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Regional variation in physician adoption of antipsychotics: Impact on US Medicare expenditures

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Abstract

Background—Regional variation in US Medicare prescription drug spending is driven by higher prescribing of costly brand-name drugs in some regions. This variation likely arises from differences in the speed of diffusion of newly-approved medications. Second-generation antipsychotics were widely adopted for treatment of severe mental illness and for several off-label uses. Rapid diffusion of new psychiatric drugs likely increases drug spending but its relationship to non-drug spending is unclear. The impact of antipsychotic diffusion on drug and medical spending is of great interest to public payers like Medicare, which finance a majority of mental health spending in the U.S.

Aims—We examine the association between physician adoption of new antipsychotics and antipsychotic spending and non-drug medical spending among disabled and elderly Medicare enrollees.

Methods—We linked physician-level data on antipsychotic prescribing from an all-payer dataset (IMS Health's Xponent™) to patient-level data from Medicare. Our physician sample included 16,932 U.S. psychiatrists and primary care providers with ≥10 antipsychotic prescriptions per year from 1997-2011. We constructed a measure of physician adoption of 3 antipsychotics introduced during this period (quetiapine, ziprasidone and aripiprazole) by estimating a shared frailty model of the time to first prescription for each drug. We then assigned physicians to one of 306 U.S. hospital referral regions (HRRs) and measured the average propensity to adopt per region. Using

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2010 data for a random sample of 1.6 million Medicare beneficiaries, we identified 138,680 antipsychotic users. A generalized linear model with gamma distribution and log link was used to estimate the effect of region-level adoption propensity on beneficiary-level antipsychotic spending and non-drug medical spending adjusting for patient demographic and socioeconomic characteristics, health status, eligibility category, and whether the antipsychotic was for an on- vs. off-label use.

Results—In our sample, mean patient age was 62 years, 42% were male, and 86% had low-income. Half of antipsychotic users in Medicare had an on-label indication. The weighted average propensity to adopt the three new antipsychotics varied four-fold across HRRs. For every one standard deviation increase in the propensity to adopt there was a 5% increase in antipsychotic spending after adjusting for covariates (adjusted ratio of spending = 1.05, 95% CI 1.01-1.08, p= 0.005). Physician propensity to adopt new antipsychotics was not associated with non-drug medical spending (adjusted ratio 0.96, 95% CI 0.91-1.01, p<0.117).

Discussion—These findings suggest wide regional variation in physicians' propensity to adopt new antipsychotic medications. While physician adoption of new antipsychotics was positively associated with antipsychotic expenditures, it was not associated with non-drug spending. Our analysis is limited to Medicare and may not generalize to other payers. Also, claims data do not allow the measurement of health outcomes, which would be important to evaluate when calculating the value of rapid vs. slow technology adoption.

Implications for Health Policies—This study will provide important insight on the relationship between the speed of adoption of new antipsychotic medications and drug and non-drug medical spending for payers and policymakers seeking to maximize the value of health care expenditures.

The two-fold variation in prescription drug spending in Medicare Part D is largely driven by higher utilization of costly brand-name drugs relative to generics in some regions.(1) For example, the share of antidepressant prescriptions filled for brand-name drugs varies from 0.15 to 0.51 across hospital referral regions in Medicare even after adjusting for patient demographic and health status differences across regions.(1) While some of the regional variation in brand name drug use may be due to differences in Part D plan benefit design and cost-sharing(2), the majority of the variation is likely due to patient or prescriber preference for brand name drugs.(3-6) This cross-sectional variation in brand-name drug use may arise from regional differences in the speed with which physicians adopt new drugs into practice.

Six second-generation antipsychotics (SGAs) introduced in the US market between 1989 and 2002, after receiving initial FDA approval for the treatment of schizophrenia, have been widely adopted both for on-label and for off-label uses.(7) SGAs now comprise over 90 percent of the antipsychotic market.(8) The speed with which psychiatrists and other physicians adopted new antipsychotics varied by drug from a mean of 22 months for olanzapine to 43 months for quetiapine.(9) But there was even more variation in adoption at the physician-level, with some adopting new SGAs within their first year on the market and other physicians waiting more than 5 years. However, whether the rate of adoption of SGAs differs by region in the US is unknown. Understanding regional variation in SGA adoption has implications for the Medicare program, which finances a large share of mental health

treatment in the US,(10) faces significant long-term financing problems,(11) and experiences tremendous regional variation in spending, much of it unaccounted for by variation in need.(12) Rapid diffusion of new drugs to treat mental illnesses likely increases drug spending but its relationship to non-drug spending will depend on the effectiveness of the drugs and the appropriateness of the utilization.(13) On the one hand, if the newer drugs are more effective and prescribed appropriately, regions that rapidly adopt them may see reductions in non-drug use and spending. On the other hand, regions rapidly adopting SGAs may see increases in non-drug spending if those medications are used primarily for off-label purposes and increase the risk of adverse drug events with long-term health effects.(14)

To fill this gap in our understanding of the link between antipsychotic diffusion and health care expenditures, we examined the association between region-level measures of physician adoption of new SGAs from a large sample of psychiatrists and primary care physicians, and antipsychotic and non-drug medical spending measured in a random sample of disabled and elderly Medicare enrollees using antipsychotics.

Data and Methods

Overview

We linked patient-level data from 2010 Medicare claims to physician-level data, **aggregated to the HRR**, on antipsychotic prescribing from an all-payer prescribing dataset from IMS Health (Xponent™) and to the American Medical Association (AMA) Masterfile. The patient-level data from Medicare were used to construct measures of antipsychotic and medical spending. The physician-level prescribing data were used to construct a physician-level measure of his/her propensity to adopt new antipsychotic measures; the physician-specific propensities were then aggregated to the hospital referral region (HRR)-level (described in detail later).

Patient-level data source and sample

We obtained 2010 data from the Centers for Medicare and Medicaid Services for a 10% sample of Medicare beneficiaries (N = 4,891,885), who were continuously enrolled in fee-for-service Medicare Parts A and B, and a stand-alone Part D plan (N = 1,522,031). We obtained the Prescription Drug Event (PDE) file which contains information for date of each prescription filled, National Drug Code (NDC), days supply, and total cost (amounts paid by the beneficiary and the Part D plan). The Medi-Span database was used to determine the drug name and category based on NDC. We included in the analytic sample any beneficiary who filled 2 or more prescriptions for any first- or second-generation antipsychotic medication in 2010 and conducted a sensitivity analysis (described in statistical analysis section) limiting the sample to chronic users of antipsychotics. We also obtained inpatient and skilled nursing facility claims from MEDPAR, and claims from the outpatient, carrier, home health, hospice, and durable medical equipment files to calculate non-drug medical spending and to identify diagnoses for which antipsychotics have FDA-approved indications.

Physician-level prescribing data and sample

We did not use the Medicare data to construct physician-level measures of antipsychotic adoption because the Prescription Drug Event files contain only encrypted prescriber identifiers, a large share of antipsychotic prescriptions in the US are financed by other payers, and Medicare Part D was implemented in 2006, long after most of the SGAs were introduced. Our goal was to create a single measure of new drug adoption behavior across all payers. We instead used the Xponent™ database, which directly captures over 70% of all US prescriptions filled in retail pharmacies and uses a patented proprietary projection methodology to represent 100% of prescriptions filled in these outlets. Physician-level prescribing data were obtained for all US psychiatrists and a random sample of 5% of primary care providers (specializing in family medicine or internal medicine) (N = 42,915 physicians). We then obtained data on all monthly antipsychotic prescriptions filled by the patients of these physicians between 1997 to 2011 for all first- and second-generation antipsychotic products, regardless of payer, and for patients of all age-groups. For inclusion in the analytic sample, physicians in both psychiatry and primary care specialties were required to be regular prescribers of antipsychotics (i.e., write at least 10 antipsychotic prescriptions) in 2011 and be observed in Xponent™ from 1997-2011 so that we could measure antipsychotic adoption behavior over that time period. Furthermore, we limited the analytic sample of physicians to those with at least one antipsychotic patient enrolled in Medicare. The final physician sample was 16,932.

Dependent variables

We constructed two measures of 2010 Medicare expenditures for our patient sample which only included antipsychotic users. First, we calculated total antipsychotic spending per beneficiary. Second, we calculated total non-drug Medicare spending including inpatient and skilled nursing facility claims from MEDPAR, outpatient claims, carrier claims, post-acute claims (home health and hospice), and durable medical equipment claims.

Key independent variable

We constructed a measure of physician propensity to adopt new SGAs on the basis of 3 SGAs introduced during the period for which we had data on physician prescribing and a sufficiently long follow up period over which to observe adoption (1997-2011). Those SGAs were quetiapine, which was introduced in September 1997; ziprasidone, introduced in February 2001; and aripiprazole, introduced in November 2002.

For each physician and for each of the new SGAs, we identified the month when a first prescription was written. We then estimated a shared frailty model of the multivariate adoption times, adjusting for physician-specific covariates. The frailty parameter characterizes the individual physician's propensity to adopt new SGAs and forms the basis of our key independent predictor. The frailty is an unobserved variable for each physician, positive, and interpreted as a multiplier of the instantaneous probability of adopting a new SGA. Physicians having frailties of 1 have an average risk of adoption; those having frailties larger than 1 are faster than average to adopt; and those having frailties less than 1 are slower than average. We assumed the baseline hazard function for the multivariate first adoption times was Weibul and the frailty parameters arose from a gamma distribution. We adjusted

for the physician's age, sex, specialty (psychiatry vs. primary care), medical school (US or foreign medical graduate, and medical school ranking based on 2011 *US News and World Report*), practice type (e.g., solo, group practice), total antipsychotic prescribing volume, urban or rural office location, and Census region. The frailty model was estimated using the R function *parfm*.

We then constructed a region-level adoption measure by assigning the 16,932 physicians to one of 306 U.S. hospital referral regions (HRRs) and computed the average physician frailty per HRR weighted by physician prescribing volume such that high-volume prescribers would contribute more to the region-level measure of propensity to adopt than low-volume prescribers. Because our HRR measure of propensity to adopt may be associated with measurement error, we determined the reliability for the HRR with the smallest number of antipsychotic prescriptions in Medicare (n = 3,584). This was accomplished assuming additive measurement error using an errors-in-variables approach via the *stata* function *eivreg*.

Patient-level covariates

We adjusted our estimates of spending for patient demographic characteristics including patient age, sex, race (white, black, or other), and health status using the Medicare Hierarchical Condition Categories (HCC) score for community-based beneficiaries which is used to risk adjust Medicare Advantage plan payments for health status differences.(15) We also controlled for disability status, socioeconomic status, and the presence or absence of a diagnosis for a FDA approved use for antipsychotics using a combined set of indicators because these factors were correlated both with each other and with spending. First, we defined on-label use as having antipsychotic use in the same calendar year as a diagnosis for schizophrenia, bipolar disorder, or major depressive disorder, using a hierarchical approach (i.e., a beneficiary could only have bipolar in the absence of a schizophrenia claims, and could only have major depressive disorder in the absence of claims for schizophrenia or bipolar). Off-label use was defined as antipsychotic use in the absence of one of these conditions recorded on a Medicare claim. Our measure of socioeconomic status was an indicator of participation in the Medicare Part D low-income subsidy program (available to beneficiaries with incomes <135% federal poverty level). Finally, we included an indicator of eligibility for Medicare due to disability. This combination of these 3 dichotomous variables resulted in 8 indicator variables. Beneficiaries who were not disabled, not low-income subsidy recipients, and had off-label antipsychotic use served as the reference category.

Data analytic procedures

We first described the characteristics of the patient sample from Medicare and the physician sample from Xponent and checked the distribution of all covariates. We adjusted our physician adoption measure for the physician characteristics listed above (e.g., demographics, specialty, practice setting, prescribing volume). The range in number of physicians per HRR varied from 1 to 770 across the 306 HRRs in the US. Reliability was virtually 1 (0.997); therefore, we did not adjust our measure of adoption propensity for error in measurement. We did, however, conduct a sensitivity analysis limiting the study sample to

HRRs in the bottom decile of numbers of antipsychotic prescribers (fewer than 9). The results were nearly identical to the main results.

To account for the skewed distribution of the expenditure data, a generalized linear model with gamma distribution and log link was used to estimate the effect of the propensity to adopt on beneficiary-level antipsychotic spending and non-drug medical spending among antipsychotic users adjusting for all covariates described above. We included a HRR random effect to account for clustering within a HRR.

We conducted a secondary analysis stratifying by on- vs. off-label use of antipsychotics because we assumed that any cost-offsets associated with rapid adoption of antipsychotics would be in patient groups for whom there is evidence of effectiveness (i.e., on-label use). These results are presented in an on-line appendix.

We conducted several sensitivity analyses. First, we limited our sample to chronic users of antipsychotics, defined as filling 6 or more prescriptions in 2010. We examined whether our findings were robust to different model specifications (e.g., gamma model with a log link but no HRR random effect; gamma model with a robust estimator). Finally, to assess whether our results were sensitive to high cost outliers we replaced beneficiaries in the top 1% of expenditures with the spending value for the 99th percentile to test the outlier impact.(16) The results from these sensitivity analyses were qualitatively similar to the main analyses so we do not present them in the paper.

Results

Characteristics of Medicare patients

In 2010, 138,680 (9.1%) of the 1,522,031 beneficiaries in our random sample filled 2 or more prescriptions for antipsychotics **(Table 1)**. The mean age of antipsychotic users was 62.1 years and 58.4% were female. More than half (56.3%) were eligible for Medicare due to disability, 80.6% were dually eligible for Medicaid and 85.9% were enrolled in the Part D low-income subsidy program. Antipsychotic use was on-label for half (49.6%) of our sample: 25.7% carried a diagnosis of schizophrenia, 13.9% bipolar disorder, and 10.1% major depressive disorder. The mean HCC risk score was 1.8 indicating that antipsychotic users had more comorbidities (worse health status) than the average Medicare beneficiary.

Characteristics of physician prescribers

The mean age among the 16,932 physicians in our sample was 60.7 and 74.1% were male **(Table 2)**. Nearly all (95.7%) of the physicians in our sample were psychiatrists; the rest were family medicine physicians (2.5%) or internists (1.8%). Mean total antipsychotic prescribing volume from 2007-2011 was 7,250 (standard deviation = 8,100). One in seven (13.9%) attended a top 20 medical school (according to *US News and World* Report rankings) and 27.4% attended a non-US medical school. The vast majority (91.1%) of physicians practiced in urban areas and were more likely to practice in solo or 2-person practices (42.4%) or group practices (27.2%) than other settings (e.g., inpatient only).

Antipsychotic and medical spending

Mean antipsychotic spending among the 9% filling at least 2 antipsychotic prescriptions using their Medicare Part D benefit was $3,444 but there was wide variability from $50 for beneficiaries in the 5th percentile to $12,146 for beneficiaries in the 95th percentile **(Table 3)**. Person-level mean non-drug medical spending showed similar variability with a mean of $18,759 and range of $368 to $75,959 from 5th to 95th percentiles, respectively.

Propensity to adopt new antipsychotics

There was also wide geographic variability in physician propensity to adopt the three SGAs introduced during our study period (1997-2011 for adoption measure). The difference between the regions with the lowest and the highest propensity to adopt new antipsychotics was four-fold with Mason City, IA having the lowest propensity to adopt new SGAs (0.37) and Rome, GA having the highest propensity to adopt (1.60). Despite this wide geographic variation in the propensity to adopt, no obvious regional pattern was discerned **(Figure 1)**.

Adoption and antipsychotic spending

The propensity among physicians in a patient's hospital referral region to adopt new antipsychotics was positively associated with antipsychotic drug spending. For every one standard deviation increase in the propensity to adopt there was a 5% increase in antipsychotic spending after adjusting for other covariates (adjusted ratio of spending = 1.05, 95% CI 1.01-1.08, p= 0.005) **(Table 4)**. The results of our secondary analysis stratifying by on- vs. off-label use indicate that this association was higher among on-label users **(Appendix Table 2a and 2b).**

All other covariates were significantly associated with antipsychotic drug spending. Spending was 11% lower among black beneficiaries and 8% lower among beneficiaries in other racial/ethnic minority groups compared to white beneficiaries (both p<0.0001). Antipsychotic spending was higher among males (adjusted ratio 1.10, 95% CI 1.09-1.12, p<0.0001). Low socioeconomic status, disability, and on-label antipsychotic use were strongly associated with antipsychotic spending. For example, beneficiaries who were enrolled in the low-income subsidy program, were disabled and had on-label use of antipsychotics spent had an adjusted ratio of spending that was 3.53 times higher than beneficiaries who fell into none of these categories (95% CI 3.41-3.64, p<0.0001). HCC risk score was slightly negatively associated with antipsychotic spending (adjusted ratio of spending 0.96, 95% CI 0.96-0.96, p<0.0001).

Adoption and medical spending among antipsychotic users

The propensity to adopt new antipsychotics was not associated with non-drug medical spending among antipsychotic users (adjusted ratio 0.96, 95% CI 0.91-1.01, p<0.117) **(Table 5)**. The results of our secondary analyses stratifying by on-label vs. off-label use also yielded similar results.

Other covariates were significantly associated with non-drug medical spending. Black beneficiaries and beneficiaries in other racial/ethnic minority groups had lower non-drug medical spending. Our combined indicators of low-income subsidy status, eligibility for

Medicare due to disability and on- vs. off-label use were also associated with medical spending. Of these three factors, Medicare eligibility due to disability was most consistently associated with lower medical spending. HCC risk score was strongly positively associated with medical spending (adjusted ratio 1.54, 95% CI 1.53-1.55, p<0.0001).

Discussion

These findings suggest wide geographic variation in the propensity to adopt new antipsychotic medications. Medicare beneficiaries living in areas where physicians have a higher propensity to adopt new drugs have higher average antipsychotic spending. However, we did not find that physician propensity to adopt antipsychotics was associated with non-drug spending. Our study sheds light on the relationship between the speed of adoption of new antipsychotic medications, and drug and non-drug medical spending for payers and policymakers seeking to maximize the value of health care expenditures.

Technological change in health care-- adoption of new drugs, devices, diagnostic tests, surgical procedures, and other technologies -- is the main driver of non-price-related increases in health care spending.(17) Regional variation in US health care spending is well-documented, particularly in Medicare.(12) Although the effect of supply-side factors (i.e., availability of hospital beds, supply of physicians and devices) on this variation has been well documented, less is known about the impact of variation in physician propensity to adopt new drugs. We found greater than 4-fold variation across HRRs in propensity to adopt antipsychotics in our sample of physicians, primarily psychiatrists. Antipsychotic medication spending was higher, even several years after our study SGAs had been introduced to the market, for Medicare beneficiaries living in areas where physicians had a higher propensity to adopt.

We did not find an association between physician propensity to adopt new antipsychotics and non-drug medical spending among antipsychotic users. That no association was found even when we stratified analyses by whether use was on- or off-label indicates that this result holds regardless of indication (or regardless of whether the antipsychotic is used for a condition where evidence of effectiveness exists). Likewise, previous studies have not found a cost-offset associated with greater use of newer antipsychotics.(18) This is perhaps not surprising given that clozapine, the only antipsychotic with a clear outcome advantage in schizophrenia also has the highest risk of metabolic side effects.(19-22) It is possible that any savings yielded from improvement in symptoms of schizophrenia are offset by increased medical costs associated with treatment of metabolic syndrome; however, we did not examine the composition of spending in our analyses. It is also worth noting that we measured spending over a short time period – one year. Results may have been different had we had a longer time horizon for evaluating effect of adoption on non-drug spending. Furthermore, we may have found a different relationship had we evaluated adoption of each SGA separately because of variability in metabolic risk among the three drugs for which we measured adoption (aripiprazole and ziprasidone have lower incidence of metabolic side effects than does quetiapine).(19)

Our findings are important to consider in light of recent policy debates over Medicare Part D formulary policy. Since Medicare Part D was implemented in 2006, the Centers for Medicare and Medicaid Services (CMS) have required plans to cover all or substantially all drugs in 6 protected classes, including antipsychotics. Plans can impose quantity limits or prior authorization requirements but cannot remove antipsychotics from the list of covered drugs. In January 2014, CMS issued a proposed rule signaling a willingness to change this policy to give plans more flexibility to limit antipsychotic coverage on their formularies. However, CMS announced it would delay implementation of the rule in March 2014 after vocal opposition from the pharmaceutical industry and groups representing patients and providers.(23, 24)

It is also worth noting that roughly half of antipsychotic use in Medicare was in the absence of a diagnosis for an FDA approved indication. While this could be due, in part, to under-coding of mental illnesses in claims data, this high rate of off-label is consistent with other studies.(7, 25) In fact, a recent report by the US Government Accountability Office found that one-third of elderly Medicare beneficiaries with dementia living in nursing homes and 14% of community-dwelling elderly beneficiaries with dementia used antipsychotics in 2012, years after a black box warning by the FDA on the mortality risks associated with antipsychotic use in the elderly.(26, 27) Both the American Geriatrics Society and the American Psychiatric Association have urged providers to avoid prescribing antipsychotics to elderly patients with dementia through the Choosing Wisely campaign.(28, 29)

Our study is subject to several limitations. First, our claims data were limited to Medicare, thus our spending results may differ from other payers with different limits on formulary coverage of SGAs or different patient populations. Second, we only examined physician propensity to adopt three SGAs and our findings may not generalize to other drugs in the antipsychotic category. Third, we required physicians to be regular prescribers of antipsychotics over a long time period (1997-2011) in order to characterize physicians' propensity to adopt new drugs across multiple new drug introductions. Our study sample is older, more likely to be male, includes more psychiatrists vs. primary care physicians, and prescribes a higher volume of antipsychotics than the average antipsychotic prescriber. These characteristics are all positively associated with more rapid adoption of new drugs(30) and we may estimate higher adoption propensities as a result. Fourth, our propensity to adopt measure was constructed at the HRR-level and included prescriptions financed by all payers although we limited our sample to those with at least some Medicare patients. Fifth, one of our predictors of adoption was medical school ranking as of 2011. Although medical school rankings are quite stable in the short run,(31) there may be some measurement error due to the fact that we were unable to obtain earlier rankings more proximal to the graduation date of our study sample. Finally, we measured the association between the propensity to adopt SGAs introduced in the late 1990s and early 2000s on Medicare spending in 2010. It is possible that provider preferences changed substantially during that period although the drugs for which we measured adoption were still dominant in terms of market share in 2010.

In sum, we detected wide variation in the propensity of physicians to adoption new antipsychotic medications across hospital regions in the US. While adoption was positively

associated with antipsychotic expenditures in Medicare, it was not associated with non-drug spending. These findings may inform efforts on the part of payers and policymakers seeking to maximize the value of health care expenditures.

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Appendix tables

1. Results of frailty model used to estimate physician propensity to adopt

Frailty distribution: gamma

Baseline hazard distribution: Weibull

Loglikelihood: −176375.784

	ESTIMATE	SE	p-val	
theta	0.414	0.009		
rho	1.336	0.006		
lambda	0.037	0.002		
allmaleMale	0.192	0.017	0.000	***
allage50-59	−0.039	0.026	0.134	
allage>59	−0.237	0.026	0.000	***
allforeignForeign Trained	−0.063	0.018	0.000	***
allpracticeUnknown	−0.047	0.028	0.090	.
allpracticeOther	0.005	0.019	0.800	
allpracticeGroup	0.092	0.019	0.000	***
allanyYes	0.179	0.015	0.000	***
allspecialPsy	−0.140	0.020	0.000	***
allspecialFamily	−1.882	0.039	0.000	***
alltop25Top 25	−0.035	0.022	0.109	
allurbanUrban	−0.019	0.026	0.467	
allregionEast North Central	−0.088	0.029	0.003	**
allregionWest North Central	0.123	0.031	0.000	***
allregionSouth Atlantic	0.151	0.040	0.000	***
allregionEast South Central	0.109	0.030	0.000	***
allregionWest South Central	0.179	0.042	0.000	***
allregionMountain	0.114	0.036	0.002	**
allregionPactific	0.182	0.040	0.000	***
allregionMiddle Atlantic	−0.030	0.031	0.319	
allcvolume	0.547	0.009	0.000	***

Signif. codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Kendall's Tau: 0.172

2. Antipsychotic spending models stratified by on vs. off-label antipsychotic use

a. Association between patient-level factors and adoption time and *antipsychotic drug spending* among OFF-LABEL users

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	1.04	1.00	1.08	0.066
Age	0.99	0.99	0.99	<0.0001
Black (ref: White)	0.89	0.86	0.91	<0.0001
Other (ref: White)	0.95	0.91	0.99	0.006
Male	1.08	1.06	1.10	<0.0001
LIS, Disabled (ref: non-disabled, non-LIS)	2.22	2.13	2.32	<0.0001
Non-LIS, disabled	1.17	1.09	1.26	<0.0001
LIS, non-disabled	1.46	1.42	1.50	<0.0001
HCC risk score	0.95	0.94	0.95	<0.0001

b. Association between patient-level factors and adoption time and *antipsychotic drug spending* among ON-LABEL users

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	1.07	1.02	1.11	0.002
Age	1.00	0.99	1.00	<0.0001
Black (ref: White)	0.90	0.88	0.92	<0.0001
Other (ref: White)	0.93	0.90	0.96	<0.0001
Male	1.12	1.10	1.14	<0.0001
LIS, Disabled (ref: non-disabled, non-LIS)	2.18	2.08	2.28	<0.0001
Non-LIS, disabled	1.05	0.99	1.11	0.105
LIS, non-disabled	1.71	1.64	1.78	<0.0001
HCC risk score	0.98	0.97	0.98	<0.0001

3a. Association between patient-level factors and adoption time and *non-drug medical spending* among OFF-LABEL antipsychotic users

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	0.95	0.9	1.01	0.077
Age	1.00	1.00	1.01	<0.0001
Black (ref: White)	1.00	0.97	1.03	0.897
Other (ref: White)	0.91	0.87	0.94	<0.0001
Male	0.97	0.95	0.98	0.001
LIS, Disabled (ref: non-disabled, non-LIS)	0.58	0.56	0.61	<0.0001
Non-LIS, disabled	0.61	0.57	0.66	<0.0001
LIS, non-disabled	0.96	0.93	0.98	0.002
HCC risk score	1.49	1.48	1.5	<0.0001

3b. Association between patient-level factors and adoption time and *non-drug medical spending* among ON-LABEL antipsychotic users

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	0.98	0.92	1.05	0.621
Age	1.00	1.00	1.00	<0.0001
Black (ref: White)	0.96	0.94	0.99	0.004
Other (ref: White)	0.91	0.88	0.94	<0.0001
Male	0.87	0.86	0.89	<0.0001
LIS, Disabled (ref: non-disabled, non-LIS)	0.79	0.75	0.82	<0.0001
Non-LIS, disabled	0.7	0.66	0.74	<0.0001
LIS, non-disabled	0.98	0.94	1.02	0.341
HCC risk score	1.53	1.52	1.55	<0.0001

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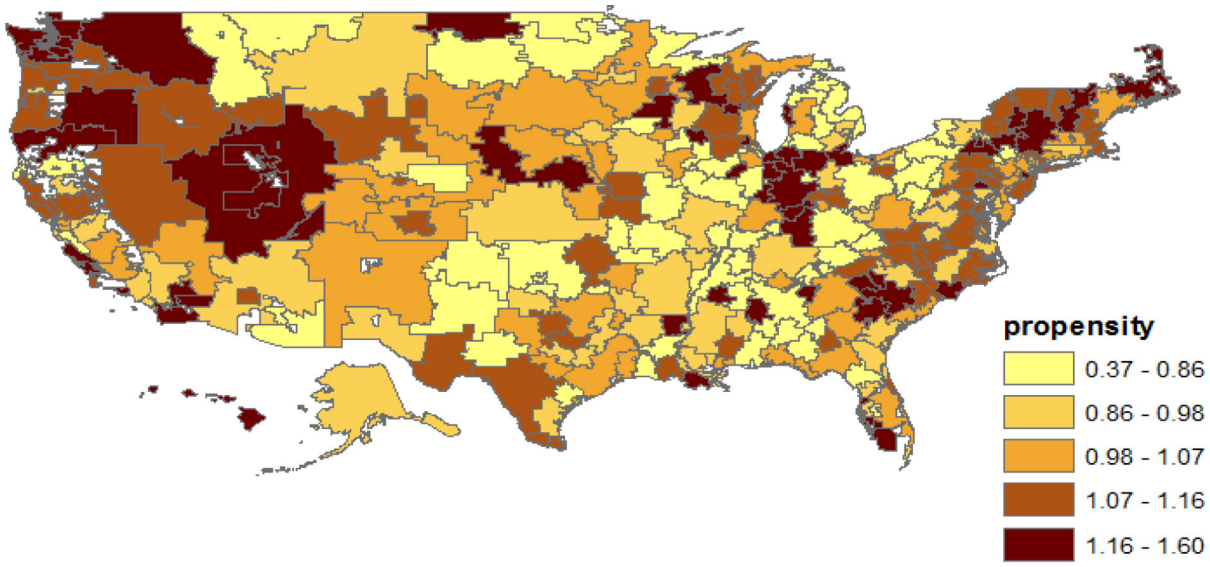

Notes: Data from IMS Health Xponent™

Figure 1.
Physician propensity to adopt antipsychotics by hospital referral region

Table 1

Characteristics of Medicare beneficiaries who used antipsychotics, 2010

Total sample	138,680
	Mean(SD)/%
Age	62.07 (18.4)
Male	41.6%
Disabled	56.3%
Race/ethnicity	
Black	15.0%
Other	7.3%
White	77.7%
Dually eligible for Medicaid	80.6%
Low-income subsidy recipient	85.9%
On-label users	49.6%
Schizophrenia	25.7%
Bipolar disorder	13.9%
Major depressive disorder	10.1%
HCC Risk Score	1.81 (1.45)

Notes: Includes continuously enrolled Medicare beneficiaries drawn from a national random sample of enrollees in fee-for-service Medicare and a stand-alone Part D plan in 2010. Inclusion in study sample depended on filling ≥2 antipsychotic prescriptions in 2010.

Table 2

Characteristics of physician study sample used to construct adoption measures, n = 16,932

	Mean(Std) or %
Age in 2011	60.7 (8.9)
Male	74.1%
Specialty	
Psychiatry	95.7%
Family Practice	2.5%
Internal Medicine	1.8%
Total antipsychotic prescribing volume (1997-2011)	7,250.4 (8,100.0)
Top 20 medical school graduate	13.9%
Foreign medical school graduate	27.4%
Urban office location	91.1%
Practice Type	
Solo or 2-person practice	42.4%
Group practice	27.2%
Other	21.7%
Missing	8.7%

Notes: Data from IMS Health Xponent™ and the AMA masterfile.

Table 3

Distribution of Medicare expenditures among antipsychotic users

	Antipsychotic spending	Non-drug medical spending among antipsychotic users
Minimum	$3	$1
5th percentile	$50	$368
25th percentile	$491	$2,054
Median	$1,744	$7,150
Mean	$3,444	$18,759
75th percentile	$4,989	$22,176
95th percentile	$12,146	$75,959
Maximum	$76,104	$751,643

Notes: Table displays raw, unadjusted spending on all antipsychotics and non-drug medical spending among antipsychotic users. Non-drug spending includes inpatient, post-acute, outpatient, physician, laboratory and other spending.

Table 4

Association between patient-level factors and adoption time and antipsychotic drug spending

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	1.05	1.01	1.08	0.005
Patient age	0.99	0.99	0.99	<0.0001
Black race (ref:White)	0.89	0.88	0.91	<0.0002
Other race/ethnicity (ref:White)	0.92	0.9	0.94	<0.0003
Male (ref: female)	1.1	1.09	1.12	<0.0004
Non-LIS, non-disabled, on-label use (ref: non-LIS, non-disabled, off-label use)	1.75	1.67	1.83	<0.0005
Non-LIS, disabled, off-label use	1.26	1.18	1.35	<0.0006
Non-LIS, disabled, on-label use	1.72	1.64	1.82	<0.0007
LIS, non-disabled, on-label use	1.45	1.42	1.49	<0.0008
LIS, non-disabled, on-label use	2.97	2.88	3.06	<0.0009
LIS, disabled, off-label use	2.40	2.32	2.48	<0.0010
LIS, disabled, on-label use	3.53	3.41	3.64	<0.0011
HCC risk score	0.96	0.96	0.96	<0.0012

Notes:

LIS stands for low-income subsidy recipient in Medicare Part D. Disabled corresponds to Medicare eligibility category. On-label use includes beneficiaries with a medical claim with a diagnosis of schizophrenia, bipolar disorder, or major depressive disorder. Otherwise antipsychotic use was considered off-label. HCC risk score is a measure of comorbidities based on dozens of diagnosis codes used by Medicare to risk adjust payments.

Table 5

Association between physician antipsychotic adoption, patient characteristics and non-drug medical spending

	Ratio of spending	95% CI		P-Value
Propensity to adopt new antipsychotics	0.96	0.91	1.01	0.117
Age	1.00	1.00	1.00	0.001
Black race (ref: White)	0.98	0.96	1.00	0.05
Other race/ethnicity (ref: White)	0.92	0.89	0.94	<0.0001
Male (ref: female)	0.89	0.88	0.90	<0.0001
Non-LIS, non-disabled, on-label use (ref: non-LIS, non-disabled, off-label use)	1.02	0.96	1.08	0.575
Non-LIS, disabled, off-label use	0.55	0.50	0.60	<0.0001
Non-LIS, disabled, on-label use	0.74	0.69	0.79	<0.0001
LIS, non-disabled, on-label use	0.96	0.93	1.00	0.034
LIS, non-disabled, on-label use	1.00	0.96	1.03	0.827
LIS, disabled, off-label use	0.56	0.54	0.59	<0.0001
LIS, disabled, on-label use	0.90	0.87	0.94	<0.0001
HCC risk score	1.54	1.53	1.55	<0.0001

Notes:

LIS stands for low-income subsidy recipient in Medicare Part D. Disabled corresponds to Medicare eligibility category. On-label use includes beneficiaries with a medical claim with a diagnosis of schizophrenia, bipolar disorder, or major depressive disorder. Otherwise antipsychotic use was considered off-label. HCC risk score is a measure of comorbidities based on dozens of diagnosis codes used by Medicare to risk adjust payments.