, 2010; Lewis, 2017). Analyses were performed in SAS version 9.4 and Stata version 15.1. The Emory University Institutional Review Board approved this study.

Results

Descriptive findings. N = 1448 participant-year records met the sample inclusion

criteria. Of those, 1311 (91%) contained at least one prescription for a HF-related drug during the year of observation, representing 876 unique patients. Accounting for sampling weights, this subpopulation was 56% female; 25% non-white, Latino, and/or multiracial; 29% non-urban; and 58% unmarried at the time of survey (Table 1). Median annual income was $17,900, including Social Security, pension, and retirement account payments for the participant and his or her spouse, and about a quarter were below the 2012 federal poverty line for an individual (U.S. Department of Health and Human Services, 2012). Thirty-nine percent did not finish high school, and 45% received the LIS at least part of the year. MA plan subscribers made up 39% of the subpopulation.

In terms of health status, about 54% rated their health as fair or poor compared to others the same age, and 60% could walk 2-3 blocks or ¼ mile only with "a lot" of difficulty or not at all (Table 1). Median BMI was 28.2, and about 20% were entitled to Medicare benefits because of a qualifying disability or disease (rather than age alone). No data on HF class or ejection fraction were available, but 40% rated their health as worse than one year before, and 48% used three or more HF-indicated drug classes during the year of observation. Prevalence of self-reported comorbid conditions was 32% for type 2 diabetes and 40% for depression.

Median [interquartile range (IQR)] OOP payment per HF-related prescription was $2.50 [0.88–4.86] for a 30-day supply (Table 1). Median [IQR] OOP payment for all HF-related prescriptions during the year of observation was $44.00 [13.20–113.80]. Accounting for sampling weights, mean inpatient costs were $5771 per participant-year for Medicare and $8275 per participant-year for all payers. Total health care costs per participant-year averaged $18,447 for Medicare and $27,403 for all payers.

Multivariate models. The adjusted association between average OOP payment per HF prescription and total Medicare costs trended toward statistical significance, $p = .073$ (Table 2). The interaction of mean OOP payment with LIS status was also significant in the model of total Medicare costs, $p < .001$. Because of the interaction term, the LIS modifies the effect of average OOP drug payment. Among non-LIS participants, predicted Medicare costs rose by an average of $126, 95% CI [-10–261], with each additional $1 spent per prescription, $p = .068$ (Figure 1).

Estimation of marginal effects showed that predicted average Medicare costs were $10,450, 95% CI [8721–12,178], at the 25th percentile of OOP drug spending ($2.77 per prescription) compared to $10,644 [8972–12,316] at the 50th percentile of OOP spending ($4.36 per prescription), a difference of $194 per year (Table 4). Likewise, predicted average Medicare costs were $10,915 [9285–12,546] at the 75th OOP percentile ($6.53 per prescription), $271 more per year than at the 50th OOP percentile. These risk-adjusted estimates were conditional on not receiving the LIS.

Average OOP payment per prescription was not significantly associated with Medicare inpatient costs, $p = .56$, total inpatient costs, $p = .58$, or total health care costs, $p = .21$ (Table 2). However, using three or more HF drug classes was associated with elevated health care spending compared to using only one drug class, ranging from 30% higher overall Medicare costs, 95% CI [5–62%], to six times higher inpatient Medicare costs, 95% CI [3.5–10.1]. Total annual OOP spending on HF drugs was not significantly related to any of the cost outcomes, but again using three or more HF drug classes was a significant predictor in all four models (Table 3). Of note, MA plan enrollment was

associated with 31% [6–50%] lower inpatient costs, 75% [68–80%] lower Medicare costs, and 38% [26–48%] lower total costs compared to traditional Medicare.

Discussion

This study of community-dwelling Part D enrollees with self-reported HF found that OOP payment for the average 30-day HF prescription was borderline significantly associated with total Medicare costs. Because of an interaction term in the model, this effect was modified by receipt of the LIS during the observation year. For patients who did not receive the LIS, predicted Medicare costs rose by an average $126 for each additional dollar the patient spent per prescription. This equates to a 1.2% increase in median annual Medicare cost. However, the confidence interval for this effect straddled zero, so the null hypothesis of no association between OOP drug spending and Medicare costs cannot be rejected.

There was no evidence of an effect by OOP drug spending on Medicare inpatient costs, total inpatient costs, or total costs for all payers. Likewise, there was no evidence that total OOP drug payments over the year observation were associated with any of the cost outcomes. However, number of HF drug classes used was predictive of inpatient and overall health care costs, which may reflect that patients who used more drug classes were sicker and required more care. Although the analysis accounted for several health status variables, MCBS contains no clinical data relevant to HF, such as ejection fraction, so this measure of total HF drug burden may have captured HF-specific health status.

It is unclear why patient drug payments were generally not associated with health care costs. A positive association had been hypothesized, because the rationale of V-BID is that lower copays for effective chronic disease medications promote adherence and

have the potential to reduce costs (Chernew et al., 2007; Lee et al., 2013). Likewise, several studies have demonstrated a link between higher OOP drug payments and greater downstream health care costs (Colombi, Yu-Isenberg, & Priest, 2008; Park et al., 2015; Subramanian, 2011; Thornton Snider, Seabury, Lopez, McKenzie, & Goldman, 2016). However, a prior study in a commercially insured HF population found no significant effect of medication copay on health care costs (Cole et al., 2006), and a systematic review of V-BID studies found no evidence of significant effects on total or non-drug costs after one year (Lee et al., 2013). Our sample of Medicare beneficiaries with drug coverage may have enjoyed good access to preventive medications, averting the need for costlier, more intense care.

In addition, compared to other chronic disorders, HF remains a serious illness with a generally poor prognosis (Go et al., 2014). The severity of HF and consequences of non-adherence may make patients less price-sensitive. Many prior studies of the effect of prescription cost sharing on health outcomes have focused on subclinical or slower-onset conditions, such as hypertension, lipidemia, and diabetes. In contrast, the clinical effects of non-adherence to HF treatment can quickly become serious, and even modest gains in adherence among Medicare beneficiaries with HF have been linked to lower 3-year cumulative Medicare spending (Lopert et al., 2012). Adherence was not examined in the present study, but a previous analysis of three drug classes in our sample found high median adherence (McGee, Phillips, Higgins, & Butler, 2017), and an earlier study of commercially insured HF patients showed no effect on β-blocker adherence at copays below $20 (Patterson et al., 2011). Average out-of-pocket drug costs in our sample were far below that threshold, at just $4 per prescription.

It has also been shown that health plans with greater cost sharing for all services may lead to lower health care costs. The RAND Health Insurance Experiment of the 1970s-80s was a randomized trial in which participants assigned to health plans with coinsurance incurred lower overall costs than participants with free care after 3-5 years of follow up (Manning et al., 1987). Yet, subsequent analysis showed that almost all the reduction in hospital use in the cost-sharing plans could be attributable to greater attrition in those groups (Nyman, 2007). Moreover, low-income participants with hypertension had higher predicted mortality in plans with cost sharing (Newhouse, 2004). In contrast, our study showed that receiving the LIS was associated with higher Medicare costs, including inpatient costs, even though the LIS should have promoted access to prescribed medications. This finding suggests that low-income HF patients are vulnerable to worse health outcomes independent of out-of-pocket liability for prescriptions.

Nonetheless, among patients who did not benefit from LIS offsets, there was some evidence that prescription drug spending was associated with total Medicare costs. Increasing the average OOP payment from $2.77 to just $4.36 per prescription was associated with a predicted average rise of $194 in Medicare costs per patient over the year of observation. Likewise, increasing the mean OOP payment from $4.36 to $6.53 per prescription was linked with a predicted average rise of $271 in Medicare costs per patient-year. Although this effect only approached (but did not reach) statistical significance, it suggests that caution is warranted before raising HF prescription copays.

Notably, MA enrollment was consistently associated with lower costs in this study. As explained above, MCBS does not contain complete encounter data for MA plan members (Cubanski et al., 2014). Therefore, cost outcomes for those patients were based

primarily on survey-reported events, which may be subject to bias. In this sample, just 26% of MA participants had an inpatient event for any reason during the year of observation, compared to 41% of traditional Medicare beneficiaries. Yet, this discrepancy is consistent with a prior study of risk-adjusted 30-day readmission rates by MA status (Lemieux, Sennett, Wang, Mulligan, & Bumbaugh, 2012), and MA plans may attract healthier members in the first place (Maciejewski et al., 2009). Therefore, MA plan enrollment may be linked with lower health care costs in this sample because of favorable selection, under-reporting of events, more efficient care, or some other factor.

Limitations. Inferences from this study are limited by its cross-sectional design. Costs were aggregated over the year of observation, so inpatient and other health care costs may have accrued before the prescription drug costs. Moreover, OOP drug spending may take longer than 12 months to affect non-drug costs, which could have underestimated the main effects. Identifying HF cases with a single survey question may have led to misclassification, because some patients may not have fully understood the question or their diagnosis. Furthermore, HF diagnosis may have occurred after baseline, since respondents who denied HF in prior years were again asked the HF survey question during the last four months of the observation year.

As noted above, no HF-specific clinical data were available, so the effect of drug spending by stage of illness could not be directly assessed, though adjustment for number of drug classes used and multiple health status variables may have captured some of this variation. Patients may evaluate the cost-sharing requirements of their Part D plan before a drug is prescribed or purchased, which could have been a source of endogeneity. Pooling data from multiple survey years could have underestimated standard errors,

because observations from multi-year participants are not truly independent. Yet, according to Sarndal and Swensson, the necessity of correcting for this source of clustering in complex samples is unclear if the primary sampling unit is specified correctly (Briesacher et al., 2012).

Exclusion of survey-reported prescriptions that did not appear in Medicare records may have biased spending estimates. However, only 6% of unmatched survey prescriptions reflect true out-of-plan use for Part D enrollees with common chronic disorders in MCBS data; many of the rest could be matched to Medicare records with a more sensitive algorithm (Roberto & Stuart, 2014). Likewise, the inclusion of MA plan subscribers may have resulted in under-reporting of health care encounters and costs for that group, as explained above. And as with any analysis of administrative data sets, results may be spurious because of omitted variables or sampling error.

Implications for policy or practice. With the discovery of new therapeutic drug classes and the addition of costly, new therapies (e.g., sacubitril and ivabradine) to the HF management arsenal, questions about the effects of prescription cost sharing are freshly relevant for HF patients. Given the growing interest in and use of V-BID, it is notable that our study of a generalizable sample of Part D enrollees with HF found little evidence that higher OOP spending on essential medications resulted in greater inpatient or total health care costs.

That is not to say that V-BID has no useful or effective role in optimal health coverage for this population, but further disaggregation by clinical status, risk profile, and drug class is warranted. Furthermore, the marginally significant finding that each additional dollar spent per HF prescription predicted an average rise of $126 in annual

Medicare costs per non-LIS patient signals the need for caution. Future studies should address the design limitations described above, such as temporality, time horizon, and disaggregation, before these findings inform policy decisions.

Conclusions

The findings from this study suggest that Part D plans may levy moderate cost sharing for essential drugs without spiking total or inpatient care costs for community-dwelling HF patients. There is some evidence that higher out-of-pocket drug spending is associated with modestly increased Medicare costs in the non-LIS population, so caution is warranted. Longitudinal analysis would better inform the optimal design of prescription drug coverage for HF patients. Nonetheless, this study extends previous research on the effects of out-of-pocket drug spending on adherence and health care use in HF.

Table 4.1. *Sample characteristics*

Variable		Count (unweighted)	Percent (weighted)	95% CI (design-adjusted)	
TOTAL		1311			
Gender					
	Male	584	44.3	40.3	48.3
	Female	727	55.7	51.7	59.7
Race/ethnicity					
	Non-white[a] or Latino	341	25.3	21.2	29.3
	White, non-Latino	966	74.7	70.7	78.8
Education					
	No schooling	21	1.4	0.6	2.2
	Nursery-8th grade	214	15.1	12.5	17.8
	9th-12th grade	297	22.6	19.3	25.9
	High school diploma	361	28.1	24.9	31.3
	Vocational, some college or associate's	300	23.9	20.8	27.1
	Bachelor's degree	65	5.3	3.6	6.9
	Post-graduate	51	3.5	1.8	5.1
Marital status					
	Married	515	41.5	37.6	45.5
	Unmarried	795	58.5	54.5	62.4
Urbanicity					
	Metropolitan area	898	70.6	66.0	75.2
	Non-metro. area	413	29.4	24.8	34.0
Region					
	Southeast or PR	639	47.9	42.9	52.8
	Other	672	52.1	47.2	57.1
Health vs. others the same age					
	Excellent	52	3.8	2.6	5.1
	Very good	182	12.7	10.7	14.7
	Good	389	29.2	26.1	32.3
	Fair	423	33.3	30.4	36.2
	Poor	257	20.9	18.2	23.6
Health now vs. one year ago					
	Much better	71	5.9	4.5	7.2
	Somewhat better	173	13.3	11.1	15.5
	About the same	557	41.3	37.7	44.9
	Somewhat worse	410	31.7	28.8	34.6
	Much worse	97	7.8	6.1	9.5
Difficulty walking ¼ mile or 2-3 blocks					
	None	226	17.8	15.1	20.5
	A little	136	10.2	8.3	12.1
	Some	153	12.0	10.2	13.8
	A lot	226	17.0	15.0	18.9
	Unable	563	43.0	39.4	46.6
Medicare entitlement					
	Disability/ESRD	228	20.5	17.0	24.0
	Age only	1083	79.5	76.0	83.0
Type 2 diabetes					
	Yes	397	31.7	28.5	34.9

	No	905	68.3	65.1	71.5
Depression					
	Yes	500	40.1	36.6	43.7
	No	811	59.9	56.3	63.4
No. of HF-indicated drug classes used					
	1	227	18.2	15.0	21.4
	2	456	33.9	31.0	36.8
	3 or more	628	47.9	44.2	51.6
Medicare plan type					
	Medicare Advantage	492	39.0	34.7	43.4
	Traditional (FFS)	819	61.0	56.6	65.3
Low-income subsidy					
	Received	586	44.7	41.0	48.3
	Not received	725	55.3	51.7	59.0
Censoring					
	Died or LTFU	53	4.1	2.9	5.2
	Alive, retained	1258	95.9	94.8	97.1
Year of observation					
	2010	438	32.3	29.9	34.8
	2011	429	33.0	31.1	34.9
	2012	444	34.7	32.3	37.1

Variable	**Median** (unweighted)	**Interquartile range** (unweighted)		**Mean** (weighted)	**SE** (design-adjusted)
Age (in years)	77	69	83	73.6	0.42
Annual income ($'000)[b,c]	17.9	11.4	30.0	25.0	0.97
Body mass index	28.2	24.4	32.8	30.0	0.30
Average OOP payment per HF prescription[b,d]	$2.50	$0.88	$4.86	$4.00	0.24
Total OOP payments for HF prescriptions[b]	$44.00	$13.20	$113.80	$89.16	4.70
Inpatient costs, all payers[b]	$0	$0	$8967	$8275	596.9
Inpatient costs, Medicare[b]	$0	$0	$3308	$5771	533.0
Total costs, all payers[b]	$14,644	$6674	$34,548	$27,403	1092.3
Total costs, Medicare[b]	$7160	$2737	$22,176	$18,447	985.1

Note. CI = confidence interval; ESRD = end-stage renal disease; FFS = fee-for-service; HF = heart failure; LTFU = lost to follow-up; OOP = out-of-pocket; PR = Puerto Rico; SE = standard error.
[a] Includes multiracial participants
[b] Adjusted to 2012 dollars
[c] Includes Social Security, pension and retirement account payments for participant and spouse
[d] Normalized to a 30-day supply

Table 4.2. *Effect of mean out-of-pocket payment per heart failure prescription on health care costs, modified by LIS status, Medicare Current Beneficiary Survey (2010-12)*

Effect	All inpatient costs		Medicare inpatient costs		Total health care costs		Total Medicare costs	
	exp(*B*)	95% CI	exp(*B*)	95% CI	exp(*B*)	95% CI	exp(*B*)	95% CI
Mean payment per HF Rx[a]	0.99	0.98-1.01	1.01	0.97-1.06	1.00	1.00-1.01	1.01[c]	1.00-1.02
LIS receipt	1.10	0.70-1.72	2.97[d]	1.41-6.25	1.15	0.96-1.39	1.71[d]	1.36-2.15
LIS*payment interaction	0.86[c]	0.72-1.02	0.75[d]	0.60-0.93	0.94[d]	0.91-0.98	0.92[d]	0.88-0.96
Health vs. age group[b]	1.28[d]	1.11-1.49	1.74[d]	1.33-2.27	1.17[d]	1.08-1.27	1.23[d]	1.11-1.36
Health vs. one year ago[b]	1.03	0.90-1.16	0.96	0.74-1.24	0.93	0.86-1.01	0.89[d]	0.80-1.00
Difficulty walking[b]	1.25[d]	1.14-1.38	1.11	0.97-1.28	1.15[d]	1.10-1.20	1.13[d]	1.07-1.20
BMI	0.96[d]	0.94-0.98	0.98	0.95-1.01	0.98[d]	0.98-0.99	0.99[d]	0.98-1.00
Disability	1.56[d]	1.09-2.23	1.18	0.71-1.97	1.63[d]	1.37-1.95	1.48[d]	1.17-1.88
Type 2 diabetes	0.93	0.69-1.24	0.67	0.39-1.15	1.01	0.87-1.18	1.00	0.85-1.17
Depression	1.09	0.82-1.45	0.95	0.62-1.45	1.20[d]	1.02-1.40	1.16	0.94-1.42
Male gender	1.93[d]	1.45-2.56	1.17	0.71-1.91	1.18[d]	1.02-1.35	1.02	0.86-1.22
Non-white/Latino	1.04	0.73-1.48	1.01	0.53-1.91	1.03	0.88-1.21	1.07	0.84-1.35
Married	0.79[c]	0.60-1.03	1.18	0.68-2.06	0.88[c]	0.76-1.01	0.93	0.75-1.15
Annual income	1.00	0.99-1.00	1.01[d]	1.00-1.01	1.00	1.00-1.00	1.00	1.00-1.01
Education level	1.11	0.98-1.25	1.13	0.91-1.40	1.08[d]	1.01-1.16	1.08[c]	0.99-1.17
Metro. area	1.06	0.84-1.34	1.36[c]	0.95-1.96	1.10	0.96-1.26	1.12	0.95-1.31
South or PR	0.84	0.66-1.07	0.49[d]	0.31-0.80	0.92	0.81-1.06	0.85[c]	0.72-1.02
Died or lost to follow-up	0.72	0.37-1.39	0.64	0.30-1.40	0.86	0.64-1.16	0.80	0.58-1.09
Year of survey (*ref.*=2012)								
2010	1.33[c]	0.97-1.82	1.41	0.78-2.56	1.02	0.87-1.20	1.09	0.88-1.35
2011	1.50[d]	1.08-2.09	0.71	0.42-1.20	1.05	0.91-1.21	0.91	0.76-1.10
Medicare Advantage	0.69[d]	0.51-0.94	0.04[d]	0.02-0.09	0.62[d]	0.52-0.74	0.25[d]	0.20-0.32
Drug classes used (*ref.*=1)								
2	1.42	0.93-2.17	2.15[d]	1.32-3.52	1.19[c]	1.00-1.41	1.09	0.86-1.37
3 or more	2.74[d]	1.79-4.20	5.95[d]	3.52-10.08	1.40[d]	1.18-1.67	1.30[d]	1.05-1.62
Intercept ('000)	0.99	0.46-2.16	0.22[d]	0.05-0.97	8.62[d]	5.40-13.75	6.06[d]	3.28-11.19

Note. BMI = body mass index; CI = confidence interval; LIS = low-income subsidy; HF = heart failure; OOP = out-of-pocket; *ref.* = reference; Rx = prescription; PR = Puerto Rico.
[a] Normalized to a 30-day supply
[b] 5-point scale; higher score reflects worse health or function
[c] Significant at the $p < .10$ level
[d] Significant at the $p < .05$ level

Table 4.3. *Effect of total annual out-of-pocket payments for heart failure drugs on health care costs, modified by LIS status, Medicare Current Beneficiary Survey (2010-12)*

Effect	All inpatient costs		Medicare inpatient costs		Total health care costs		Total Medicare costs	
	exp(*B*)	95% CI	exp(*B*)	95% CI	exp(*B*)	95% CI	exp(*B*)	95% CI
Total OOP payments on all HF Rxs[a]	1.00	1.00-1.00	1.00	1.00-1.00	1.00	1.00-1.00	1.00	1.00-1.00
LIS receipt	0.96	0.62-1.47	2.86[d]	1.46-5.60	1.13	0.92-1.38	1.69[d]	1.33-2.14
LIS*payment interaction	1.00	0.99-1.00	0.99[d]	0.98-0.99	1.00[d]	1.00-1.00	1.00[d]	0.99-1.00
Health vs. age group[b]	1.29[d]	1.11-1.49	1.81[d]	1.39-2.36	1.17[d]	1.08-1.27	1.24[d]	1.12-1.37
Health vs. one year ago[b]	1.02	0.90-1.16	0.94	0.73-1.21	0.93	0.86-1.01	0.89[d]	0.79-0.99
Difficulty walking[b]	1.25[d]	1.14-1.38	1.09	0.95-1.26	1.15[d]	1.09-1.20	1.13[d]	1.07-1.20
BMI	0.96[d]	0.95-0.98	0.98	0.95-1.01	0.99[d]	0.98-1.00	0.99[c]	0.98-1.00
Disability	1.54[d]	1.07-2.22	1.03	0.61-1.74	1.60[d]	1.34-1.92	1.44[d]	1.14-1.83
Type 2 diabetes	0.90	0.68-1.21	0.67	0.39-1.17	1.01	0.87-1.17	0.99	0.85-1.15
Depression	1.09	0.82-1.44	0.88	0.58-1.35	1.20[d]	1.02-1.40	1.15	0.94-1.42
Male gender	1.90[d]	1.43-2.52	1.18	0.72-1.93	1.17[d]	1.01-1.35	1.01	0.85-1.20
Non-white/Latino	1.06	0.75-1.50	1.00	0.52-1.89	1.02	0.87-1.21	1.04	0.82-1.32
Married	0.77[c]	0.59-1.01	1.04	0.61-1.76	0.87[c]	0.76-1.00	0.92	0.74-1.14
Annual income	1.00	0.99-1.00	1.01[d]	1.00-1.01	1.00	1.00-1.00	1.00	1.00-1.01
Education level	1.10	0.98-1.24	1.16	0.93-1.44	1.08[d]	1.01-1.16	1.08[c]	0.99-1.18
Metro. area	1.08	0.86-1.36	1.48[d]	1.03-2.12	1.10	0.96-1.27	1.12	0.94-1.33
South or PR	0.82	0.65-1.04	0.47[d]	0.30-0.75	0.92	0.81-1.06	0.86[c]	0.72-1.02
Died or lost to follow-up	0.72	0.37-1.39	0.69	0.32-1.47	0.87	0.64-1.16	0.81	0.60-1.10
Year of survey (*ref.*=2012)								
2010	1.30	0.95-1.77	1.27	0.68-2.35	1.03	0.88-1.20	1.10	0.89-1.36
2011	1.49[d]	1.07-2.07	0.69	0.40-1.18	1.05	0.91-1.21	0.92	0.76-1.10
Medicare Advantage	0.69[d]	0.50-0.94	0.04[d]	0.02-0.08	0.62[d]	0.52-0.74	0.25[d]	0.20-0.32
Drug classes used (*ref.*=1)								
2	1.51[c]	1.00-2.29	2.48[d]	1.50-4.11	1.21[d]	1.03-1.44	1.11	0.89-1.40
3 or more	3.08[d]	1.97-4.81	7.04[d]	3.96-12.51	1.47[d]	1.25-1.74	1.36[d]	1.09-1.70
Intercept ('000)	0.99	0.45-2.17	0.17[d]	0.04-0.79	8.58[d]	5.38-13.69	5.92[d]	3.20-10.95

Note. BMI = body mass index; CI = confidence interval; LIS = low-income subsidy (for Medicare Part D); HF = heart failure; OOP = out-of-pocket; *ref.* = reference; Rx = prescription; PR = Puerto Rico.
[a] Normalized to a 30-day supply
[b] 5-point scale; higher score reflects worse health or function
[c] Significant at the $p < .10$ level
[d] Significant at the $p < .05$ level

Table 4.4. *Predicted Medicare costs by prescription drug spending quartile, non-LIS*

OOP payment per prescription	OOP payment percentile	Predicted average Medicare costs	95% CI	Difference in predicted costs per patient-year
$2.77	25th	$10,450	8721-12,178	--
$4.36	50th	$10,644	8972-12,316	+$194
$6.53	75th	$10,915	9285-12,546	+$271

Note. CI = confidence interval; LIS = low-income subsidy; OOP = out-of-pocket.

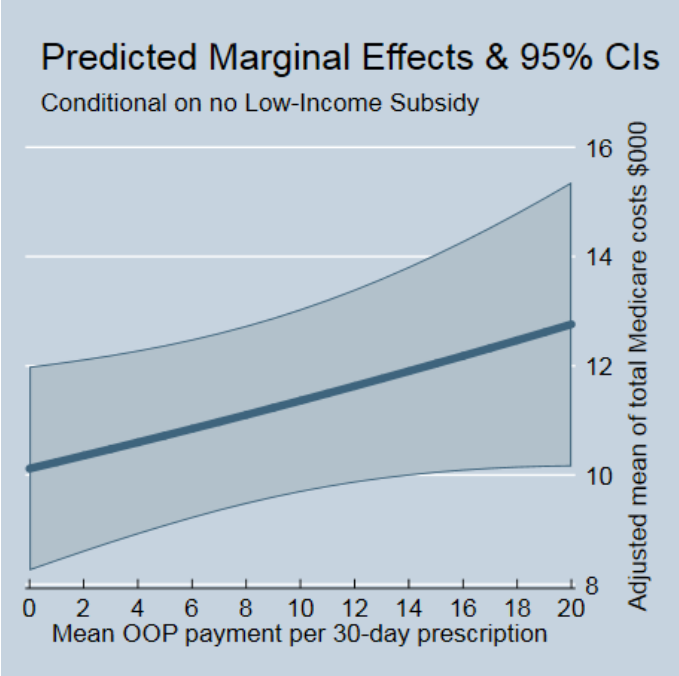

Figure 4.1. Converted to 2012 dollars; OOP = out-of-pocket.

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CHAPTER 5

Conclusion

Summary of findings

This purpose of this dissertation was to evaluate the relationship between prescription cost sharing and medication adherence, acute care use, and health care costs among community-dwelling Medicare Part D beneficiaries with heart failure (HF). It found no evidence of an association between out-of-pocket spending and adherence for angiotensin receptor blockers or angiotensin-converting enzyme (ACE) inhibitors. It also found no evidence of an association between out-of-pocket spending per HF prescription and the odds of HF-specific hospitalization or emergency care. And it found no evidence of an association between out-of-pocket drug spending and total health care costs, total inpatient costs, or inpatient costs to Medicare. Yet, it did detect a modest, statistically significant, inverse association between out-of-pocket spending and adherence for β blockers. Likewise, it detected associations of borderline statistical significance between out-of-pocket spending on HF drugs and frequency of HF-related hospitalization, number of HF-related inpatient days, and total Medicare costs.

Aim 1. The analysis of adherence excluded recipients of the Low-Income Subsidy (LIS) but retained participants in Medicare Advantage (MA) plans. Prescription cost sharing was approximated by the average out-of-pocket expenditure on a relevant prescription, standardized to a 30-day supply and expressed as a percentage of average monthly income. Adherence was estimated with the medication possession ratio (MPR), which permitted variable observation periods. MPR was dichotomized into adherent (≥80%) or non-adherent (<80%), and extreme values were discarded for the linear

models. Notably, each of the three drug classes was analyzed independently, at least two purchases of the same agent were required for the MPR calculation, and participants who switched agents within the same drug class were excluded.

Logistic models of the adjusted odds of non-adherence to ACE inhibitors and angiotensin receptor blockers (ARBs) showed no significant effect from out-of-pocket spending as a share of income. In the logistic model for β blockers, on the other hand, the adjusted odds of non-adherence were significantly associated with the share of income spent on that β blocker, odds ratio (OR) = 1.41, 95% CI [1.01, 1.98], $p = .046$. Similarly, the linear models for ACE inhibitors and ARBs showed no significant association between adherence and out-of-pocket spending. In the linear model for β blockers, however, there was a significant inverse association between share of income spent on the β blocker and MPR, $B = -3.63$, $SE = 1.57$, $p = .022$. Assuming a linear relationship, an increase of 0.1 in percent of income spent on a β blocker (equivalent to a shift from the 25th to 50th cost-sharing percentile) was associated with 4% increased odds of non-adherence and an absolute decline of 0.4 in the MPR.

Aim 2. In the analysis of acute care use, MA plan subscribers were excluded, due to incomplete reporting by plan sponsors of the encounter data used to define the outcomes. However, LIS recipients were retained, and participants who otherwise met the sample criteria were included if they had any prescription from a HF-indicated drug class in the Medicare pharmacy records. The predictor of interest was average out-of-pocket payment per HF-related prescription, normalized to a 30-day supply. The outcomes were odds of hospitalization or emergency department (ED) use with a principal or secondary diagnosis of HF; frequency of such hospitalizations; and number of HF-related inpatient

days during the year of observation. Logistic, Poisson, and negative binomial models were built for each effect, respectively, and models included an interaction of prescription drug spending with Medicaid eligibility.

Conditional on the effect of no Medicaid entitlement, average out-of-pocket expenditure per HF prescription was not significantly associated with odds of HF-related hospitalization, OR = 1.01, 95% CI [0.98, 1.05], p = .401, or ED use, OR = 1.02, 95% CI [0.97, 1.08], p = .419. Average expenditure per prescription was borderline significantly associated with frequency of HF-related hospital admission, rate ratio (RR) = 1.02, 95% CI [1.00, 1.05], p = .060, and hospitalized days, RR = 1.04, 95% CI [1.00, 1.07], p = .057. These effects were smaller and non-significant in zero-inflated versions of the models. Notably, Medicaid status moderated the associations between drug spending and number of hospitalizations and inpatient days, $p < .05$: the associations between drug spending and hospital use were flat to weakly positive for patients without Medicaid but significantly negative for Medicaid-eligible patients.

Aim 3. The analysis of health care costs retained both MA plan subscribers and LIS recipients. The predictors of interest were average out-of-pocket payment per HF-related prescription, normalized to a 30-day supply, and total out-of-pocket payments for HF drugs in the year of observation. The outcomes were total and Medicare-specific payments for inpatient and all health care services during the observation year. The data set contained imputed payments for non-Medicare-covered services for participants with incomplete survey data. Gamma regression models with a log link were constructed, because cost variables were non-negative and right-skewed. Moderation of the cost-sharing effect by LIS status was hypothesized, based on the significant interaction with

Medicaid from Aim 2. (All LIS recipients were also Medicaid-eligible.) Therefore, models included an interaction between out-of-pocket drug spending and LIS receipt.

Conditional on not receiving the LIS, predicted Medicare costs per patient rose by an average of $126, 95% CI [-10, 261], $p = .068$, for each additional $1 spent per prescription. This effect trended toward statistical significance. Predicted Medicare costs were an average $194 higher per patient at the 50th versus 25th drug cost-sharing percentile, and they were $271 higher at the 75th versus 50th percentile. Again, the interaction term was significant, indicating that receipt of the LIS moderated the drug spending effect on Medicare costs. Average payment per prescription was not significantly associated with Medicare inpatient costs, total inpatient costs, or total health care costs. Annual out-of-pocket spending on all HF drugs was not significantly related to any of the cost outcomes.

Contribution to the literature

This dissertation is the first known study of HF prescription cost sharing and outcomes in the Medicare population. Prior studies of HF patients analyzed claims databases from commercial insurance plans in primarily working-age samples. Medicare beneficiaries may be distinct from those samples in important ways. For example, they might have more advanced illness, which in turn may make them less price-sensitive. Although HF-specific clinical information was not included in this data set, large proportions of participants reported only fair to poor health, worse health than a year earlier, and difficulty walking short distances. In addition, they were older on average than the parent Medicare sample, and at least among the fee-for-service (i.e., non-MA) beneficiaries, the average person had multiple comorbidities. The overall lack of

significant cost-sharing effects observed in this study, compared to previous work, could be partly a function of older, sicker patients who felt more compelled to adhere to prescribed drug regimens.

Furthermore, average out-of-pocket spending on HF-indicated prescriptions was very low in this sample. The two published studies from the last 12 years that focused on HF patients both detected copay effects at levels much higher than average drug payments in this study. Modeling by Cole, Norman, Weatherby, and Walker (2006) predicted that a $10 copay rise was associated with a 2.6% decline in MPR for ACE inhibitors and a 1.8% decline in MPR for β blockers. Those effects are modest (though they were linked to significantly higher odds of HF-related hospitalization), and the vast majority of participants in the present study paid less than $10 for those drug classes. Likewise, Patterson, Blalock, Smith, and Murray (2011) detected increased odds of non-adherence only in the groups with copays over $20, and they only reported results for β blockers. This dissertation analyzed data from participants with continuous enrollment in Part D, which provides federally mandated levels of prescription drug coverage (Hoadley, Cubanski, & Neuman, 2016), and the data were collected at a time when many of the drugs in use were off patent. Coupled with disease severity, the low out-of-pocket prices faced by this sample may have promoted adherence.

Nonetheless, some significant or near-significant cost-sharing effects were observed despite low out-of-pocket drug costs and potentially severe disease. Percent of income spent on a β blocker was associated with non-adherence among non-LIS patients; average out-of-pocket payment per HF prescription was borderline significantly associated with HF-related hospital admissions and inpatient days in non-Medicaid

patients; and for each $1 spent per prescription by non-LIS patients, predicted Medicare costs rose by a borderline significant $126, on average. These effect sizes are modest, but they are not wholly dissimilar from previous research in healthier populations with more copay variability. For example, a 2012 literature review estimated a 3.8% average drop in adherence per $10 rise in drug copay across 24 primary studies (Eaddy, Cook, O'Day, Burch, & Cantrell, 2012). The cost-sharing effect on β-blocker MPR in this study was roughly equivalent to a 0.3% decrease in average adherence per $2.20 rise in out-of-pocket payment (or 1.4% decrease per $10 rise).

Finally, this dissertation appears to be the first study of HF prescription cost sharing to use population-level survey data. The Medicare Current Beneficiary Survey (MCBS) is a powerful data source, because it combines detailed interviews with verifiable events in Medicare records, and the Cost and Use files are designed to be representative of the ever-enrolled Medicare population during the survey year (U.S. Centers for Medicare and Medicaid Services, 2016). Therefore, findings from this dissertation can be generalized to community-dwelling Medicare patients with self-reported HF and continuous Part D coverage nationally. (Notable exceptions are that the findings for Aim 1 cannot be extrapolated to LIS recipients, and Aim 2 findings do not apply to MA plan subscribers.) Perhaps more importantly for future work, this study demonstrates that analysis of MCBS data is a viable option for researching cost-sharing effects in the Medicare population generally.

Application of conceptual framework

Frick and Chernew's (2009) theory of beneficial moral hazard provided the conceptual framework for this dissertation. Like Nyman's (2004) alternative view of

moral hazard as an income transfer effect, their theory recognizes that some of the additional health care consumed at lower out-of-pocket prices is efficient and leads to welfare gains. This phenomenon occurs primarily with high-value services that prevent costlier complications down the road. One scenario in which beneficial moral hazard arises is when the demand curve for a service ought to be more inelastic, or less sensitive to price changes, as with highly cost-effective services like preventive care (Frick & Chernew, 2009). Yet, the actual demand curve may be more elastic, depending on how patients understand their health care, make decisions amid uncertainty or stress, and value future gains against present losses (Chernew, Rosen, & Fendrick, 2007; Newhouse, 2006). To the extent that lower out-of-pocket costs promote uptake of a high-value service and nudge the quantity consumed closer to the ideal, "perfectly informed" demand curve, the better for the market and society (Frick & Chernew, 2009).

Findings from this study suggest that HF patients with Part D coverage may already consume high-value care, such as recommended prescription medications, at optimal or near-optimal amounts. Indeed, median adherence was high in the analysis of non-LIS recipients: 95% for β blockers and ACE inhibitors, and nearly 98% for ARBs (though it is worth remembering that at least two fills of the same drug in the same year were required to compute the MPR, implying a minimum level of adherence; Patterson et al., 2011). Low Part D cost-sharing liability for the average prescription in this study may have ensured that the actual quantity demanded was close to the quantity dictated by the perfectly informed demand curve. The lack of evidence for increased odds of HF-related hospitalization, total inpatient costs, Medicare inpatient payments, and total health care

costs at higher drug expenditures may represent welfare gains from modest prescription cost sharing overall.

On the other hand, the negative effect of relative cost sharing on adherence to β blockers, though small, suggests there may have been room for lower prices to move the quantity consumed closer to optimality for some patients. Likewise, the near-significant cost-sharing effects on rates of HF-specific hospital admissions and inpatient days and on total Medicare costs may reflect a small welfare loss due to below-optimal prescription use. It is unclear whether still lower out-of-pocket prices would have nudged consumption of prescriptions closer to ideal demand, and if so, for which drugs in which plans. Yet, future rises in medication copays or coinsurance without regard to clinical value may risk growing this potential welfare loss to a more appreciable size. This implication will become more salient as data emerge from more recent Medicare cohorts, where the use of newer, costlier HF therapies (e.g., sacubitril and ivabradine) is likely to be more widespread.

Strengths and limitations

One important advantage of this study was its use of data from the MCBS. As described previously, in-depth questionnaires conducted three times annually for four years are supplemented by data from administrative and claims records from the Centers for Medicare & Medicaid Services (CMS) (DiMartino, Shea, Hernandez, & Curtis, 2010; Lopert et al., 2012). Most prior studies of cost sharing in chronic diseases have been limited to a single employer, insurance provider, managed care organization, or state program, but the MCBS has high external validity for Medicare beneficiaries nationally. It also links verifiable events from Medicare records, such as prescription drug fills, with

key survey-reported variables, such as income (including from retirement sources), race and ethnicity, and self-reported measures of health and function. Many prior studies have lacked these variables, or they have relied on very imperfect proxies, such as the proportion of Black residents in a ZIP code to estimate a participant's race (Choudhry et al., 2012).

The limitations relevant to each specific aim are detailed in the preceding chapters but will be summarized here. Despite the high external validity of the data source, inferences from this study are limited by its cross-sectional design. Costs and use were aggregated over the year of observation, so outcomes such as non-adherence, hospitalization, and medical costs may have occurred before at least some of the observed prescription drug payments. Moreover, out-of-pocket drug spending may take longer than 12 months to affect outcomes, especially total health care costs, which could have underestimated effects. Identifying HF cases with a single survey question may have led to misclassification, because some patients may not have fully understood the question or their diagnosis. An interrater agreement analysis of the questionnaire item with a claims-based case definition (DiMartino et al., 2010) yielded an unweighted kappa of just .40, suggesting only fair to moderate agreement (McHugh, 2012). Furthermore, HF diagnosis may have occurred after baseline, since respondents who denied HF in prior years were again asked the HF survey question in the last four months of the observation year, and it was impossible to distinguish between the two types of "yes" responses in the data set.

Despite the availability of self-reported measures of health and function, the data set contained no HF-specific clinical data, such as HF class or ejection fraction, so the effect of drug spending by stage of illness could not be directly assessed. Patients may

evaluate the cost-sharing requirements of their Part D plan before enrolling, or they may discuss out-of-pocket price with their prescriber in advance, either of which could have biased results toward the null hypothesis. Exclusion of participants who switched drugs within a class during the observation year for the adherence analysis obscured any cost-sharing effect that contributed to the switch; however, including them would have introduced instability to model estimates and overestimated adherence due to leftover supply of the discontinued drug (Cole et al., 2006; Kim et al., 2011). Pooling data from multiple survey years could have underestimated standard errors, because observations from multi-year participants are not truly independent. Yet, the necessity of correcting for this source of autocorrelation in complex survey analysis is unclear, as long as the primary sampling unit is correctly specified (Briesacher, Tjia, Doubeni, Chen, & Rao, 2012).

Exclusion of survey-reported prescriptions that did not appear in Medicare records may have biased spending estimates. However, only 6% of unmatched survey prescriptions reflect true out-of-plan use for Part D enrollees with common chronic disorders in MCBS data; many of the rest are probably duplicates (Roberto & Stuart, 2014). The inclusion of MA plan subscribers for Aim 3 may have resulted in under-reporting of health care costs for that group, because MA plan sponsors do not report complete encounter data to CMS (Cubanski, Swoope, Damico, & Neuman, 2014). Nonetheless, the survey asks about health care use extensively, and missing payment data for events not in the Medicare records undergo a rigorous imputation process (CMS, 2016). Finally, as with any analysis of secondary data, results may be spurious because of omitted variables or sampling error.

Implications for policy and future research

There is growing interest in value-based insurance design (V-BID), including within the Medicare program (Hirth, Cliff, Gibson, McKellar, & Fendrick, 2016). To better inform V-BID policies, evidence of the effects of cost-sharing exposure for additional high-value services, such as recommended pharmacotherapy in chronic HF, is needed. This dissertation found that, with average patient payments for HF medications below $5, there was little evidence of statistically or clinically significant effects on important cost and use outcomes. Yet, even at these low average out-of-pocket levels, there was evidence of slightly decreased adherence to β blockers, which have been shown to prevent hospitalization in HF (Packer, 1998), and possibly increased inpatient use and Medicare costs at higher prescription cost-sharing amounts. To the extent that health insurers are interested in adopting V-BID principles, these findings offer preliminary evidence for cost-sharing levels that promote clinical value in HF.

Nonetheless, additional research is warranted before these findings inform policy design. Prospective data collection, or at least a retrospective analysis that addresses temporality, e.g., a controlled before-and-after design, would improve the internal validity of study findings. Likewise, a time horizon of longer than 12 months may be necessary to detect cost and use outcomes from increased prescription cost sharing (or averted outcomes from reduced cost sharing), if they exist. Certain benefit design information, such as deductible and copay amounts for specific drugs, would improve measurement precision. And further disaggregation of patients by clinical status, risk profile, and specific drugs used would help tease out the value implications of cost-sharing amounts. For example, the results for Aims 2 and 3 showed significant

interactions of the main effects with low-income assistance (i.e., Medicaid or LIS) despite adjustment for annual income and other sociodemographic characteristics. Mechanisms that render low-income patients vulnerable to worse outcomes despite the availability of cost offsets to promote use of high-value care should be explored.

Concluding remarks

HF remains a leading cause of morbidity and mortality in the U.S. (Go et al., 2014) yet has received little attention in the literature on prescription drug cost sharing. This dissertation analyzed data from a national sample of community-dwelling HF patients with Medicare Part D coverage. It found no evidence of an association between out-of-pocket drug spending and: adherence to ACE inhibitors or ARBs; odds of HF-specific hospitalization or emergency care; or total health care costs, total inpatient costs, or inpatient costs to Medicare. Yet, it did detect a small inverse association between out-of-pocket spending and adherence for β blockers, as well as associations of borderline statistical significance between out-of-pocket drug spending and rates of hospital admission and hospitalized days due to HF and total Medicare costs. With the discovery of novel therapeutic drug classes and the addition of these costly agents to the HF management arsenal, questions about the effects of prescription cost sharing are freshly relevant for HF patients both within and outside Medicare.

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