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Teresa B. Gibson* Mary Beth Landrum† Amber Batata‡

A. Mark Fendrick** Sara Wang†† Michael E. Chernew‡‡

*Thomson Reuters, teresa.gibson@thomsonreuters.com

†Harvard Medical School, landrum@hcp.med.harvard.edu

‡Pfizer Inc., amber.batata@pfizer.com

**University of Michigan, Amfen@umich.edu

††Formerly of Thomson Reuters, csshw@yahoo.com

‡‡Harvard Medical School, chernew@hcp.med.harvard.edu

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Teresa B. Gibson, Mary Beth Landrum, Amber Batata, A. Mark Fendrick, Sara Wang, and Michael E. Chernew

Abstract

An extensive literature has demonstrated geographic variation in medical services and this variation has been largely attributed to the health care system and not to regional differences in patient behavior. We use empirical Bayes shrinkage models, conditional on patient, firm, and market covariates, to investigate geographic variation in adherence to prescription medications across hospital referral regions (HRRs). Models are estimated for commercially insured patients in 11 combinations of chronic diseases and drug classes. We use factor analysis to create a market-level composite measure of adherence that we relate to adjusted market-level spending on non-drug services. We find that there is a very small amount of variation in adherence to prescription drugs across HRRs supporting the widely held assumption that geographic variation is attributable to the health system. Markets with high adherence have systematically lower medical spending, and this inverse correlation is more likely due to unobserved market traits.

KEYWORDS: regional variation, prescription medication, adherence, commercial insurance

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Introduction

The existing literature on geographic variation in the use of health care services is extensive. For example, Fisher et al. (2004) reported geographic variation in the frequency of hospitalization, diagnostic testing and physician visits for chronically ill populations. Several studies have identified marked geographic variation in the treatment of patients with acute myocardial infarctions (i.e., use of invasive versus non-invasive management strategies) (Pilote et al., 1995; Wennberg et al., 1996; Mark et al., 1994; Tu et al., 1997). Geographic variation in the use of discretionary surgical procedures such as hip, knee and spine surgeries has also been identified (Weinstein et al., 2004;Weinstein et al., 2006). In each of these cases, the observed geographic variation is not explained by regional differences in patient preference or illness levels, but rather seems to be a function of characteristics and behaviors of the providers of care within the local health care system.

The geographic variations literature focuses almost exclusively on medical procedures and hospitalizations, with little research examining variation in the use of prescription drugs. One recent study examined regional variation in prescription drug spending patterns among Medicare beneficiaries with standalone Part D drug plans, and found that drug spending varies across regions, although the variation in drug spending was less than that of medical spending (Zhang et al., 2010).

Prescription drug utilization is an important omission because medications are recognized as a significant component of medical care. Prescription drug treatment for chronic conditions also differs from many other inputs to the patient's production function for health. Once prescribed by the provider, the patient must adhere to the prescription drug regimen of care over time, largely shifting responsibility for health maintenance and improvement to the patient. Thus far, the role of and extent to which patient behavior contributes to geographic variation in spending and utilization has been relatively unexplored. The extent to which patient behavior varies across geographic regions has also been largely unquantified. In this study, we assess the mostly untested assumption that variations in patient inputs into the production of medical care services is small.

Prescription drugs are a routine and essential part of treatment for several chronic conditions including hypertension, hypercholesterolemia, diabetes and congestive heart failure (National Heart, Lung and Blood Institute, 2004; National Cholesterol Education Program, 2001; Nathan et al. 2009; Hunt et al., 2001). They are often important substitutes for or compliments to surgeries and other medical services (e.g., the use of selective serotonin reuptake inhibitors as a complement to psychotherapy) and in some cases, prescription drugs are the only,

or one of a handful of, treatment options available to patients (e.g., protease inhibitors for acquired immunodeficiency syndrome). Proper use of prescription drugs has been associated with reduced risk of hospitalization and acute illness, lower mortality and morbidity and higher quality of life for various patient populations (SOLVD Investigators, 1991; The Scandanavian Simvastatin Survival Study Group, 1994; Soumerai et al., 1997; Rosenheck et al., 1997). Moreover, research demonstrates widespread underutilization of medications.

To study medication utilization, we may analyze two components of use: treatment initiation and treatment adherence. Treatment initiation refers to commencement of treatment. Treatment adherence focuses on compliance to medication prescribed to treat chronic disease conditional on initiation. We focus on adherence because we cannot identify patients in the disease cohorts who initiate treatment.

Even among patient populations that stand to benefit from medication adherence underuse is prevalent. For example, despite the proven efficacy of statin treatment for coronary heart disease, primary and secondary prevention populations failed to adhere to treatment regimens between 27.3% and 56.2% of the time, depending on the definition of adherence (Ellis et al., 2004). In general, estimates of non-adherence range from two-thirds to one-half of patients (Osterberg & Blaschke, 2005).

The consequences of underuse and nonadherence are serious: nonadherence reduces treatment benefits and is associated with poorer overall prognosis for patients (Gordis, 1979; Irvine et al., 1999). Reasons for medication underuse vary, but include a dislike of precription drugs, a belief that the prescribed drugs were not necessary, discomfort with associated side effects, cost-related underuse and improvement without the use of medication (Kirking et al., 2006).

Conceptual framework

To determine whether geographic variations found for medical procedures and hospitalizations extends to patient behavior, we examine the presence of regional variation in adherence to prescription drugs, and if found, we assess the extent of regional variation in adherence. If regional variation in adherence is small, then this supports the assumption that regional variation in care extends mainly from provider behaviors. If it is large, this would suggest that patient behaviors in addition to provider behaviors vary across regions and current efforts to quantify and minimize these variations should also include patients. We focus on adherence, which pre-supposes a prescription was filled by the patient. This avoids confounding physician and patient behavior, and avoids measurement issues associated with identifying patients eligible for particular classes of

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medications. Thus we explicitly do not focus on use, but instead focus on adherence, which is conditional on at least one prescription being filled.

We quantify variation in adherence across Hospital Referral Regions (HRRs) for patients in 11 different disease/medication cohorts. We also assess the correlation between measures of regional variation across different disease/medication cohorts. Further, we examine the extent to which patient, plan or employer, and market traits explain regional variation in adherence. Finally, we assess the extent to which observed regional variation in use of prescription drugs is correlated with regional measures of non-drug services.

New contribution

The topic and study design make significant contributions to the literature in several ways. First, we focus on a relatively unexplored topic; geographic variation in medication adherence among the commercially insured. We employ case mix adjustment methods to account for differences in patient composition across HRRs and extend the methodological approaches used in much of the geographic variations literature by estimating variation using statistical methods including random effects models and Bayes shrinkage estimators to account for differences in sample size across HRRs. Bayes shrinkage estimators are based on hierarchical methods and improve reliability of estimates when comparing aggregate measures for units (such as geographic areas, providers or hospitals) with unbalanced underlying sample sizes. Using this approach, HRR-specific estimates of mean adherence are a weighted combination of adjusted HRR-specific estimates and the national mean adherence. HRRs where reliability is lower (smaller HRRs) are weighted more toward the national mean, and estimates for HRRs where reliability is higher (larger HRRs) are weighted less (or not weighted at all) toward the national mean (Hox 2002, Bryk and Raudenbush 2002). Weights also depend on the degree of variation across HRRs so that disease/medication cohorts that exhibit larger variation in adherence will have less shrinkage in HRR-specific effects. Finally, to further understand regional variations we combine the HRR-level measures of adherence into a composite measure using factor analysis and correlate this aggregate measure to adjusted market-level medical utilization measures and spending.

Methods

Data

The 2006 and 2007 Medstat MarketScan® Commercial Claims and Encounters Database was utilized in this analysis. This database included de-identified health insurance claims for inpatient services, outpatient medical services, and outpatient

pharmaceutical services for millions of enrollees receiving health care insurance through plans offered by more than 110 medium and large, primarily self-insured employers in the United States. These data conformed to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) confidentiality requirements.

The sample included commercially insured enrollees who were under age 65 and continuously enrolled in 2006 and 2007. We created subsamples of beneficiaries corresponding to selected chronic diseases: asthma, congestive heart failure (CHF), diabetes, depression, and osteoporosis, (see criteria in the Appendix). Beneficiaries could be enrolled in multiple subsamples if they have multiple diseases. Within each disease, we further subset the analysis by medication class. To qualify for the study, patients with each disease had to have evidence of at least one prescription fill in at least one of the relevant classes of medications. For each patient, we created a single record summarizing their experience in 2007.

Assigning patients to geographic areas

Each patient was assigned to a Hospital Referral Region (HRR) based on their ZIP code of residence (Dartmouth Atlas, 2009). HRRs are geographic measures of the tertiary care resources available in a particular area. We chose the HRR as our geographic measure because HRRs provide the foundation for much of the geographic variations literature.

Measure of patient adherence

Adherence is measured using the Medication Possession Ratio (MPR), which captures, for each class of medication, the percentage of days an individual had medication on-hand. Following existing literature, the MPR is calculated from individual prescription drug claims, using the fill date and the intended days supply of medication from each claim (Chernew et al., 2008). If a patient refilled the same medication (and dose) before the end of the previous prescription fill then the days supplied for the new prescription were appended to the end of the previous fill. If a patient switched medication (or dose) within a medication class the remainder of the prescription for the earlier medication was discarded, and coverage commenced with the supply of the new medication. In order to carry over days supplied from prescriptions filled in late 2006 into early 2007, we examined filling behavior starting in the fourth quarter of 2006. Each patient was assigned an index date for each medication class corresponding to the date of the first fill of the medication in the year, or January 1 if the prescription was filled on or before January 1. The denominator of the MPR represented the amount of time between the index date and December 31.

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Measures of spending and utilization

We computed the HRR average total medical spending in 2007 as the sum of all non-drug expenditures, including both the employer and employee out-of-pocket share, divided by the number of enrollees in each HRR. Utilization measures included the number of inpatient admissions, the number of inpatient days, and the number of emergency room visits per enrollee in each HRR 2007.

Explanatory variables

Explanatory variables fell into three categories: patient characteristics; plan and employer level characteristics; and area characteristics. We combined plan and employer characteristics because the large firms that form our sample influence many plan traits (such as benefit design) and these employers can influence utilization through unobserved benefit programs such as disease management or worker education initiatives.

Patient-level characteristics included socio-demographic characteristics: age, gender, beneficiary type (e.g., contract holder), employment classification (e.g., salary), employee status (e.g., retired), and health status. Health status was controlled for in part by examining samples with selected clinical conditions (e.g. diabetes) and including, within each disease, the Charlson Comorbidity Index (CCI), which is a numeric scale reflecting the risk of death or serious disability in the next year based on the presence of a diagnosis for one of 19 conditions (e.g., diabetes, heart disease, cancer) in the 12-month pre-index period (Romano et al., 1993). We also included a measure of household income at the ZIP code level from the Census Bureau files (U.S. Census Bureau, 2003).

Plan and employer characteristics included benefit plan type (e.g., Preferred Provider Organization) and two patient cost-sharing measures, because patient out-of-pocket costs are related to adherence rates (Ellis et al., 2004; Huskamp, 2003; Cunningham, 2002; Leibowitz et al., 1985; Goldman et al., 2007). The first cost-sharing measure was the office visit cost sharing for doctor office visits. The second was the calculated weighted prescription drug copayment index that was calculated as a weighted average of cost sharing amounts for brand name and generic medications in each class. Dummy variables representing each firm were also included.

Market level variables that measure health care infrastructure, and obtained from the Area Resource File, were included as covariates in our models to investigate the impact of resource availability and capacity on underuse of medications. Area characteristics included: primary care and specialist physicians in 2006, number of nurses in 2006, and hospital beds in 2005 (all per 1,000 population). Area characteristics were merged onto each patient year record by county of residence.

Statistical models

We used random effects linear probability models to estimate HRR adjusted adherence levels to estimate variance in adherence across HRRs. MPR is bounded by 0 and 1, and linear models are not ideal, but are a useful functional form for computing conditional means of adherence by HRR. We also used random effects linear probability models to estimate HRR adjusted spending. If the purpose of our investigation was to predict individual level spending conditional on the covariates we would have had to address the problem of skewed spending data with a large mass-point at zero expenditures. Consequently, we would have utilized a different approach and estimated a two-part model (Duan et al.,1983; Duan et al., 1984) or bivariate sample selection model such as Type-2 Tobit (Vella, 1998). Empirically, however, Buntin and Zaslavsky (2004) note that all of these estimators give very similar results.

We estimated four models for each disease/drug class combination. They include (1) unconditional model (empty model with an HRR random effect), (2) a model including patient traits that results in demographic and health adjusted conditional means in MPR (the variance captures regional variation not attributable to patient traits), (3) a model including patient and plan/employer traits, which results in mean MPR adjusted for patient traits, benefit design and any unobserved employer effects, and (4) a model that includes patient traits, plan/employer traits and market traits. The resulting HRR random effects capture residual HRR variation in adherence not captured by any of our covariates. We used these models to quantify regional variation based on the size and significance of the variance of the HRR-level random effects in each model.

We also used random effects models to compute empirical Bayes shrinkage estimates of market-level adherence to each medication class. These estimates were calculated as a weighted average of the conditional mean adherence level in each HRR adjusted for patient characteristics and the national adherence level. The weight was based on the reliability of the estimate. For example, for HRRs with a small number of patients in the medication class, the shrinkage estimate will weight toward the overall mean, and in large HRRs the shrinkage estimate will weight toward the HRR mean.

We then used factor analysis to generate a market specific adherence measure that aggregates the market level adherence shrinkage estimates into a single, market level adherence measure. Specifically, we computed an aggregate adherence rate as a weighted average of the 11 individual adherence rates using factor loadings as weights. This single factor was able to explain 66% of the total variation in market level adherence.

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We correlated the market (HRR) level adherence estimate to market level spending and utilization estimates to determine the strength of association between area-level adherence, spending, and utilization.

Results

Study sample

Our sample size ranges from about 12,000 patients with Congestive Heart Failure prescribed Angiotension Converting Enzyme (ACE) Inhibitors to over 315,000 individuals with diabetes mellitus who filled a prescription for oral antidiabetic medications (Table 1). All of the 306 HRRs in the United States (not shown) are represented, except for the Osteoporosis cohort which has 305 HRRs.

Table 1: Sample sizes by Medication Class and Chronic Disease Cohort

	Asthma	CHF	Diabetes	Major Depression	Osteoporosis
Inhaled Corticosteroids	60,361				
ACE Inhibitors		12,190	160,118		
ARB		5,629	91,078		
Beta Blockers		15,634			
Statins			134,061		
Oral Antidiabetic Medications			317,981		
SSRI/SNRI				231,464	
Other Antidepressants				110,452	
All Antidepressants				267,188	
Antiresorptive Therapy					39,541

Descriptive statistics for each disease cohort (counting all patients only once for each disease, even if they are in multiple medication classes) are provided in Table 2. Demographic characteristics vary across conditions: the average age of patients ranges from 31.4 years for asthma to 57.6 years for osteoporosis. Almost all (94.8%) patients with osteoporosis are female, and slightly less than half of patients with congestive heart failure are female (42.9%). Patients with congestive heart failure have the highest comorbidity burden with an

average Charlson Comorbidity Index of 2.43, and patients with major depression have the lowest comorbidity burden, with a CCI of 0.44.

Table 2: Descriptive statistics (all medications)

	Asthma		CHF		Diabetes		Major Depression		Osteoporosis	
n	60,361		19,987		160,118		267,188		39,541	
PATIENT TRAITS										
Age in Years, mean(std)	31.4	(18.16)	55.3	(7.24)	53.0	(8.37)	44.7	(11.48)	57.6	(3.73)
Female (%)	57.7		42.9		47.7		71.7		94.8	
Charlson Comorbidity Index, mean(std)	0.79	(0.88)	2.14	(2.22)	1.55	(1.43)	0.44	(1.08)	0.61	(1.19)
Relationship to Employee										
Employee(%)	37.7		63.4		67.6		58.6		53.2	
Spouse (%)	22.4		35.8		31.5		35.5		46.6	
Dependent(%)	39.8		0.8		0.9		5.9		0.1	
Employee Class										
Salary(%)	30.6		15.0		19.0		25.5		24.9	
Hourly(%)	19.0		30.7		27.7		19.6		22.3	
Unknown(%)	50.4		54.3		53.3		55.0		52.8	
Employee Status										
Active(%)	80.8		47.6		58.7		71.5		48.0	
Retired(%)	6.0		36.4		27.4		13.9		40.9	
Unknown(%)	13.2		16.0		13.9		14.6		11.1	
Household Income (000s), mean(std)	51.03	(18.67)	43.70	(14.93)	45.21	(15.61)	49.81	(17.22)	50.12	(18.64)
PLAN TRAITS ASSIGNED TO PATIENTS										
Plan Type										
Comprehensive(%)	3.7		7.3		4.9		4.4		7.4	
EPO(%)	0.9		1.0		1.0		0.7		0.8	
HMO(%)	21.3		16.9		17.8		20.9		13.8	
POS(%)	12.8		13.5		14.5		13.3		12.9	
Capitated POS(%)	0.8		0.4		0.6		0.6		0.7	
CDHP(%)	3.1		1.8		2.0		2.7		2.1	
PPO(%)	55.7		57.7		57.8		56.2		61.1	
Unknown(%)	1.7		1.5		1.5		1.3		1.2	
Medication Copayments, mean(std)	26.26	(10.07)	9.31	(3.20)	15.16	(5.01)	13.08	(3.60)	20.23	(7.33)
Physician Visit Copayments, mean(std)	26.14	(12.34)	29.20	(13.60)	28.17	(12.82)	26.14	(12.30)	28.75	(13.44)
MARKET TRAITS ASSIGNED TO PATIENTS (per 1,000 population)										
Total GPs (2006), mean(std)	3.0	(1.42)	3.0	(1.40)	3.0	(1.43)	3.2	(1.49)	3.0	(1.40)
Total Specialists (2006), mean(std)	9.2	(7.87)	8.4	(6.91)	8.4	(7.43)	9.5	(9.52)	9.0	(7.48)
Total Nurses (2006), mean(std)	65.2	(42.20)	59.7	(42.10)	60.3	(43.06)	65.9	(44.33)	63.5	(41.16)
Total Hospital Beds (2005), mean(std)	32.1	(26.11)	34.3	(27.70)	33.6	(28.03)	32.5	(26.89)	32.4	(25.07)

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Regional adherence

The analysis reveals statistically significant regional variation in medication adherence. The likelihood ratio test rejects the hypothesis that the random effects equal zero (at $p<0.05$) for all samples and all sets of covariates. The magnitude of the variation across areas is small. The percent of variation explained by the HRR random effects is also consistently small, less than 2% when no covariates are added. As expected, this percentage decreases further when covariates are included (Table 3).

Table 3: Percent of variation explained by HRR random effects

		n	HRR Only	Patient/HRR	Patient-Plan-Firm/HRR	Patient-Plan-Firm-Area/HRR
Asthma	Inhaled Corticosteroids	60,361	1.50	1.35	0.73	0.61
CHF	ACE Inhibitors	12,190	1.60	1.00	0.34	0.32
	Beta Blockers	5,629	1.86	1.36	0.68	0.63
Diabetes	ACE Inhibitors	160,118	1.24	0.90	0.70	0.68
	ARB	91,078	1.52	1.06	0.60	0.58
	Statins	134,061	1.52	0.96	0.55	0.54
	Oral Antidiabetic Medications	317,981	0.52	0.46	0.41	0.39
Major Depression	SSRI/SNRI	231,464	0.61	0.66	0.49	0.44
	Other Antidepressants	110,452	0.54	0.42	0.24	0.21
	All Antidepressants	267,188	0.61	0.62	0.47	0.43
Osteoporosis	Antiresorptive Therapy	15,634	0.99	0.89	0.50	0.46

Note: Cells contain the percent of variation explained by the HRR random effect

Table 4 displays the 50th percentile of the shrinkage estimates of average adherence for HRRs. The ratio of the shrinkage estimates of average adherence for HRRs at the 90th percentile is between 4 and 13% greater than average adherence for HRRs in the 10th percentile (not shown). This generally

corresponds to less than 25 days per year or a 3 to 8 percentage point difference in the average MPR at the 10th percentile compared to the average MPR at the 90th percentile.

Table 4: Shrinkage estimates of adherence

		50th percentile
Asthma	Inhaled Corticosteroids	0.391
CHF	ACE Inhibitors	0.634
	Beta Blockers	0.630
Diabetes	ACE Inhibitors	0.670
	ARB	0.668
	Statins	0.571
	Oral Antidiabetic Medications	0.695
Major Depression	SSRI/SNRI	0.604
	Other Antidepressants	0.537
	All Antidepressants	0.635
Osteoporosis	Antiresorptive Therapy	0.688

Note: n=306, except the Osteoporosis cohort where n=305

We report selected results of the regressions in the Appendix. However, we do not focus on individual, plan, or employer traits here because the effects of those are well studied and our focus is on geographic variation. Yet our models, which are estimated on individual level data, do reveal results consistent with existing literature. For example, age is associated with higher adherence. Adding covariates improves the model fit across patient cohorts as indicated by the R^2 values in the Appendix. R^2 values range from 0.05 to over 0.33 across the cohorts with higher values (approaching 1) indicating the degree to which the covariates improve upon the null model.

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Market traits and adherence

Several market traits were associated with adherence (Table 5). The coefficient estimate of the number of primary care physicians per capita was positive and statistically significant in 7 of 11 models and never negative and statistically significant. This suggests primary care physicians are associated with better medication adherence. Similarly, the coefficient on the number of specialist physicians per capita was negative and statistically significant in 7 of 11 models and positive and statistically significant in one model. This suggests specialist physicians are associated with worse adherence. Results were weaker for other market traits, but suggest nurses have a positive association with adherence and the number of hospital beds have a negative association. It is important to note that, like much of the geographic variations literature, we do not infer that these relationships are causal.

Table 5: Summary of regression coefficients for market traits

	Positive and significant	Positive not significant	Negative not significant	Negative and significant
Total GPs (2006)	7	3	1	0
Total Specialists (2006)	1	2	1	7
Total Nurses (2006)	3	7	1	0
Total Hospital Beds (2005)	0	2	6	3

Note: Cells contain counts of the number of models with the direction and significance indicated in the row heading

Because geographic variation in adherence is small, the magnitude of these relationships on actual medication adherence is small. For example, a 1 standard deviation increase in primary care physicians per capita is associated with 0.63 percentage point higher adherence to asthma medications. A 1 standard deviation increase in specialist physicians per capita is associated with a 0.42 percentage point lower adherence to asthma medications.

The geographic measures of adherence are positively correlated across the 11 models (correlation table not reported, but the correlations were generally between 0.4 and 0.8 and the correlation was over 0.5 for 89 percent of the disease/condition measures.) This may reflect common market traits, as well as overlap in patients across samples. Factor analysis allowed us to aggregate the random effects across the different samples to generate a single HRR level adherence measure.

The HRR medication adherence measure was inversely correlated with random effect measures for models of non-drug spending and utilization. (Table

6). This is consistent with the evidence that adherence to prescription drugs reduces use of medical services (Sokol et al., 2005) and medical spending (Roebuck et al., 2011). However, because the magnitude of the prescription drug adherence variation is small, we believe these correlations more likely reflect unobserved market traits that are correlated with both high adherence and low spending. Certainly the primary care and specialist results are consistent with this view. This extends the notion of area level practice culture, discussed by Baicker and Chandra (2004) and Chandra and Staiger (2007) to include patient behavior. Some areas, perhaps due to system traits or the general culture, appear to perform better on a wide range of indicators.

Table 6: Correlations of HRR-level adherence with HRR average spending and use

	Correlation	
Medical and Prescription Drug Spending	-0.0109	***
Number of Admissions	-0.1309	***
Length of Stay	-0.2109	***
Number of ER visits	-0.1424	***

Note: Correlations were calculated between the aggregate HRR-level adherence measure and the average HRR-level spending and utilization measures. n=305, one HRR did not have information on all measures of adherence and utilization, *** $p<0.01$

Discussion

A growing body of research demonstrates important regional variation in use of many commonly used health care services. Many authors attribute much of this variation to attributes of providers and the health care delivery system. We extend that research to examine whether geographic variation in patient behavior can be detected via analyzing adherence rates to several high value drug classes. While we find statistically significant variation, the magnitude is modest and less substantial than the variation found in previous studies of non-drug services. This variation could be due to many possible factors including regional cultural differences, unmeasured differences in demographics, or effects of health systems to boost adherence. We cannot distinguish between these, but collectively their effects are small. These results imply that factors driving the use of a prescribed medication are likely different than procedures and hospitalizations, and suggest that there is less of a 'patient' signature for drugs in areas than 'health system'

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signatures. It also provides some confirmation of the assumption that geographic variation in spending largely emanates from the health care delivery system.

These results may shed some light on the likely source of the regional variation in drug spending among Medicare beneficiaries identified by Zhang et al. (2010) who found non-negligible variation in spending among Medicare beneficiaries with stand alone Part D plans. By decomposition, variation in spending comes from variation in prices and variation in utilization – and variation in utilization comes from variation in initiation and adherence. To the extent that these results generalize to the Medicare population and to the extent that within Part D there is little variation in drug prices, when interpreted in conjunction with Zhang et al.'s results our findings suggest that much of the variation that Zhang et al. find in spending is due to variation in medication initiation. Further research exploring the extent of variation in medication initiation will help illuminate the sources of geographic variation in drug spending.

Our measure of adherence, the medication possession ratio, calculates the percentage of days after the index date that a patient had medications on-hand. Other measures of adherence such as persistence, which is time from initiation to discontinuation, could also be studied to gain insight into other dimensions of compliance with medication regimens. The medication possession ratio takes into consideration persistence to some extent, as all uncovered days resulting from discontinuation will lower the medication possession ratio.

In addition, these regional differences in adherence are likely to be conservative as the empirical Bayes shrinkage estimators are known to have a small amount of bias toward the mean, but are generally closer to the actual (unknown) values of the area means (Hox 1992, Bryk and Raudenbush 1992).

Our research finds that markets with high medication adherence have lower spending on non-drug medical services. However, given the modest variation in adherence, this correlation is highly likely to be related to unobserved traits that affect both adherence and spending, rather than to a direct effect of better adherence. Given our findings, future adherence research should focus on factors that directly affect patient behavior and such an approach may be more fruitful than interventions aimed at health systems. That said, innovative programs that align incentives for both the “demand” (patient) and “supply” (provider) side to improve the use of high value services are likely to yield better clinical and economic results than those that focus on only one.

Colophon

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Dr. Batata is a full-time employee of Pfizer Inc.
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Appendix Table: Coefficient estimates from adherence (MPR) models with patient, plan/firm, market characteristics and HRR random effects

	Asthma Inhaled Corticosteroids N = 60,361			CHF ACE N = 12,190			CHF Beta Blockers N = 15,634			Diabetes ACE Inhibitors N = 160,118		
	β	SE	P>|z|	β	SE	P>|z|	β	SE	P>|z|	β	SE	P>|z|
Age	0.004	0.000	0.000	0.004	0.000	0.000	0.005	0.000	0.000	0.006	0.000	0.000
Female	-0.031	0.002	0.000	-0.033	0.006	0.000	-0.007	0.004	0.118	-0.024	0.001	0.000
Charlson Comorbidity Index	0.011	0.001	0.000	-0.014	0.001	0.000	-0.007	0.001	0.000	-0.008	0.000	0.000
Spouse (Ref is Employee)	-0.010	0.003	0.000	-0.009	0.006	0.121	-0.006	0.005	0.212	-0.006	0.002	0.000
Dependent	0.003	0.006	0.608	-0.038	0.029	0.195	-0.013	0.024	0.602	-0.045	0.010	0.000
Salaried Employee (Ref is Unknown)	-0.002	0.008	0.803	0.027	0.017	0.116	0.034	0.013	0.010	0.038	0.004	0.000
Hourly Employee	-0.027	0.008	0.001	0.011	0.017	0.523	0.004	0.013	0.725	0.013	0.004	0.002
Active Employee (Ref is Unknown)	0.008	0.010	0.424	0.073	0.014	0.000	0.053	0.010	0.000	0.029	0.005	0.000
Retired Employee	0.016	0.011	0.137	0.071	0.014	0.000	0.053	0.010	0.000	0.027	0.005	0.000
R^2	0.3418			0.1566			0.3103			0.1657		

	Diabetes ARB N = 91,078			Diabetes Statins N = 134,061			Diabetes Oral Antidiabetic Medications N = 347,252			Major Depression SSRI/SNRI N = 231,646		
	β	SE	P>|z|	β	SE	P>|z|	β	SE	P>|z|	β	SE	P>|z|
Age	0.006	0.000	0.000	0.005	0.000	0.000	0.003	0.000	0.000	0.004	0.000	0.000
Female	-0.008	0.002	0.000	-0.036	0.002	0.000	-0.023	0.001	0.000	0.014	0.001	0.000
Charlson Comorbidity Index	-0.009	0.001	0.000	-0.004	0.001	0.000	0.013	0.000	0.000	-0.002	0.001	0.001
Spouse (Ref is Employee)	-0.003	0.002	0.190	0.002	0.002	0.337	-0.005	0.001	0.000	0.014	0.001	0.000
Dependent	-0.009	0.018	0.613	0.001	0.015	0.962	0.038	0.006	0.000	0.000	0.003	0.992
Salaried Employee (Ref is Unknown)	0.038	0.005	0.000	0.052	0.005	0.000	0.018	0.003	0.000	0.028	0.004	0.000
Hourly Employee	0.012	0.005	0.025	0.028	0.005	0.000	0.013	0.003	0.000	0.004	0.004	0.304
Active Employee (Ref is Unknown)	0.039	0.006	0.000	0.024	0.006	0.000	0.020	0.004	0.000	0.010	0.004	0.010
Retired Employee	0.040	0.006	0.000	0.029	0.006	0.000	0.017	0.004	0.000	0.019	0.004	0.000
R^2	0.2083			0.1195			0.0581			0.1420		

	Major Depression Other Antidepressants N = 110,452			Major Depression All Antidepressants N = 267,188			Osteoarthritis Antiresorptive Therapy N = 39,541		
	β	SE	P>|z|	β	SE	P>|z|	β	SE	P>|z|
Age	0.006	0.000	0.000	0.005	0.000	0.000	0.005	0.000	0.000
Female	-0.003	0.002	0.163	0.011	0.001	0.000	0.007	0.006	0.260
Charlson Comorbidity Index	-0.003	0.001	0.004	0.001	0.001	0.341	-0.012	0.001	0.000
Spouse (Ref is Employee)	0.014	0.002	0.000	0.020	0.001	0.000	-0.005	0.003	0.087
Dependent	0.011	0.005	0.042	-0.001	0.003	0.678	-0.038	0.038	0.321
Salaried Employee (Ref is Unknown)	0.033	0.006	0.000	0.031	0.004	0.000	0.017	0.008	0.036
Hourly Employee	-0.001	0.006	0.854	0.007	0.004	0.049	-0.012	0.008	0.116
Active Employee (Ref is Unknown)	0.015	0.006	0.010	-0.006	0.004	0.090	0.039	0.008	0.000
Retired Employee	0.020	0.006	0.001	0.003	0.004	0.510	0.050	0.008	0.000
R^2	0.1025			0.1517			0.1421		

Note: Model also included plan/firm, market characteristics and HRR random effects (not shown). R^2 was calculated by comparing the full model to the empty model with HRR random effect.

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