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How quickly do physicians adopt new drugs? The case of second-generation antipsychotics

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Abstract

Objective—To examine physician adoption of second-generation antipsychotic medications and identify physician-level factors associated with early adoption.

Methods—Using IMS Health Xponent™ data, which captures over 70% of all prescriptions filled in the U.S., and AMA Masterfile data on prescriber characteristics for each of 9 second-generation antipsychotics introduced from 1996–2008 for 30,369 physicians who prescribed antipsychotics, we estimate drug-specific Cox proportional hazards models of time to adoption and conduct descriptive analysis of the total number of agents prescribed.

Results—On average, physicians waited two or more years before prescribing new second-generation antipsychotics, but there was substantial heterogeneity across products in time to adoption. General practitioners were much slower to adopt second-generation antipsychotics than psychiatrists (hazard ratios (HRs) ranged from 0.10–0.35); solo practitioners were slower to adopt most products than group practitioners (HRs ranged from 0.77–0.89). Physicians in the highest quartile of antipsychotic prescribing volume adopted second-generation antipsychotics much faster than physicians in the lowest quartile (HRs ranged from 0.15–0.39). Psychiatrists tended to prescribe a broader set of antipsychotics (median of 6) than other specialties (median of 2 for general practitioners and neurologists and 1 for pediatricians).

Conclusions—Policymakers are searching for ways to control rapid health spending growth, which is driven primarily by use of new technologies such as second-generation antipsychotics. Understanding the factors that influence physician adoption of new medications will be crucial in the implementation of efforts aimed at maximizing value of care received by individuals with mental disorders as well as efforts to improve medication safety.

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Keywords

prescription drugs; mental health; antipsychotics

Rapidly-rising health care spending is a great concern of policymakers, and the diffusion and use of new treatment technologies is generally viewed as the primary driver of spending increases (1). Antipsychotic medications represent one of the most important new mental health treatment technologies from the past several decades. Beginning in 1989, several second-generation antipsychotics were introduced, and subsequently, several reformulations of those drugs (e.g., extended-release formulations). A large body of early research concluded that second-generation antipsychotics were more efficacious and had a lower incidence of extrapyramidal symptoms such as tardive dyskinesia (2,3) than first-generation antipsychotics (4,5). Second-generation antipsychotics quickly became first-line treatment for psychotic disorders (6).

More recently, two publicly-funded trials conducted in the US and UK showing that second-generation antipsychotics (with the exception of clozapine) are no more effective than their predecessors (7,8) made some experts question the wholesale shift of clinicians away from first-generation antipsychotics (9,10). Evidence of substantially-increased risk of weight gain and metabolic side effects associated with second-generation drug use (11–13), along with recent evidence suggesting a far smaller advantage with regard to the risk for tardive dyskinesia (14), have intensified the re-assessment of their role in schizophrenia treatment (15,16). The cost-effectiveness of second-generation antipsychotics is particularly salient to payers like Medicaid because of the drugs' high prices and the strain their use has put on state budgets (17).

Little is known about the factors that contributed to physicians' adoption of second-generation antipsychotics. Studies of other medications indicate that most of the variation in prescribing is explained not by patient clinical characteristics but rather physician preferences for a particular drug (18–21). Few empirical studies have identified influences on physician adoption behavior, other than small age and gender effects (22,23). For example, there has been little study of the role of medical training or practice setting.

We use data on dispensed prescriptions for a large random sample of physicians from multiple specialties who prescribe antipsychotics to examine physician adoption of second-generation drugs, and to identify physician-level factors associated with early adoption over the period 1996–2008.

Methods

Data

We used monthly physician-level data on the number of prescriptions dispensed for every antipsychotic (both first- and second-generation) for the period January 1996 through September 2008 from IMS Health's Xponent™ prescription database. The Xponent™ database directly captures over 70% of all outpatient prescriptions filled in the U.S. and uses a patented projection methodology to represent 100% coverage of outpatient prescriptions (Appendix). We obtained data for a 10% national random sample of physicians from each of the ten specialties with the highest antipsychotic prescribing volume who prescribed at least one dispensed antipsychotic prescription in 1996. To this sample we added new antipsychotic prescribers in each subsequent year of the study (10% of physicians who did not prescribe in 1996 but did in 1997, 10% of physicians who did not prescribe in 1996 or 1997 but did in 1998, and so on). Our sample includes 30,369 physicians. The prescribing

data were linked to data on physician characteristics from the American Medical Association Physician Masterfile, which includes current and historical information on physicians, residents, and medical students in the U.S., including foreign medical school graduates (24).

Outcome measures

We examine three primary outcomes: the proportion of physicians who have adopted a drug at different points in time (e.g., one year after a drug becomes commercially available, two years after), the number of months until a physician adopts a new drug product after it becomes available, and the median number of different antipsychotics prescribed in a year across physicians.

Predictors

Each model adjusts for physicians' demographic characteristics (age in 1996, sex), education and training (specialty, whether the physician attended a top 25 medical school as measured using the 2010 U.S. News and World Report rankings, and whether the physician was a foreign medical school graduate), practice setting (solo, other, or unknown versus group practice; whether the physician practiced in a hospital either part- or full-time); and total (first- plus second-generation) antipsychotic prescribing volume in the year before a drug becomes available using dummy variables for volume quartiles. For specialty, we use four categories: general practice (internal medicine, family medicine, family practice, and general practice), psychiatry (general, child/adolescent, and geriatric), pediatrics, and neurology (general and child). To adjust for characteristics of the area in which a physician practices, the models include contextual variables of the zip code of the physician's practice using data from the 2002 Area Resource File (%black, %Hispanic, %enrolled in an HMO, %who completed high school, and %65 years or older). We also include state fixed effects to control for time-invariant characteristics of the state where a physician practices.

Statistical analysis

To assess time to adoption, we first use Kaplan-Meier analysis (the procedure that computes the empirical survival curve for the sample) to tabulate the proportion of physicians who had not yet adopted a given drug at the end of each year after the drug became available. The Kaplan-Meier calculation accounts for censored observations by restricting the risk set at each point in time to just those providers who had yet to adopt. The adoption rate is calculated by subtracting the non-adoption rate from 1.

Next, we estimate drug-specific Cox proportional hazard models (25) of the number of months until a physician's first prescription for each orally-administered second-generation antipsychotic introduced during our study period: four original formulations (olanzapine, quetiapine, ziprasidone, and aripiprazole) and five reformulations (Zyprexa Zydis, Risperdal M-Tab, Seroquel XR, Symbyax, and Invega). We do not study clozapine or risperidone because they were introduced before 1996. To focus on physicians who prescribe antipsychotics with some regularity, we exclude physicians with fewer than 10 antipsychotic prescriptions in the year before a drug was released. We censor physicians who died or retired from clinical practice at the point of their last prescription.

The Cox proportional hazards regression models (25) simultaneously account for the effects of the predictors, isolating their independent effects. For ease of visual presentation, we compute survival probabilities over a range of values of the predictor of interest with the value of other predictors set to their mean if continuously-valued, and to their most common value if discrete-valued. The corresponding survival curves show the probability that a physician remains a non-adopter at a given point in time as a function of a single predictor

with the other predictors fixed at realistic values in the sample. These curves adjust separately for the characteristics that we hypothesized would be the most important determinants of adoption speed: age, sex, specialty, practice setting, antipsychotic volume, top 25 medical school, and foreign medical graduate. Because certain types of physicians adopt at a much faster rate than others (e.g., psychiatrists, in the case of specialty), for ease of presentation the vertical axes in some curves are truncated near the low point of the survival curve for the second fastest type of adopter, allowing differences between the provider types (including types for which most physicians have yet to adopt) to be depicted more clearly.

The Cox models themselves yield parameter estimates whose exponentials are the change in the hazard ratio of a unit change in the predictor (in the case of a categorical variable, a unit-change in the predictor corresponds to changing from the baseline level to the level of interest). We use the statistical inferences and tests associated with these (e.g., confidence intervals and p-values) to assess the level of statistical evidence for each predictor having a non-zero effect on time to adoption.

Finally, using data from the last 12 months of our study period (October 2007–September 2008), we examine the median number of different antipsychotic products prescribed (where reformulations are counted separately), by specialty.

Results

Characteristics of study sample

Approximately two-thirds (68%) of the sample's antipsychotic prescribers were men, and most (56%) were between the ages of 30 and 49 (Table 1). Approximately two-thirds (66%) were general practitioners, 16% psychiatrists, 14% pediatricians, and 4% neurologists; a total of 16% (including pediatricians) specialized in treating children. Approximately one-fifth (21%) worked in solo practices, 42% practiced in groups, and 18% practiced in other types of settings such as the Veterans Health Administration (the Masterfile listed no classification for 19%). In terms of medical training, 12% graduated from a top 25 ranked U.S. medical school, and 27% were foreign medical graduates.

Proportion of prescribers adopting each drug

During their first year on the market, each of the four original formulations was prescribed by a minority of antipsychotic prescribers (13–31%) (Table 2). Olanzapine, the third on the market (after clozapine and risperidone), was adopted the fastest, with 31% of physicians prescribing it during the first year, 48% during the first two years, and 61% during the first three years. After ten years on the market almost all prescribers (91%) had prescribed olanzapine. Adoption was slightly slower for the other three original formulations, although even aripiprazole (the last new molecule approved) had been prescribed by 59% of prescribers after five years on the market. In contrast, the reformulations had been adopted by only a minority of prescribers several years after their introduction.

Time to adoption

Among physicians who adopt each product, there was considerable variation across products in adoption speed. For the four original formulations, median time to adoption among adopters was 22 months for olanzapine, 24 months for aripiprazole, 27 months for ziprasidone, and 43 months for quetiapine. The median number of months to adoption among adopters varied more for reformulations (8 for Seroquel XR, 9 for Invega, 11 for Symbyax, 25 for Risperdal M-Tab, and 38 for Zyprexa Zydis).

Predictors of time to adoption

Results from the drug-specific Cox models were consistent across drugs (Tables 3 and 4). A hazard ratio greater than 1.0 indicates that a physician with that characteristic was faster to adopt the drug, on average, relative to the reference group (and adjusting for the other variables), while a hazard ratio less than 1.0 indicates that a physician with that characteristic was slower to adopt the drug relative to the reference group.

For 8 of 9 products (results were null for the ninth), physicians under age 50 were faster to adopt than those age 50+ (for example, hazard ratios (HRs) for physicians under age 30 relative to those 50+ ranged from 1.21 to 2.00). Female physicians were slower to adopt new products than male physicians (HRs from 0.76 to 0.91). For 8 of 9 products, psychiatrists were much faster to adopt than general practitioners, pediatricians, and neurologists (for example, HRs for general practitioners relative to psychiatrists ranged from 0.10 to 0.35), although generalists were significantly faster to adopt Symbyax than psychiatrists (HR=1.61). For all 9 products, physicians in the top volume quartile adopted the drug much faster than physicians with lower antipsychotic volume (HRs for lowest quartile relative to highest ranged from 0.15 to 0.39).

Solo practitioners were slower to adopt 5 of 9 antipsychotics than physicians practicing in groups (HRs for solo relative to group practitioners were 0.77 to 0.89); results were null for the other 4. Physicians who graduated from a top 25 medical school were slower to adopt 6 of 9 products (results null for other 3) than physicians who attended other schools (HRs 0.69 to 0.87), and foreign medical graduates were faster to adopt 8 of 9 products (HRs 1.09 to 1.50; results null for ninth) than U.S. medical graduates. For 2 products, physicians who practiced in a hospital setting were faster to adopt than those who had no hospital practice (HR=1.07 for quetiapine and HR=1.10 for Zyprexa Zydis; results null for other 7). For illustration, we present curves of survival probabilities at specific values of the predictors for time to adoption of the original formulation of olanzapine in the Appendix.

Number of agents prescribed

Psychiatrists tend to prescribe a much broader set of antipsychotic medications than the other types of specialists. For the last year of our data, the median number of different antipsychotic products that psychiatrists prescribed was 6, versus a median of 2 for general practitioners and neurologists, and a median of 1 for pediatricians.

Discussion

In this study of a large, national sample of antipsychotic prescribers we found that the vast majority of prescribers (two-thirds of whom were general practitioners) did not adopt new drugs immediately after they became available. We also found substantial heterogeneity across physicians in adoption speed. In particular, physician specialty and prescribing volume were key drivers of time to adoption, although other factors like practice setting, training, and physician demographics are also important influences.

While most second-generation antipsychotics were eventually adopted by a majority of antipsychotic prescribers, the majority of prescribers waited two or more years before prescribing a new product. This behavior could be due to a variety of factors, such as a lack of awareness of a drug's introduction, a change in prescribing after new clinical indications are approved by the FDA, or an intentionally cautious approach to adopting new drugs in an effort to ensure patient safety. Rates of adoption did vary by product, however. Variation in adoption rates could be influenced by order of entry and the number of alternatives available in the class. In fact, olanzapine, the third atypical on the market, and the first drug whose adoption patterns we could observe, was adopted relatively quickly. Variation in adoption

by drug can also be influenced by perceived clinical advantages (e.g., the relatively rapid adoption of aripiprazole may have been influenced by its relatively low incidence of metabolic side effects (11,26)). Rates of reformulation adoption were generally much lower than rates of original formulation adoption, although the physicians who did adopt these products did so relatively quickly.

Psychiatrists adopted new antipsychotics much sooner on average and generally prescribed a much broader set of antipsychotics than physicians from other specialties that commonly prescribe antipsychotics, who may be more likely to prescribe antipsychotics for off-label indications such as sleep disorders. These results are consistent with those of a study by Taub and colleagues using a similar dataset (27). The results are also consistent with evidence that physicians often follow norms (e.g., prescribing one or two drugs to all patients with a condition) to guide treatment decisions rather than customize treatment for a given patient due to substantial time and cognition costs of customization (21, 28). Use of norms may be more common among non-psychiatrists, for whom antipsychotic treatment may represent a much smaller proportion of their prescribing (and thus cognition and time costs associated with learning the nuances of antipsychotic treatment may be greater), than for psychiatrists.

The highest-volume antipsychotic prescribers were much faster to adopt than low-volume antipsychotic prescribers even after controlling for specialty. It could be that high-volume prescribers are disproportionately likely to treat treatment-refractory patients, and thus more likely to try new products soon after they come on the market. Alternatively, high-volume prescribers may be more likely to be targeted by drug manufacturer marketing efforts (29,30).

Speed of adoption also varied on the basis of characteristics of the physician's practice setting and training. Physicians in solo practice were often slower to adopt than those practicing in group settings, although the differences were relatively small. We are unable to isolate the features of solo practice that may contribute to slower adoption. However, physicians who practice alone may have less exposure to a variety of influences on prescribing, including quality improvement initiatives, guideline dissemination, and pharmaceutical sales representatives, than physicians who practice in groups. In addition, social influences within organizations have long been acknowledged as an important determinant of technology diffusion (31–33); physicians are likely to be influenced by their peers within their practice organizations, and solo practitioners may have fewer interactions with peers that could influence prescribing behavior.

Interestingly, physicians who graduated from the highest-ranked medical schools were slower to adopt most new antipsychotics. It could be that higher-ranked medical schools are more likely to emphasize a more "conservative" approach to adopting new drugs (34) or grant less exposure to pharmaceutical representatives, but there is no evidence to support this conjecture.

Our study has several limitations. First, we lack information on the patients filling the prescriptions, including the specific disorder for which an antipsychotic was prescribed or the disorder's severity. Psychiatrists treating patients with treatment-resistant mood or psychotic disorders may be faster adopters than those treating less severely ill patients. Second, we are unable to study the adoption of clozapine and risperidone, although our thirteen years of data allow us to look at the adoption of all other second-generation original formulations and most reformulations currently available on the market. Third, we lack data on prescriptions filled by in-hospital pharmacies. Further, to the extent that we do not have data on prescriptions written but not dispensed, our results are confounded by factors

affecting patient decisions to fill prescriptions. Fourth, we lack data on the number of free samples distributed by each physician, and use of patient assistance programs, although use of the latter is quite low (35). In addition, we are unable to identify a physician's residency training program, which may have more influence on prescribing than medical school attended. Finally, due to lack of data we are unable to adjust for some of the external influences on prescribing behavior such as manufacturer promotional efforts directed at physicians, characteristics of the specific organizations in which physicians practice, and health plan coverage of different antipsychotics.

Conclusions

Physician decisions about whether or not to adopt new drugs into practice can have profound implications for patient care, both in terms of the quality and safety of care received. These decisions also have important implications for health care spending. As policymakers and payers grapple with how to control rising health care expenditures, there will likely be increased pressure to maximize the value of care received by patients, including individuals with mental disorders. By identifying physician characteristics associated with decisions to adopt new medications, our findings enable the targeting of efforts to increase high-value, evidence-based prescribing through training/education programs, academic detailing (36), guideline dissemination, financial incentives, utilization management, or other initiatives.

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Table 1

Characteristics of Physician Prescribers of Antipsychotics in the Study Sample (n=30,369)

Characteristic	N	%
Female	9681	31.9
Age (years):		
<30	6853	22.6
30–39	8731	28.8
40–49	8164	26.9
50 or more	6621	21.8
Specialty:		
General practice	20125	66.3
Psychiatry	4767	15.7
Pediatrics	4147	13.7
Neurology	1330	4.4
Practice type:		
Solo	6238	20.5
Group	12841	42.3
Other	5554	18.3
No classification	5736	18.9
Some hospital practice	11568	38.1
Top 25 medical school	3676	12.1
Foreign medical graduate	8025	26.5

Note: These data were obtained from IMS Health, Xponent™, 1996–2008. “General practice” includes internal medicine (n=9628), family medicine (n=7497), family practice (n=1821), and general practice (n=1179). “Psychiatry” includes psychiatry (n=4115), geriatric psychiatry (n=37), and child/adolescent psychiatry (n=615). “Neurology” includes neurology (n=1217) and child neurology (n=113). Antipsychotic prescribers in the sample prescribed at least one first- or second-generation antipsychotic during the study period (January 1996–September 2008).

Table 2

Percentage of Second-Generation Antipsychotic Prescribers Who Have Adopted a Drug within 10 Years of Its Introduction

% of Antipsychotic Prescribers Who Have Adopted a Drug												
Product (Brand Name)	**Active Ingredient**	**FDA Approval Date**	**1 yr**	**2 yrs**	**3 yrs**	**4 yrs**	**5 yrs**	**6 yrs**	**7 yrs**	**8 yrs**	**9 yrs**	**10 yrs**
Original Formulations												
Zyprexa	olanzapine	9/96	30.5%	47.9%	60.6%	69.3%	77.9%	83.7%	87.4%	89.3%	90.4%	91.2%
Seroquel	quetiapine	9/97	13.4%	25.7%	37.4%	48.6%	59.5%	69.1%	76.7%	82.8%	87.1%	90.4%
Geodon	ziprasidone	2/01	16.4%	25.2%	32.1%	38.2%	44.1%	49.5%	53.7%	--	--	--
Abilify	aripiprazole	11/02	20.0%	32.5%	42.8%	52.0%	59.0%	--	--	--	--	--
Reformulations												
Zyprexa Zydis	olanzapine	4/00	2.1%	6.2%	11.1%	15.4%	18.2%	20.5%	22.3%	24.3%	--	--
Risperdal M-Tab	risperidone	4/03	4.4%	8.1%	11.1%	13.6%	15.7%	--	--	--	--	--
Symbyax	olanzapine + fluoxetine	12/03	12.0%	16.9%	19.4%	21.2%	--	--	--	--	--	--
Invega	paliperidone	12/06	9.4%	--	--	--	--	--	--	--	--	--
Seroquel XR	quetiapine	5/07	7.6%	--	--	--	--	--	--	--	--	--

Note: These data were obtained from IMS Health, Xponent™, 1996–2008. The numbers are product-limit survival estimates from Kaplan-Meier survival models. The data cover the period 1996–2008, so we are unable to provide 10 years of data on drugs introduced later in the study period. For example, we have only 5 full years of data for Abilify, which was introduced during 2002.

Table 3

Results from Cox Model Regression Analyses of Time to Adoption for Four Original Second-Generation Antipsychotic Formulations

Variables	Olanzapine Hazard ratio	P-Value	Quetiapine Hazard ratio	P-Value	Ziprasidone Hazard ratio	P-Value	Aripiprazole Hazard ratio	P-Value
Sex								
Female	.84	<.001	.86	<.001	.87	<.001	.91	.001
Male	Reference		Reference		Reference		Reference	
Age								
<30	1.07	.545	1.48	<.001	1.52	<.001	1.43	<.001
30–39	1.33	<.001	1.45	<.001	1.47	<.001	1.45	<.001
40–49	1.33	<.001	1.38	<.001	1.34	<.001	1.34	<.001
50+	Reference		Reference		Reference		Reference	
Specialty								
General Practice	.28	<.001	.35	<.001	.18	<.001	.22	<.001
Pediatrics	.24	<.001	.25	<.001	.21	<.001	.38	<.001
Neurology	.33	<.001	.54	<.001	.16	<.001	.16	<.001
Psychiatrist	Reference		Reference		Reference		Reference	
Practice Setting								
Solo	.89	<.001	.86	<.001	.95	.087	.96	.167
Other	.88	.003	.81	<.001	.88	.001	.90	.003
No Classification	.78	<.001	.83	<.001	.84	<.001	.83	<.001
Group	Reference		Reference		Reference		Reference	
Any Hospital Practice								
Yes	1.04	.072	1.08	.001	.97	.272	.99	.664
No	Reference		Reference		Reference		Reference	
Antipsychotic Volume								
1st quartile	.34	<.001	.39	<.001	.33	<.001	.28	<.001
2nd quartile	.40	<.001	.46	<.001	.38	<.001	.35	<.001
3rd quartile	.51	<.001	.55	<.001	.52	<.001	.47	<.001

Variables	Olanzapine Hazard ratio	P-Value	Quetiapine Hazard ratio	P-Value	Ziprasidone Hazard ratio	P-Value	Aripiprazole Hazard ratio	P-Value
4th quartile	Reference		Reference		Reference		Reference	
Top 25 Medical School								
Yes	.94	.082	.94	.055	.87	.001	.98	.628
No	Reference		Reference		Reference		Reference	
Foreign Medical Graduate								
Yes	1.13	<.001	1.13	<.001	1.09	.005	1.15	<.001
No	Reference		Reference		Reference		Reference	

Note: These data were obtained from IMS Health, Xponent™, 1996–2008. Hazard ratios are presented in this table, with p-values provided in parentheses. A hazard ratio greater than 1.00 suggests that a physician with that characteristic was faster to adopt the drug on average relative to the reference group (and adjusting for the other variables in the model), while a hazard ratio less than 1.00 suggests that a physician with that characteristic was slower to adopt the drug on average relative to the reference group. These models also include for state fixed effects and variables characterizing the population residing in the zip code of the physician's practice using data from the 2002 Area Resource File (percent black, percent Hispanic, percent enrolled in an HMO, percent who have completed high school, and percent 65 years or older).

Table 4

Results from Cox Model Regression Analyses of Time to Adoption for Five Second-Generation Antipsychotic Reformulations

Variables	Zyprexa Zydis Hazard ratio	P-Value	Risperdal M-Tab Hazard ratio	P-Value	Symbyax Hazard ratio	P-Value	Invega Hazard ratio	P-Value	Seroquel XR Hazard ratio	P-Value
Sex										
Female	.89	.013	.93	.144	.89	.015	.76	<.001	.87	.030
Male	Reference		Reference		Reference		Reference		Reference	
Age										
<30	2.00	<.001	1.61	<.001	1.76	<.001	1.21	.029	1.44	.001
30–39	1.53	<.001	1.55	<.001	1.48	<.001	1.42	<.001	1.38	.002
40–49	1.35	<.001	1.36	<.001	1.28	<.001	1.19	.001	1.19	.034
50+	Reference		Reference		Reference		Reference		Reference	
Specialty										
General Practice	.22	<.001	.20	<.001	1.16	.007	.12	<.001	.10	<.001
Pediatrics	.21	<.001	.64	<.001	.23	<.001	.12	<.001	.13	<.001
Neurology	.18	<.001	.34	<.001	.19	<.001	.06	<.001	.05	<.001
Psychiatrist	Reference		Reference		Reference		Reference		Reference	
Practice Setting										
Solo	.82	<.001	.77	<.001	1.03	.586	.87	.035	.93	.366
Other	.98	.691	1.04	.523	.81	.001	.89	.076	.91	.263
No classification	.96	.488	.97	.698	.74	<.001	1.01	.848	.90	.231
Group	Reference		Reference		Reference		Reference		Reference	
Any Hospital Practice										
Yes	1.10	.028	.94	.162	1.01	.743	.99	.816	.95	.386
No	Reference		Reference		Reference		Reference		Reference	
Antipsychotic Volume										
1st quartile	.27	<.001	.22	<.001	.19	<.001	.15	<.001	.16	<.001
2nd quartile	.36	<.001	.28	<.001	.31	<.001	.22	<.001	.21	<.001
3rd quartile	.44	<.001	.41	<.001	.48	<.001	.30	<.001	.33	<.001

Variables	Zyprexa Zydis Hazard ratio	P-Value	Risperdal M-Tab Hazard ratio	P-Value	Symbyax Hazard ratio	P-Value	Invega Hazard ratio	P-Value	Seroquel XR Hazard ratio	P-Value
4th quartile	Reference		Reference		Reference		Reference		Reference	
Top 25 Medical School										
Yes	.85	.013	.26	.046	.70	<.001	.69	<.001	.75	.008
No	Reference		Reference		Reference		Reference		Reference	
Foreign Medical Graduate										
Yes	1.39	<.001	1.23	<.001	1.07	.130	1.50	<.001	1.42	<.001
No	Reference		Reference		Reference		Reference		Reference	

Note: These data were obtained from IMS Health, Xponent™, 1996–2008. Hazard ratios are presented in this table, with p-values provided in parentheses. A hazard ratio greater than 1.00 suggests that a physician with that characteristic was faster to adopt the drug on average relative to the reference group (and adjusting for the other variables in the model), while a hazard ratio less than 1.00 suggests that a physician with that characteristic was slower to adopt the drug on average relative to the reference group. These models also include for state fixed effects and variables characterizing the population residing in the zip code of the physician's practice using data from the 2002 Area Resource File (percent black, percent Hispanic, percent enrolled in an HMO, percent who have completed high school, and percent 65 years or older).