Do new prescription drugs pay for themselves?
The case of second-generation antipsychotics

Mark Duggan

University of Maryland and NBER, College Park, MD 20742, USA

Abstract

During the last several years, spending on prescription drugs in the U.S. increased at a 15% annual rate, with the US$ 178 billion spent in 2002 accounting for more than 11% of health care expenditures in the U.S. This growth has been largely driven by a shift to new drugs, which are typically more expensive than earlier drugs within the same therapeutic category. Recent research has suggested that the shift to new drugs may lower health care spending by reducing the demand for hospitalizations and other health care services. Using a 20% sample of Medicaid recipients from the state of California for the 1993–2001 period, I investigate this hypothesis for antipsychotic drugs—the therapeutic category that has accounted for more government spending than any other during the past decade. Using three different identification strategies, my findings demonstrate that the 610% increase in Medicaid spending on antipsychotic drugs during the study period caused by the shift to three new treatments has not reduced spending on other types of medical care, thus undermining the hypothesis that the drugs have "paid for themselves." Because of data limitations, the findings for health outcomes are necessarily more speculative but suggest that the new medications have increased the prevalence of diabetes while reducing the prevalence of extrapyramidal symptoms among the mentally ill.

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E-mail address: duggan@econ.bsos.umd.edu.

1. Introduction

From 1996 to 2002, spending on prescription drugs in the U.S. grew at a 15% annual rate, with the US$ 178 billion spent in 2002 accounting for more than 11% of all health care expenditures. This growth was mainly driven by an increase in the average price of a prescription, which rose by more than 10% per year from 1996 to 2001. Price increases were caused both by an increase in the price of existing drugs and by a shift to newly approved drugs, which tend to be more expensive than the drugs that preceded them in the same therapeutic category (NIHCM, 2002). The growth in pharmaceutical spending has been similarly rapid within the federal-state Medicaid program, with expenditures there increasing from US$ 12.3 billion in 1996 to US$ 29.6 billion in 2002.[1] State governments have differed in their response to the increase, with some requiring co-pays by Medicaid recipients, others introducing dispensing limits, and still others requiring physicians to obtain prior authorization before prescribing drugs not on the state's formulary.

Determining how optimally to respond, if at all, to the growth in Medicaid prescription drug spending is clearly a complicated problem. The program provides valuable insurance to millions of society's most disadvantaged individuals, covering the cost of more than 520 million prescriptions for nearly 47 million Medicaid recipients in 2002. But because Medicaid recipients typically do not share in the cost of their prescription drugs, the program distorts medical care purchase decisions, potentially leading a Medicaid recipient to select an expensive drug over a much cheaper alternative even if he/she is almost indifferent between the two. It is therefore plausible that, in some cases, a Medicaid recipient would derive a benefit from a drug treatment that is substantially lower than the cost to taxpayers.[2]

But as recent researchers have noted, the difference between two drug prices may not accurately reflect the difference in health care spending that would result if a patient were to choose one treatment over another (Lichtenberg, 1996, 2001). For example, a more expensive drug may deliver health benefits that reduce the patient's demand for other health care services, to some extent offsetting its higher price. A similar offset effect could occur for individuals who otherwise would take no treatment. Even with no offset effect, a more expensive treatment may deliver health or quality of life benefits that are sufficiently large to pass a cost–benefit test. In measuring the value of any drug treatment, one would like to know its effect on both spending and health, with these effects potentially varying across individuals.

In this paper, I investigate the effect of new prescription drugs on both Medicaid spending and health outcomes. This question is inherently difficult given that drug treatment is not randomly assigned and because there are thousands of drugs covered by Medicaid at a point-in-time. Rather than simultaneously considering all of them, I focus on the one therapeutic category that accounts for more Medicaid spending than any other. Antipsychotic drugs are used to treat schizophrenia, bipolar disorder, and dementia and the Medicaid program spent US$ 3.73 billion on them in 2002. Risperdal, Zyprexa, and Seroquel, three drugs that were approved by the FDA and entered the market during the mid-1990s, accounted

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[1] Dollar figures cited here and elsewhere in the paper are adjusted to 2001 dollars using the CPI-U index.

[2] This moral hazard effect is of course not unique to Medicaid. Individuals with other forms of health insurance also typically pay a small share (if any) of the costs of additional medical care.

for 88% of this spending. These three "second-generation" antipsychotics are substantially more expensive than the drug treatments that preceded them and were numbers one, two, and four, respectively, among all prescription drugs in terms of 2002 Medicaid spending.

To estimate the impact of these new drug treatments and the accompanying increase in prescription drug spending, I utilize complete claims and eligibility data for a 20% sample of Medicaid recipients from the state of California for the 1993–2001 period. I construct the initial sample by selecting the 37,369 individuals diagnosed with schizophrenia (the condition for which these drugs are most commonly prescribed) at some point during the nine-year study period. This long time period allows me to exploit changes in treatment patterns from a year when no schizophrenia patients were taking Risperdal, Zyprexa, or Seroquel until 2001, a year when nearly 70% were taking one of these drugs.

There are two central challenges for reliable estimation of the effect of these new drug treatments. The first is that drug treatments are not randomly assigned in the Medicaid program. Individuals who take a certain drug are likely to differ systematically from their counterparts who do not. While many of these differences are likely to be observable, some may not be, and this unobserved heterogeneity could lead to biased estimates. To surmount this obstacle, I employ three strategies to estimate the effect of second-generation antipsychotics. None of these methods is free from potential biases, but because each one has different limitations it can act as a check on the other two to gauge the robustness of the results.

The second main challenge for this study is that the Medicaid data will provide an incomplete picture of health for individuals in the sample. Following previous studies, I focus on the prevalence of adverse side effects when investigating whether the new drugs have influenced health. Earlier research has found that second-generation antipsychotics improve health by reducing the prevalence of extrapyramidal symptoms (EPS) including involuntary movements, tremors, and body restlessness (Leucht et al., 1999). A number of recent studies suggest that the new drugs may reduce health by increasing the prevalence of diabetes and related illnesses (Sernyak et al., 2002; Lindenmayer et al., 2001). But both sets of results are controversial, with some finding no impact of second-generation antipsychotics on EPS (Rosenheck et al., 2003) and others no effect on diabetes (Kabinoff et al., 2003).

My first identification strategy examines changes statewide in outcome variables of interest as the new medications are used by an increasing fraction of individuals with schizophrenia. This analysis demonstrates that the diffusion of second-generation antipsychotics has been associated with a substantial increase in prescription drug spending but no apparent reduction in spending on other health care services. This also holds true in those periods when there is a sharp break in trend in the diffusion rate of the new drugs. The increase in the use of these drugs was associated with a decline in the measured prevalence of extrapyramidal symptoms but also with an increase in the fraction diagnosed with diabetes.

Of course, a trend analysis for just one geographic area suffers from the difficulty that factors other than antipsychotic treatments that may influence the outcome variables of interest are changing over time. To control for these potential confounders, I next exploit variation across geographic areas in the rate at which second-generation drugs diffuse. My findings using this strategy demonstrate that the areas in which the utilization of second-generation drugs increased relatively rapidly had substantially larger increases in Medicaid spending and a significantly greater increase in the measured prevalence of diabetes than

those areas with relatively little use of the new treatments. On the plus side, my findings here suggest that increases in the use of these drugs have been associated with a modest reduction in the prevalence of extrapyramidal symptoms, though the estimates are not statistically significant.

An important limitation to this second strategy is that some of the variation across geographic areas in the rate at which the new treatments diffuse may be driven by changes in health or other factors that could lead to biased estimates of the effect of the new treatments. Thus, my third method utilizes an instrumental variables strategy with individual-level data that exploits variation across psychiatrists in the propensity to prescribe second-generation antipsychotics. This method controls for differences across psychiatrists in the baseline characteristics of their patients and aims to estimate the effect of the new drug treatments for marginal patients, individuals who would take the drug when paired with certain psychiatrists but not with others. The findings here demonstrate that psychiatrists have a substantial effect on the probability that a schizophrenia patient takes a second-generation drug and that the new treatments significantly increase Medicaid spending for the marginal patient.

Taken together, the findings presented in this paper suggest that second-generation antipsychotics did not reduce spending on other types of medical care. This finding undermines the hypothesis that the new drugs, which are several times more expensive than first-generation antipsychotics, to some extent paid for themselves. The findings for health outcomes are less clear-cut because there appear to be both positive and negative effects and because health is not perfectly measured in the Medicaid data.

2. Background and previous research

Schizophrenia is a chronic and debilitating mental illness that afflicts nearly two million individuals in the U.S. It is characterized by a range of symptoms, including delusions, hallucinations, cognitive impairments, and social withdrawal. While there is no known cure for schizophrenia, patient symptoms often improve in response to treatment with antipsychotic drugs. Until 1990, physicians typically prescribed haloperidol or some other "first-generation" antipsychotic for the treatment of schizophrenia. While these drugs were often effective in treating the symptoms of schizophrenia, one important disadvantage was their side effect profile. Patients taking the drugs frequently experienced extrapyramidal symptoms (EPS) that could include tardive dyskinesia (involuntary movements), Parkinsonism (tremors and rigidity), akathisia (restlessness), acute dystonia (muscle contractions), and neuroleptic malignant syndrome (changes in heart rate or breathing).

Treatment patterns began to change in 1990 following the FDA's approval of Clozaril, the first in a line of "second-generation" antipsychotics that appeared to reduce the prevalence of extrapyramidal symptoms while treating the positive symptoms of schizophrenia (Lamberg, 1998; Keefe et al., 1999; Meltzer et al., 1999). Though Clozaril was found to have serious side effects of its own that limited its use to schizophrenia patients who could not tolerate other drugs, the shift to second-generation antipsychotics accelerated following the introduction of Risperdal in 1994, Zyprexa in 1996, and Seroquel in 1997. These latter three drugs were several times more expensive than haloperidol and other first-generation drugs and quickly became the most commonly prescribed drugs in the treatment of schizophrenia.

2.1. Previous research

A number of previous studies have investigated the relationship between the use of second-generation antipsychotics and total health care spending. The findings from these studies are mixed, with some suggesting that the drugs reduce expenditures (Glazer and Johnstone, 1997) and others finding the opposite (Coley et al., 1999). As a recent review article notes (Hudson et al., 2003) the findings from most of the previous studies are not conclusive because of small sample sizes, short time periods, imputed data, or other design limitations. An even larger body of research has examined the effect of second-generation antipsychotics on the prevalence of adverse side effects, including extrapyramidal symptoms, diabetes, abnormal weight gain, and hyperlipidemia (Gianfrancesco et al., 2002; Koro, 2002; Leucht et al., 1999; Lund et al., 2001; Meyer, 2001; Sernyak et al., 2002). Taken together, these studies suggest that second-generation drugs have fewer adverse extrapyramidal side effects than the earlier drugs but that they may increase the prevalence of diabetes and related illnesses.[3] Both sets of results are controversial, however, with some finding, no impact of second-generation antipsychotics on EPS (Rosenheck et al., 2003) and others no effect on diabetes (Kabinoff et al., 2003).

One prominent recent study compared the effect on both health outcomes and health care spending of haloperidol and Zyprexa, the most commonly prescribed first and second-generation drugs, respectively (Rosenheck et al., 2003). The study enrolled 309 schizophrenia patients insured by the Department of Veterans' Affairs (DVA) and randomized each person to haloperidol or Zyprexa for up to one year. A wide set of outcome measures were considered, including cognitive functioning, quality of life, adverse side effects, and health care spending. The findings from this study suggest that Zyprexa did not lower hospitalization rates or other types of health care utilization. Because of this and given the substantial difference in the cost of these two drugs, spending for individuals taking Zyprexa was substantially higher than for those in the haloperidol group. The authors also found little evidence to suggest that Zyprexa increased compliance, reduced the prevalence of adverse side effects, or improved quality of life. The findings did suggest that Zyprexa reduced the prevalence of akathasia (restlessness) and led to modest improvements in cognitive functioning but also found that individuals taking this drug were more likely to gain a substantial amount of weight, potentially increasing their risk for diabetes.

While this study and previous ones using a randomized research design have made important contributions to knowledge, there are a number of limitations that motivate the current study. First, randomized studies are well-suited to estimating the average effect of a drug but are unable to estimate its effect on the marginal patient. The distinction between these two causal parameters has been emphasized in economics[4] but cannot be explored in the typical randomized study of alternative health care treatments. As previous authors have noted (McClellan et al., 1994), it is this marginal effect that may be more relevant when forecasting the effect of alternative policy interventions.

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[3] It is important to note that the magnitude of these estimates vary substantially across studies and across drugs.

[4] See, for example, many of the studies that estimate the return to schooling summarized in Card (2003).

Second, most randomized studies have small sample sizes with which it is difficult to obtain sufficient precision for a skewed outcome variable such as health care spending. The main reason for this is cost, randomized studies are very expensive to administer; and thus, the ones that consider costs often have wide confidence intervals. A third limitation of most randomized studies is their focus on just two drugs. Though the Rosenheck study does consider the most common first and second-generation drugs, these two currently account for less than one-third of antipsychotic prescriptions.

An additional limitation of randomized studies is that they are often tightly controlled. Individuals may be much less likely to adhere to a treatment regimen in real-world settings. Similarly, randomized studies usually follow individuals for just a short time, with the maximum duration typically equal to one year. A sixth limitation is that they often focus on a small subset of individuals who are possible candidates for a drug. In the case of the Rosenheck study, only males in their 40s who had recently been hospitalized were considered. And one final limitation of randomized studies is that individuals can choose not to participate. While the Rosenheck study successfully enrolled 309 individuals, there were 1530 who either refused to participate or whose clinicians would not allow them to join the study. If the individuals who enroll in a study are substantially different from those who choose not to participate then the estimates may not apply for this other group.[5]

2.2. Medicaid and the market for antipsychotic drugs

From 1996 to 2002, Medicaid spending in the U.S. on prescription drugs increased by 141% from US$ 12.3 billion to US$ 29.6 billion. This growth far outpaced Medicaid spending on other health care services, which increased by just 29% during this same period. In both years, spending for drugs used to treat central nervous system (CNS) disorders was greater than for any other therapeutic category.

Within the CNS therapeutic category, antipsychotic drugs accounted for 51% of the US$ 7.34 billion in 2002 Medicaid spending. During the 1996–2002 period, Medicaid spending on antipsychotic drugs grew at a 25% annual rate, with most of this expenditure growth explained by an increase from US$ 61 to US$ 171 in the average price of an antipsychotic prescription. Zyprexa, Risperdal, and Seroquel accounted for 88% of U.S. Medicaid spending on antipsychotic drugs in 2002 and were ranked first, second, and fourth, respectively, in terms of total Medicaid spending among all prescription drugs in that same year.

One interesting feature of this category of drugs is the importance of Medicaid. While this program paid for 18% of all prescriptions filled in the U.S. in 2002, the corresponding share for antipsychotic drugs was nearly 75% (Duggan, 2003). Given this high Medicaid market share, the current study's focus on beneficiaries of this program is not as limiting as it might otherwise be.

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[5] An additional issue with previous studies (both randomized and other) in this area is that a large fraction of them were funded by one of the three pharmaceutical companies that produce the new second-generation drugs.

3. The Medicaid sample and the diffusion of second-generation antipsychotic drugs

3.1. The Medicaid claims and eligibility data

To estimate the effect of second-generation antipsychotic drugs on health care spending and health outcomes, I use an administrative data set constructed by the California Department of Health Services (DHS) that contains all Medicaid claims and detailed eligibility data for a random 20% sample of California residents with at least one month of Medicaid eligibility between January of 1993 and December of 2001.[6] There are 2.92 million individuals in the sample, implying that approximately 14.6 million Californians were eligible for the program in one or more months during this nine-year period.

The annual Medicaid eligibility files contain demographic information for each individual in the sample, including gender, month and year of birth, race/ethnicity, and zip code of residence. The file provides Medicaid eligibility information for each of the 12 months during the year and also contains month-by-month information on the individual's aid code, which reports whether the person is eligible for Medicaid through welfare, Supplemental Security Income (SSI), or some other government program. Additionally, there are two variables in each month that indicate whether an individual is eligible for parts A or B of the Medicare program. Many Medicaid recipients are dually eligible for Medicare because of their receipt of social security benefits. Finally, the eligibility data indicate whether each recipient is enrolled in a managed care plan and if so provides the plan number.[7]

In a typical year, the Medicaid claims data for the 20% sample contain more than 30 million claims. These include every fee-for-service payment made on behalf of individuals in the sample while they are eligible for Medicaid. Each claim includes the individual's Medicaid identifier, which can be matched to the eligibility files. There are three main types of claims in the data. Inpatient claims include detailed information about admissions to hospitals and long-term care facilities. Outpatient and other ambulatory claims have similar data about payments to physicians, clinics, hospital outpatient facilities, laboratories, and other health care providers. Finally, prescription drug claims provide a drug code, which can be linked to a companion file to determine the drug and dosage amount, as well as the number of units dispensed for each prescription. The claims data include all fee-for-service payments made in the 10-year period from January of 1993 until December of 2002, though because there is often a lag in processing the claims the current study will focus on the nine-year period ending in December of 2001.

3.2. The analysis sample and the shift to second-generation antipsychotics

Following previous work (Frank et al., 2003), the current study uses diagnosis codes from the Medicaid claims data to determine whether an individual has been diagnosed with

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[6] DHS sampled by individual rather than by eligibility spell when constructing these files. Thus, if one person has multiple spells of eligibility during this nine-year period, every spell would be included.

[7] Though the utilization data will be incomplete for managed care recipients, a file with capitation rates by aid code, plan number, and month can be used to calculate Medicaid managed care spending for them (Duggan, 2004).

schizophrenia.[8] Selecting Medicaid recipients with one or more schizophrenia claims during the nine-year study period yields a sample of 37,369 individuals from the full 20% sample. Individuals ever residing in one of the seven counties that moved to a county organized health system in this period are dropped because the claims data would be incomplete for them. The final sample consists of 32,072 individuals diagnosed with schizophrenia at least once between January of 1993 and December of 2001. There is substantial variation across individuals in the number of schizophrenia claims, with 9.1% of the sample having just one schizophrenia claim while 7.1% of the sample has 500 or more claims during the study period.[9]

From 1993 to 2001, there were substantial changes in the pharmacological treatment of psychotic illness. Table 1 lists the 10 most commonly prescribed antipsychotics in the full 20% Medicaid sample in 1993 and in 2001,[10] with the table providing both the number of prescriptions and the average amount spent per prescription. As the table shows, the first-generation drugs haloperidol and thioridazine were the most commonly prescribed antipsychotics in 1993. Eight years later, the top selling drugs were Zyprexa and Risperdal, with Seroquel number three in terms of total spending and four with respect to total prescriptions. These three drugs were not available in 1993 but accounted for more than 58% of all antipsychotic prescriptions and 86% of spending on antipsychotic drugs by 2001.

3.3. The causal effect of second-generation drugs

Before proceeding to the empirical analyses, it is useful to define the structural parameters of interest for estimating the effect of second-generation antipsychotics. Define for patient j, a set of K potential outcomes for variable Y (e.g. Medicaid spending) in period t, with these outcomes representing the values of Y that would result in response to treatment with each of K possible drug treatments. For simplicity, set K equal to 3, with the three possible treatments being a second-generation antipsychotic, a first-generation drug, or no drug treatment. This simplification captures the difference across these three categories rather than within each category.[11] The effect of a second-generation drug relative to no drug treatment for individual j in period t is defined to equal $\Delta_{j0t} = Y_{j2t} - Y_{j0t}$ and the corresponding effect relative to a first generation drug is $\Delta_{j1t} = Y_{j2t} - Y_{j1t}$. Both parameters are indexed by j and t to capture the fact that the effect may vary across individuals or within a person over time. Which of the two parameters is relevant for j will depend on whether he/she would otherwise take a first-generation drug or no drug at all. The two parameters

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[8] The data uses the ICD-9 coding system, and thus a diagnosis code that begins with 295 represents schizophrenia. Prescription drug claims do not have a diagnosis code though virtually all of the inpatient and outpatient claims do.

[9] The results presented below are not sensitive to dropping individuals with just one claim.

[10] In 1993, 59% of these prescriptions are written for individuals in the schizophrenia sample, while in 2001, that number is slightly higher at 62%. The most common prescription provides a one-month supply.

[11] It would be straightforward to expand the measures of potential outcomes to allow for variation within a drug category and for outcomes to depend on both current and past treatment decisions.

Table 1
Top 10 antipsychotic drugs in 1993 and 2001

Drug name	Prescriptions		Spending in US$ 1000		Average price (US$)
	#Scripts	Percentage of total	Total paid (US$)	Percentage of total	
1993					
Haloperidol	66018	20.5	1515	12.4	23
Thioridazine	47832	14.9	579	4.8	12
Clozapine	41616	12.9	4374	35.9	105
Lithium carbonate	31381	9.8	313	2.6	10
Compazine	28585	8.9	973	8.0	34
Amitrip/Perp	28093	8.7	327	2.7	12
Fluphenazine	24131	7.5	1584	13.0	66
Thiothixene	19188	6.0	488	4.0	25
Perphenazine	10749	3.3	480	3.9	45
Prolixin	4748	1.5	558	4.6	118
All others	19322	6.0	987	8.1	51
Total	321663	100.0	12179	100.0	38
2001					
Zyprexa	113919	24.9	41120	47.6	361
Risperdal	108969	23.8	23049	26.7	212
Clozapine	50211	11.0	6494	7.5	129
Seroquel	42785	9.3	10253	11.9	240
Haloperidol	35480	7.7	1419	1.6	40
Lithium carbonate	21129	4.6	408	0.5	19
Thioridazine	13645	3.0	251	0.3	18
Fluphenazine	13136	2.9	535	0.6	41
Perphenazine	10875	2.4	233	0.3	21
Chlorpromazine	9306	2.0	405	0.5	44
All Others	38791	8.5	2170	2.5	56
Total	458246	100.0	86337	100.0	188

Medicaid spending and number of prescriptions in the 20% California Medicaid sample for the top 10 antipsychotic drugs in 1993 and 2001.

can be incorporated into the following equation for Y_{jt} as follows:

$$Y_{jt} = Y_{j0t} + \Delta_{j0t} \times \text{Second}_{jt} + (\Delta_{j0t} - \Delta_{jlt}) \times \text{First}_{jt} \tag{1}$$

with First_{jt} and Second_{jt} equal to indicator variables that are set to one if individual j takes a first or second-generation drug in period t, respectively, and zero otherwise.

The challenge for reliable identification is that only one of the three potential outcomes is ever observed for individual j in period t. If drug treatment were randomly assigned then one could obtain an unbiased estimate for the average effect of the drug simply by calculating differences in the sample means. But with observational data, one must account for the fact that treatment is not random and thus may be correlated with both observable and unobservable determinants of the potential outcomes Y_{j0t}, Y_{j1t}, and Y_{j2t}. If not properly accounted for, this could bias any estimate of the effect of the new drugs.
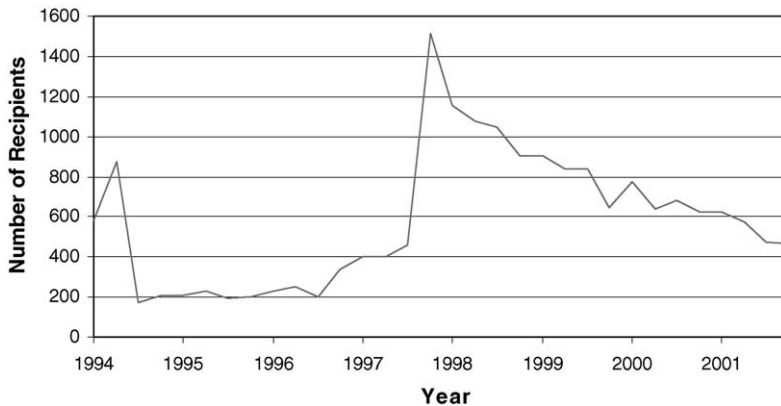
Fig. 1. Numbers taking Risperdal, Zyrexa, or Seroquel for first time.

4. Time-series trends in spending, utilization, and health outcomes

In this section, I investigate whether trends in average measures of Medicaid spending, utilization, and health appear to be affected by sharp changes in the use of Risperdal, Zyprexa, and Seroquel, three drugs approved by the FDA in the mid-1990s.[12] Each column of Table 2 includes average annual measures of more than 30 variables for Medicaid recipients with one or more schizophrenia claims in each year. One obvious concern with any examination of statewide trends is that the characteristics of individuals in the sample may change over time. The first six rows provide average characteristics for Medicaid recipients diagnosed with schizophrenia in each year to explore this issue. As is clear from the table, these averages remain fairly stable and to the extent that there are changes, they are gradual. For example, the percentage of schizophrenia patients who are male increases by an almost equal amount from 1993 to 1997 (53.4%–54.9%) as from 1997 to 2001 (54.9%–56.5%).[13] Additionally, the number of patients diagnosed with schizophrenia at least once during the year does not change much from one year to the next, ranging from a low of 12,114 in 1994 to a high of 14,083 in 2001. It is, therefore, unlikely that there are any substantial changes in the characteristics of schizophrenia patients that coincide with the sharp changes in the use of Risperdal, Zyprexa, and Seroquel summarized in the next section.

4.1. Discontinuous change in the use of second-generation antipsychotics

Fig. 1 and Table A.1 provide information on the number of individuals taking any of the three major second-generation antipsychotics for the first time in each quarter.[14] The first

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[12] I do not consider the second-generation drug Clozaril because it is recommended only for treatment-resistant patients and because it was first used more than two years before the beginning of my study period.

[13] The trends summarized in this section are almost identical if I exclude the 15% of schizophrenia patients with one or more months in a managed care plan during the nine-year study period.

[14] A person can appear in this table only once, thus if he/she takes Risperdal in 1994, Zyprexa in 1996, and Seroquel in 1997, only the first Risperdal prescription would count in this table.

Table 2
Trends in spending, utilization, and health outcomes for Medicaid recipients with schizophrenia

		1993	1994	1995	1996	1997	1998	1999	2000	2001
1	Average age	43.5	42.9	42.7	43.4	43.8	43.9	44.1	44.2	44.4
2	Average months eligible	11.4	11.4	11.3	11.4	11.4	11.4	11.4	11.4	11.4
3	%Medicare	44.0	41.0	39.4	40.9	41.2	39.6	39.6	38.8	38.3
4	%Managed care	1.2	1.0	1.5	2.1	3.6	5.3	6.0	6.2	6.7
5	%Male	53.4	54.6	55.1	55.1	54.9	55.7	56.2	56.6	56.5
6	%Black	19.4	19.3	19.2	19.8	20.1	19.8	20.2	20.3	20.8
7	Average antipsychotic RX paid	586	791	893	937	1174	1867	2294	2562	2854
8	Average other RX paid	671	686	654	775	925	1070	1259	1491	1760
9	Average schizophrenia IP/OP paid	4049	4458	3973	3931	3834	4250	4504	4467	4898
10	Average other mental health IP/OP paid	1811	1886	1573	1593	1560	1649	1680	1739	1970
11	Average all other IP/OP paid	2187	2070	2122	2266	2401	2346	2590	2456	2621
12	Average Medicaid expenditures	9304	9892	9215	9502	9895	11182	12326	12714	14103
13	%Any Risperdal	0.0	13.0	12.3	14.1	17.2	22.8	25.8	30.4	32.8
14	%Any Zyprexa	0.0	0.0	0.0	1.9	15.8	32.7	36.6	39.1	39.9
15	%Any Seroquel	0.0	0.0	0.0	0.0	0.3	4.9	9.4	13.0	17.1
16	%AnyRZS	0.0	13.0	12.3	15.1	29.3	49.7	58.1	64.7	69.0
17	%Other antipsychotic	76.7	81.7	78.1	76.5	72.9	66.6	60.1	54.6	49.1
18	%Any antipsychotic	76.7	83.2	81.1	80.7	81.6	84.9	86.2	87.1	86.7
19	Any hospitalization	32.4	34.0	34.1	33.9	32.6	33.5	34.2	34.7	34.5
20	Average hospital days	6.7	7.5	7.4	7.2	7.3	7.4	7.5	7.7	7.9
21	Any LTC/ICF	8.3	7.5	6.8	7.1	7.7	7.8	7.3	7.7	7.7
22	Average LTC/ICF days	20.0	18.7	16.7	17.9	19.3	19.3	17.8	18.1	18.6
23	Any inpatient care	36.8	37.8	37.5	37.5	36.3	37.4	37.6	38.0	37.9
24	Average inpatient days	26.7	26.3	24.1	25.1	26.5	26.6	25.4	25.8	26.5
25	%Any diabetes	7.29	5.92	6.62	7.51	8.30	8.30	8.99	9.87	10.86
26	%Any hyperlipidemia	3.69	2.91	3.57	5.17	5.80	5.10	5.42	6.61	7.24
27	%Any abnormal weight/obese	2.11	1.55	1.64	1.09	1.60	1.49	1.76	1.85	1.73
28	%Any Tardive dyskenesia	0.65	0.71	0.80	1.27	1.07	0.53	0.44	0.48	0.43
29	%Any Parkinsonian symptoms	0.81	0.48	0.47	0.60	0.71	0.41	0.61	0.51	0.63
30	%Other EPS	0.83	0.74	0.74	1.07	0.87	0.69	0.65	0.65	0.69
31	%Die this year	1.40	1.20	1.46	1.26	1.28	1.37	1.23	1.28	1.33
32	%Die this or next year	3.14	2.96	3.18	2.84	3.10	2.93	2.98	3.04	–
33	%Leave, other	2.72	2.86	3.07	2.92	3.04	2.60	2.78	2.41	–
34	Number of observations	12741	12114	12333	13578	14081	13329	13186	13481	14083

Columns provide summary statistics for Medicaid recipients with one or more schizophrenia claims in each year.

prescription for Risperdal in the sample was filled in late January of 1994. In the first quarter of 1994, there are 584 individuals in the sample who take Risperdal for the first time, with this number increasing to 878 in the second quarter. The number of new patients declines substantially in the next quarter, and is close to 200 per quarter for the next two years. Thus, the number of individuals in the sample with one or more Risperdal prescriptions in each quarter increases only gradually during this period (Fig. 2) after the initial increase in early 1994. The first Zyprexa prescription appears in the Medicaid data in early October of 1996, shortly after the FDA approval in September of that same year. As a result of this, there is a significant increase in the number of individuals taking either drug for the first time,
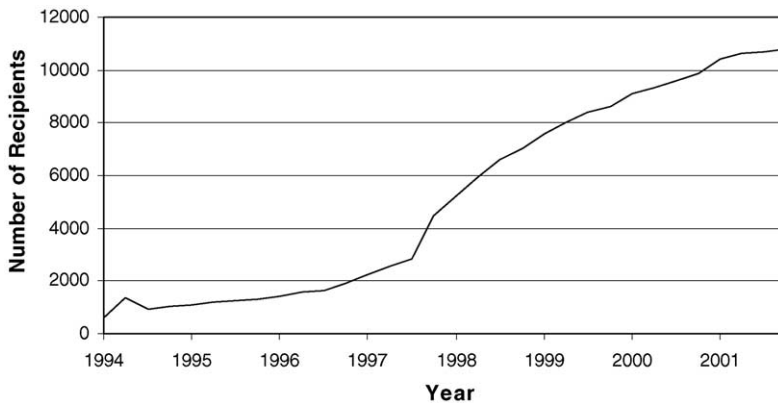
Fig. 2. Number of patients taking Risperdal, Zyprexa, or Seroquel.

which grows to 457 by the third quarter of 1997. And as Fig. 2 demonstrates, there is a slight acceleration in trend in the number of individuals with a current prescription for a second-generation drug.

A much sharper break in trend occurs in the fourth quarter of 1997. As Fig. 1 and Table A.1 demonstrate, the number of Medicaid recipients in the sample taking a second-generation drug for the first time increases from 457 to 1513, with the number of new entrants remaining above 1000 for the next three quarters. This increase was mainly caused by a state regulation that eased restrictions on prescribing second-generation antipsychotics. This increase in the number newly taking a second-generation antipsychotic translated into a sharp break in trend in the number of people taking one of the three drugs in each quarter, which more than doubled from 2849 to 5950 in just three quarters.

4.2. Did other health care spending decline?

This sharp and substantial break in trend in the use of these three second-generation drugs provides an excellent opportunity to gauge their short-term effect on several outcome variables of interest. If second-generation drugs reduced the demand for hospital care and other health care services, one would expect to detect a decline in spending on schizophrenia-related services in the fourth quarter of 1997 or shortly thereafter. Fig. 3 compares quarterly data for spending on antipsychotic drugs in the Medicaid sample with total (non-drug) spending for all care with a primary diagnosis of schizophrenia.

As this figure shows, there is no apparent decline in spending on schizophrenia-related services, which continued on a gradual upward trend following the sharp increase in spending on antipsychotic drugs. Because the number of individuals diagnosed with schizophrenia is not changing much during the study period, this trend looks almost identical if one instead summarizes costs on a per-patient rather than an aggregate basis. It is of course possible that other factors were changing in this same quarter, but the fact that there is no detectable decline in spending on schizophrenia-related services undermines the hypothesis that the new treatments substantially lowered other spending.
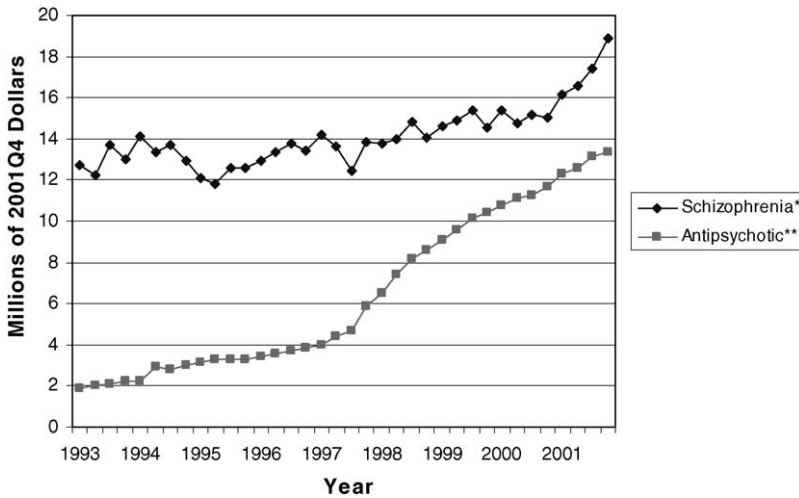
Fig. 3. Antipsychotic and (non-drug) schizophrenia spending. Spending on (✱) inpatient and outpatient care with a primary diagnosis of schizophrenia and (✱ ✱) antipsychotic drugs.

An alternative way to examine this issue is to compare the change in spending on antipsychotic drugs with the initial level of spending on schizophrenia-related inpatient and outpatient care. From the first quarter of 1993 until the final quarter of 2001, spending on antipsychotic drugs for individuals in the sample increased by 610%, from US$ 1.9 million to US$ 13.4 million,[15] with this growth almost entirely driven by the shift to the three new antipsychotic drugs. The US$ 11.5 million increase is just slightly smaller than the US$ 12.7 million in total (non-drug) schizophrenia spending in the first quarter of 1993. Thus, to a first approximation, the new drugs would have needed to lower inpatient and outpatient schizophrenia spending by more than 90% of the initial level to have reduced total health care spending.

A wider set of outcome variables is summarized in Table 2. Rows 7 through 12 provide annual averages for two categories of drug spending (antipsychotic and all other), three categories of non-drug spending (schizophrenia, other mental health, and all other diagnoses), and total spending for individuals diagnosed with schizophrenia in each year. Consistent with the quarterly data described above, there is no decline in average spending on inpatient or outpatient care in the latter half of the study period. If anything, it appears that there is a trend increase in average inpatient and outpatient spending, which actually declined by 3.1% from 1993 to 1997 but then increased by 21.7% during the subsequent four years. As a result of this increase and the accompanying growth in pharmaceutical expenditures, the growth rate of Medicaid spending for individuals diagnosed with schizophrenia increased from just 1.6% per year from 1993 to 1997 to a 9.3% annual rate during the 1997–2001

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[15] This increase is larger than the one implied by Table 2 because it considers spending for those diagnosed with schizophrenia in any year, while Table 2 only includes spending for individuals with a diagnosis in a particular year.

period. This strongly suggests that the diffusion of second-generation antipsychotics, which accelerated beginning in the last quarter of 1997, has substantially increased health care spending for individuals diagnosed with schizophrenia.

Rows 13 through 18 summarize changes in the utilization of antipsychotic drugs in the sample of schizophrenia patients. As row 16 demonstrates, nearly 70% were taking Risperdal, Zyprexa, or Seroquel in 2001. This increase in the utilization of second-generation drugs coincided with a much smaller increase in the utilization of any antipsychotic treatment, with 77% of schizophrenia patients taking one or more antipsychotic prescriptions in 1993 and this number increasing to 87% by the end of the study period. It, therefore, appears that most of the individuals taking Risperdal, Zyprexa, or Seroquel would otherwise be taking a first-generation antipsychotic rather than no drug treatment.

Rows 19 through 24 list average measures of inpatient utilization among individuals in the schizophrenia sample. The first two variables summarize hospital utilization while the next two describe the use of intermediate or long-term care facilities. As the final two rows demonstrate, the use of inpatient care did not change substantially during the study period. In 1993, approximately 37% of individuals diagnosed with schizophrenia spent one or more days in a hospital or long-term care facility and this fraction increased slightly to 38% by 2001. Similarly, the average number of inpatient days remained virtually unchanged, declining from 26.7 to 26.5. Similar trends emerge if one examines inpatient care for schizophrenia separately, with very little change during the nine-year study period.

Rows 25 through 30 examine changes in the prevalence of two sets of side effects that previous studies suggest may be affected by the use of second-generation antipsychotics. To estimate the prevalence of each condition, I simply calculate the fraction of individuals with one or more inpatient or outpatient claims with a primary diagnosis of each illness.[16] This approach is admittedly imperfect, as some individuals may have a certain illness but it may not be coded on a claim. The trends summarized in Table 2 suggest that the prevalence of diabetes and related illnesses have increased substantially during the study period. As rows 28 through 30 show, the measured prevalence of tardive dyskenesia and other extrapyramidal symptoms declines substantially beginning from 1997 to 1998. These trends are consistent with the findings from earlier studies, that second-generation drugs reduce the prevalence of EPS but may actually increase the prevalence of diabetes and related illnesses.[17]

The final three rows summarize exit rates from the Medicaid program for individuals diagnosed with schizophrenia. The first two rows summarize the fraction of individuals diagnosed with schizophrenia during the year who died during the current year or in the subsequent year. There is no obvious change in this mortality rate from 1997 forward. Interestingly, the rate at which individuals exit the program for other reasons does appear to

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[16] The diagnosis codes used for each of these side effects are as follows: diabetes (250, 362, 3572, 6480, 36,641), hyperlipidemia (272), abnormal weight gain (783, 278), tardive dyskenesia (33,382), Parkinsonian symptoms (332), and other EPS (333 excluding 33,382).

[17] It is worth noting that the prevalence of diabetes, hyperlipidemia, and abnormal weight gain did increase among other Medicaid recipients as well. But a comparison of changes in the schizophrenia sample with other Medicaid recipients that controls for age, gender, race, and other factors demonstrates that the increase has been significantly greater for schizophrenia patients. Because of space limitations, these results are not reported here.

decline substantially following the sharp increase in the use of second-generation drugs. If these drugs increased the rate at which individuals returned to the workforce and increased their earnings, one would actually expect the opposite effect.

The statewide trends summarized in this section shed some light on the effect of second-generation antipsychotic drugs. Most strikingly, the absence of a decline in spending on other types of medical care following the sharp increase in the fraction taking Risperdal, Zyprexa, or Seroquel undermines the hypothesis that the new drugs to some extent paid for themselves.

5. Variation across geographic areas in the diffusion of second-generation antipsychotics

One limitation of the analysis from the preceding section is that other factors may have been changing at the same time that the utilization of second-generation drugs exhibited a sharp increase. If these other factors also influence outcome variables of interest, then an examination of trends could provide a misleading picture of the effect of the new treatments. In an effort to control for this potential source of bias, the current section exploits variation across areas in the rate at which Risperdal, Zyprexa, and Seroquel diffused. As previous researchers have noted, there exist substantial differences across geographic areas in the use of health care treatments that cannot be explained by health differences alone (Skinner and Wennberg, 2000). If similar variation exists for second-generation drugs, one can investigate whether areas in which the new treatments penetrated relatively quickly had significantly different changes in outcomes variables of interest by estimating specifications of the following type:

$$\Delta Y_{zt} = \alpha + \beta \Delta X_{zt} + \gamma \Delta \text{AnyRZS}_{zt} + \mu_z + \lambda_t + \varepsilon_{zt} \qquad (2)$$

In this equation, z indexes geographic areas and t indexes time periods, while ΔY_{zt}, ΔX_{zt}, and $\Delta \text{AnyRZS}_{zt}$ represent changes in the outcome variable, other explanatory variables, and the use of the three new drugs, respectively, from period $t-1$ to period t in area z. The parameter γ captures the average change in Y that is associated with a one-unit change in the use of Risperdal, Zyprexa, and Seroquel.

If the variation in the use of the new treatments is not systematically related with unobserved factors that influence the outcome variable of interest and if the effect of second-generation drugs does not vary across individuals, then the parameter γ would provide an unbiased estimate for the effect of this treatment on the outcome variable Y. It is, of course, plausible that the variation across areas in the diffusion of the drugs is not strictly exogenous. For example, certain areas may exhibit a larger increase in the use of second-generation drugs simply because a larger fraction of their schizophrenia patients experience a decline or an improvement in health. If true and if these changes are not adequately captured in the ΔX_{zt} variables, then the parameter estimate for γ would be biased.

Recognizing that there is no way to rule out this type of endogeneity, I aim to minimize its potential effect by focusing on market areas with a large number of patients.

This reduces the likelihood that random changes in individual-level health would lead to substantial variation in the utilization of drug treatments. I consider the four-digit zip code rather than the county because these areas are much more similar in population within the state of California and more likely to approximate a health care market. I include the 70 four-digit zipcodes with 50 or more Medicaid schizophrenia patients in 1993 and then follow these same patients for the subsequent eight years.[18] The average distance from one Medicaid recipient to another within these four-digit zipcodes is 5.8 miles and the median distance is 4.1 miles.[19] I focus only on those diagnosed in 1993 to obtain a baseline of spending and utilization for each individual and thus reduce the likelihood of composition bias. Additionally, I pair each individual with their 1993 zip code because future residential decisions could be influenced by changes in treatment or in health.

And finally, I drop the 16% of Medicaid recipients in the sample with one or more months in a managed care plan during the nine-year study period because the utilization data will be incomplete for them.

In the first year that Risperdal was available, there was substantial variation across geographic areas in the probability that Medicaid-eligible schizophrenia patients used this drug. For example, 29% of the 149 patients in one four-digit zip code were using this drug, while less than 0.6% of the 180 patients in three low-utilization areas had one or more prescriptions filled for it. Of the 70 selected market areas with more than 50 schizophrenia patients, 18 had less than 5% utilization of this new drug while 11 had more than 15%. It is indeed implausible that this heterogeneity is entirely driven by differential health shocks. Much of it may be driven by differences in the *level* of health across areas, but by taking first-differences in the regressions I control for time-invariant differences across areas. Additionally, I include zip code-specific effects in one-half of the first-difference specifications, which controls for differential trends in spending, utilization, or health across areas.

In Table 3, I summarize the results from specifications analogous to (2) with variables defined at the four-digit zipcode-year level. Each regression controls for changes in the fraction of patients who are dually eligible for Medicare, the average number of eligible months, and the fraction of the initial 1993 sample that is still eligible for Medicaid. These specifications also include year fixed effects and control for changes in the age, gender, and race of schizophrenia patients.[20] The explanatory variable of interest is ΔAnyRZS, which is equal to the change in the fraction of individuals in the four-digit zipcode with one or more prescriptions for Risperdal, Zyprexa, or Seroquel.

As the results in the first column demonstrate, increases in the use of second-generation drugs are significantly positively related with changes in expenditures. In this column, the dependent variable is the change in the log of average Medicaid spending. The results suggest that a 10% point increase in the use of antipsychotic drugs is associated with a

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[18] A similar analysis at the county level would include just 24 counties with Los Angeles and San Diego together accounting for more than 50% of the observations. The maximum share for any four-digit zipcode is just 5.9%.

[19] I calculate these distances using the exact longitude and latitude of the center of each zipcode.

[20] Each regression includes 12 age–gender interactions (with age groups 0–17, 18–29, 30–39, 40–49, 50–64, and 65 plus) and four race variables (white, black, Hispanic, missing race).

Table 3
Area-level estimates of the effect of second-generation antipsychotics

	Δ log(total paid)		Δ Total paid		Δ %Hospitalized		Δ %EPS claim		Δ %w/Diab, etc. claim	
	1	2	3	4	5	6	7	8	9	10
Δ %AnyRZS	0.492*** (.117)	0.481*** (.125)	5383*** (1096)	4972*** (1154)	0.087* (.050)	0.087 (.055)	−0.014 (.016)	−0.014 (.017)	0.069* (.038)	0.071* (.041)
Δ %Medicare	−0.927*** (.343)	−0.944** (.378)	−8284*** (3213)	−7388** (3504)	0.002 (.148)	0.033 (.165)	−0.026 (.046)	−0.019 (.051)	0.032 (.111)	0.016 (.125)
Δ Average months	0.115*** (.025)	0.111*** (.027)	1064*** (232)	1011*** (246)	0.010 (.011)	0.012 (.012)	0.008*** (.003)	0.008*** (.004)	0.031*** (.008)	0.032*** (.009)
Δ %Remaining	0.155 (.283)	0.083 (.313)	258 (2649)	−206 (2901)	0.027 (.122)	0.028 (.137)	−0.001 (.038)	−0.005 (.042)	0.066 (.091)	0.086 (.103)
Year effects?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zip trends?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
R-squared	0.295	0.339	0.362	0.413	0.121	0.148	0.130	0.168	0.182	0.202
Number obs.	560	560	560	560	560	560	560	560	560	560

Dependent variables in each specification represent changes in average annual measures of spending, utilization, or health at the four-digit zip code level from 1993 to 2001. Individuals diagnosed with schizophrenia in 1993 are included in the regression and paired with their 1993 zip code through 2001. Specifications exclude individuals with any months in a Medicaid managed care plan and include only those four-digit zip codes with more than 50 people in 1993. %Any RZS equals one at the individual level if person has one or more Risperdal, Zyprexa, and/or Seroque scripts in the year and zero otherwise. Regressions are weighted by zip code's share of observations in each year. Specifications include year effects, 12 age × gender interactions, and four race indicator variables. Specifications summarized in the even-numbered columns include zip code-specific time effects.

  * Statistical significance at 10% level.

  ** Statistical significance at 5% level.

  *** Statistical significance at 1% level.

4.7% increase in average Medicaid spending.[21] The estimate is virtually identical when I include zipcode-specific fixed effects. The next two columns summarize the relationship with average Medicaid spending, and suggest that this increases by US$ 487 in response to a 10% point increase in the use of Risperdal, Zyprexa, or Seroquel. This would translate into an effect of approximately US$ 5000 per-patient shifted to one of the three second-generation drugs, which is within the range of estimates from the randomized study cited above (Rosenheck et al., 2003).

In the next two specifications, I investigate the relationship between changes in the use of second-generation drugs and the probability that an individual is hospitalized or admitted to a long-term care facility. If the new drugs reduce the use of inpatient care, one would expect to find a negative coefficient on the parameter of interest. Instead one finds the opposite, changes in the use of second-generation drugs are positively related with changes in the probability of staying one or more nights in a health care facility. Specifically, a 10% increase in the use of second-generation drugs is associated with a 0.87% increase in the fraction of schizophrenia patients who are hospitalized and this first estimate is significant at the 10% level. One concern with this estimate is that it may be driven by an omitted variable. For example, individuals may switch to a new drug after a hospitalization, which was itself caused by a change in their demand for medical care. To gauge the importance of this possible source of bias, I determine the date that each individual first took Risperdal, Zyprexa, or Seroquel (if ever) and explore how individuals' health care utilization changes in the days leading up to their first prescription by estimating specifications of the following type:

$$\text{ANYIP}_{jt} = \sum_{k=1}^{50} \text{PRE}(k)_{jt} + \text{FIRST}_{jt} + \sum_{k=1}^{50} \text{POST}(k)_{jt} \tag{3}$$

In this regression, ANYIP_{jt} is an indicator variable that is equal to one if individual j stayed overnight in a hospital or other health care facility on day t and zero otherwise. The variable FIRST_{jt} is equal to one if individual j's first prescription for a second-generation drug occurs on day t and zero otherwise. The PRE and POST variables are simply leads and lags for this day of the first treatment.[22] This regression also includes individual fixed effects to control for differences across patients in the use of inpatient care.

In the specifications summarized in Table 4, the unit of observation is the person-day. I use utilization data for the 50 days before and the 50 days after each individual's first prescription for a second-generation drug and thus have 101 observations for each individual. There are 22,613 individuals in the schizophrenia sample who take Zyprexa, Risperdal, or Seroquel at least once on or before November 11, 2001 (with this end date selected so that I would have 50 or more post days) and thus there are 2,283,913 person-day observations in each regression. The results summarized in column 1 suggest that there is a significant increase in the use of inpatient care in the days leading up to an individual's first prescription for one of these new drugs. Specifically, an individual is 9.2% points more likely to be in the

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[21] The analogous estimate from a county-level regression is quite similar at 0.500 with a standard error of 0.234.

[22] Thus, PRE(k) is equal to one k days before person j's first prescription and zero otherwise while POST(k) is equal to one k days after j's first prescription and zero otherwise.

Table 4
Utilization immediately before and after first RZS script

	Any inpatient care?	Any outpatient care?
Pre days 41–50	Omitted	Omitted
Pre days 31–40	0.0077*** (.0009)	0.0011 (.0008)
Pre days 21–30	0.0199*** (.0013)	0.0083*** (.0009)
Pre days 11–20	0.0432*** (.0016)	0.0148*** (.0010)
Pre days 06–10	0.072*** (.0020)	0.0329*** (.0013)
Pre days 02–05	0.0915*** (.0023)	0.0349*** (.0014)
Pre day 01	0.0843*** (.0023)	0.0514*** (.0020)
First script	0.0599*** (.0021)	0.0977*** (.0024)
Post day 01	0.0152*** (.0017)	0.0213*** (.0018)
Post days 02–05	0.0127*** (.0017)	0.0028*** (.0011)
Post days 06–10	0.0149*** (.0017)	0.0106*** (.0011)
Post days 11–20	0.0120*** (.0016)	0.0071*** (.0010)
Post days 21–30	0.0101*** (.0016)	0.0077*** (.0010)
Post days 31–40	0.0089*** (.0016)	0.0024*** (.0010)
Post days 41–50	0.0073*** (.0016)	0.0052*** (.0010)
Number of observations	2283913	2283913
Person effects?	Yes	Yes
R-squared	0.616	0.147

Specifications include 101 person-day observations for each of the 22,613 individuals in the sample with a Risperdal, Zyprexa, or Seroquel prescription by November 10, 2001. For each individual, the day of the first prescription, 50 days before this and 50 days after the first prescription are included. Dependent variable in each column is an indicator variable for whether person has inpatient or outpatient utilization on day t. Each specification includes person fixed effects and standard errors are clustered at the person level to account for serial correlation in the error term.

*** Statistical significance at 1% level.

hospital two to five days before the first prescription than they were 40 days earlier. The magnitude of the coefficient estimates declines quickly from just before to just following the first prescriptions, suggesting that individuals often fill their first prescription upon leaving the hospital.

The coefficient estimate of .092 from the person-day regression suggests that the two estimates of .087 from the zip code-year regressions are primarily driven by the increase in inpatient care preceding the first prescription for a second-generation drug. But the fact that the estimates are almost identical also suggests that, for the remaining 90% of individuals who were not hospitalized just days before their first prescription, there was not a substantial decline in the likelihood of being hospitalized.

In the next two columns of Table 3, I investigate whether the increase in the use of second-generation drugs was associated with a change in the measured prevalence of extrapyramidal side effects. In this regression, the dependent variable is equal to the fraction of patients in the four-digit zipcode with one or more Medicaid claims that has a primary diagnosis of one or more extrapyramidal side effects. In both cases, the coefficient estimate for the ΔAnyRZS variable is negative, though neither is statistically significant. In the final two columns I summarize the results from analogous specifications for diabetes, hyperlipidemia, and abnormal weight gain. The estimates for the ΔAnyRZS coefficient suggest that areas in which the drugs were taken up relatively rapidly did have greater increases in the fraction of

schizophrenia patients with one or more of these illnesses, and in both cases the estimates are significant at the 10% level. It, therefore, appears that while the new antipsychotic drugs may have reduced the prevalence of certain adverse side effects, their effects on health were not uniformly positive.

6. Individual-level estimates of the effect of second-generation antipsychotics

One limitation with the results from the previous section that use aggregate zip code-level data is that some of the differential use of these drugs across geographic areas appears to be driven by a change in individuals' health and thus in their demand for medical care. Specifically, almost 10% of individuals who initiate treatment for a second-generation drug are hospitalized just a few days before their prescription but were not in the hospital several weeks earlier. Thus, the coefficient estimates for the ΔAnyRZS variable will confound the actual causal effect of these drugs on the outcome variables of interest with the effect of this change in the demand for medical care.

In this section, I attempt to surmount this obstacle to identification with individual-level analyses that exploit variation across psychiatrists in their propensity to prescribe second-generation drugs. I use this variation to estimate the effect of second-generation drugs for the marginal patient and divide the sample into two distinct periods. The first consists of the period up through and including the third quarter of 1997. Until this time, the penetration of second-generation drugs was fairly gradual, as shown in Figs. 1 and 2. But beginning in the fourth quarter of 1997, the diffusion of second-generation drugs accelerated, with more individuals taking Risperdal, Zyprexa, or Seroquel for the first time in the subsequent nine months than in the preceding 45. This increase was likely driven by legislation enacted in 1997 that made it easier for psychiatrists and other physicians to prescribe the new drugs.

6.1. OLS estimates of the effect of second-generation antipsychotics on Medicaid spending

I begin by estimating OLS specifications that examine the relationship between Medicaid spending for individual j in period $t + \tau$ as a function of her spending and utilization in period t and an indicator for whether she takes a second-generation antipsychotic in period $t + \tau$:

$$\text{SPEND}_{j,t+\tau} = \alpha + \beta X_{j,t+\tau} + \theta \text{SPEND}_{jt} + \gamma \text{RZS}_{jt} + \lambda \text{UTILIZATION}_{jt} + \varepsilon_{jt} \quad (4)$$

In this equation, the variable RZS_{jt} is defined to equal one if individual j has one or more Risperdal, Zyprexa, or Seroquel claims in period t and zero otherwise. Following previous work (Manning et al., 1987), I take the log of Medicaid spending because health care expenditures are quite skewed to the right and this produces a distribution that is much closer to the standard normal. The parameter of interest in this equation is γ, which represents the average effect of the new treatments on the log of Medicaid spending. As emphasized above, the challenge for reliable estimation of this parameter is the endogeneity of treatment, individuals who take the drug may differ in unobservable ways from those who do not.

The 12 specifications summarized in Table 5 examine the relationship between the use of the new drug treatments and the log of Medicaid spending in the four years from 1994 to 1997. The sample includes the 9664 individuals from the 20% Medicaid sample who are at least 18 years old in 1993, have one or more schizophrenia claims (two or more if only outpatient) and 12 months of Medicaid eligibility in that year, and who have no months in a managed care plan from 1993 to 1997. Because I take the log of Medicaid spending, individuals with no spending in a year will not be included in the regressions.[23] Additionally, those who die or become ineligible for Medicaid will also not be included.

The first column summarizes results from a regression that controls for each individual's age, gender, race,[24] the number of Medicaid-eligible months in 1994, and the fraction of those months also covered by Medicare. The statistically significant estimate of .926 on the AnyRZS coefficient suggests that the use of Risperdal increased Medicaid spending in 1994, the first year that this drug was available. In transforming this into the implied dollar effect for each person, I account for heteroscedasticity and for deviations from the assumption of a normally distributed error term by using the smearing estimate developed by Duan (1983). Using this retransformation method, I estimate the median effect of Risperdal on Medicaid spending in 1994 to be US$ 5396 with the mean slightly lower at US$ 5244.

In the next column, I summarize the results from a specification that controls for the log of Medicaid spending in 1993. The addition of this one variable substantially increases the explanatory power of the regression, with the R-squared increasing from .094 to .524. The coefficient estimate of interest declines to 0.596 with the median effect on Medicaid spending falling by 46% to US$ 2921. The magnitude of this change suggests that failing to control for baseline spending, which to some extent captures the variation across individuals in illness severity, would bias the estimates. The inclusion of 15 measures of health care utilization[25] in 1993 in the third column reduces the point estimate further to .550, with the implied median effect falling to US$ 2769. Given the small standard errors on the estimate for AnyRZS, this parameter is quite precisely estimated, with the 95% confidence interval for the median effect ranging from US$ 2626 to US$ 2921.

This first set of results suggests that the inclusion of detailed pre-treatment information on both Medicaid spending and health care utilization for each individual reduces the bias that is present in specifications analogous to the one summarized in column 1. The next several columns replicate these first analyses for 1995, 1996, and the first three quarters of 1997. In every case, I use Medicaid spending and utilization data from 1993, a period when individuals could not have taken one of the three new second-generation drugs. Consistent with the results for 1994, the inclusion of 1993 Medicaid spending and utilization substantially lowers the point estimate for γ in each year. The implied median effect in the

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[23] Given that just 2–3% of the sample has zero spending in each subsequent year while eligible for Medicaid, excluding these observations should not be too problematic, though by dropping low-spenders from the "no treatment" group, it will bias down the estimate for the effect of the new drugs on spending.

[24] The regressions include 12 age–gender interactions (with age groups 0–17, 18–29, 30–39, 40–49, 50–64, and 65 plus) and four race variables (white, black, Hispanic, missing race).

[25] These measures include an indicator variable for whether or not an individual was hospitalized with a primary diagnosis of schizophrenia, the number of days that the person spent in the hospital with this diagnosis, and the number of days squared. Analogous measures are constructed for four other types of claims: antipsychotic drug claims, other drug claims, outpatient claims, and days spent in long-term care with a schizophrenia diagnosis.

Table 5
OLS estimates of the effect of second-generation antipsychotics on Medicaid spending: 1994–1997Q3

	log(total paid$_{94}$)			log(total paid$_{95}$)			log(total paid$_{96}$)			log(total paid$_{97Q1-Q3}$)		
	1	2	3	4	5	6	7	8	9	10	11	12
AnyRZS$_t$	0.927	0.596	0.551	0.921	0.660	0.617	0.922	0.697	0.656	1.016	0.795	0.757
	(.046)	(.033)	(.033)	(.047)	(.038)	(.038)	(.043)	(.036)	(.036)	(.037)	(.033)	(.032)
log(total paid$_{93}$)		0.737	0.683		0.649	0.582		0.568	0.487		0.511	0.428
		(.008)	(.011)		(.009)	(.012)		(.010)	(.013)		(.010)	(.013)
Medicare fraction$_t$	−0.475	−0.151	−0.203	−0.536	−0.288	−0.388	−0.399	−0.194	−0.251	−0.309	−0.128	−0.178
	(.031)	(.023)		(.032)	(.026)	(.026)	(.031)	(.027)	(.027)	(.031)	(.027)	(.027)
Eligible months$_t$	0.130	0.165	0.160	0.114	0.147	0.141	0.146	0.162	0.158	0.202	0.227	0.226
	(.011)	(.008)	(.008)	(.010)	(.008)	(.008)	(.010)	(.009)	(.009)	(.016)	(.014)	(.014)
R-squared	0.094	0.524	0.541	0.099	0.420	0.444	0.107	0.363	0.390	0.135	0.347	0.372
Utilization controls?	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
#Observations	9492	9492	9492	9053	9053	9053	8642	8642	8642	8216	8216	8216
#No longer eligible	0	0	0	391	391	391	815	815	815	1195	1195	1195
#With zero spending	172	172	172	220	220	220	207	207	207	253	253	253
Median effect	5396	2921	2769	4527	2674	2435	4571	3608	3230	4262	3270	2953

Sample includes the 9664 individuals eligible for Medicaid for 12 months in 1993, with one or more (two or more if only outpatient) schizophrenia claims in that year, who are eligible for at least one month in 1994, and who have zero months in a managed care plan from 1993 through the third quarter of 1997. Dependent variable in each column is equal to the log of Medicaid spending in a certain year, with the final measure including spending for just the first three quarters of 1997. All regressions include 12 age × gender interactions and four race indicator variables. Specifications in columns 3, 6, 9, and 12 include 15 controls for hospital long-term care, outpatient, and prescription drug utilization (with any, #days or claims, and #days or claims squared). The number of observations declines from one year to the next because individuals die, become ineligible for Medicaid, or have no spending in the year.

specification with all of the control variables remains fairly stable overtime, ranging from a low of US$ 2435 in 1995 to a high of US$ 3230 in 1996.[26]

In Table 6, I estimate a similar set of specifications for the second half of the nine-year study period. I focus on the period from the fourth quarter of 1997 forward, a time when the diffusion of second-generation drugs accelerated rapidly. I include individuals diagnosed with schizophrenia at some point during the 12 months prior to this break in trend and exclude individuals with one or more prescriptions for a second-generation drug during that time period. Using the fourth quarter of 1996 through the third quarter of 1997 as my baseline year, I estimate a set of specifications analogous to those presented in Table 5 for the four years from 1998 through 2001. Because it includes expenditure data for the last quarter of 1997, the spending data for 1998 include five quarters of information.

Consistent with the results from the previous table, the findings here suggest that the use of the new treatments was associated with a substantial increase in Medicaid spending, with the estimates for γ declining in every case when pre-treatment spending and utilization data are included. The estimated effects are substantially larger during this period and increase over time. For example, the estimate for the median effect of the new treatments on Medicaid spending in the third and final column for each year increases from a low of US$ 5055 in 1998 to a high of US$ 7011 by 2001. This trend could be partially driven by changes in the characteristics of patients taking the drug, as the effect of the new treatments may vary across individuals. Additionally, average spending on antipsychotic drugs for individuals taking Risperdal, Zyprexa, or Seroquel is increasing during this period. Given that AnyRZS is an indicator variable and thus does not capture increases in the intensity of treatment, one would expect an increase from one year to the next if the effect on other health care spending remained constant.

Even with detailed information on spending and health in a pre-treatment year, however, it is possible that treatment decisions are correlated with unobservable factors that also influence the outcome variable of interest. This motivates a search for a source of variation in treatment decisions that is unlikely to be driven by a change in an individual's health.

6.2. Variation across psychiatrists in the use of second-generation antipsychotics

As previous researchers have noted, there is substantial variation across physicians in prescribing patterns even after controlling for differences in patient mix (Hellerstein, 1998). In this section, I aim to exploit this variation when estimating the effect of Risperdal, Zyprexa, and Seroquel on Medicaid spending. I begin by pairing each Medicaid-eligible individual diagnosed with schizophrenia during the 1993 calendar year with the psychiatrist they visited during that year.[27] By constructing the sample in this way, I exclude schizophrenia patients who did not visit a psychiatrist in 1993 or who visited a psychiatrist without an

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[26] Given that the 1997 specifications include just three quarters of spending, the estimate of US$ 2953 for that nine-month period suggests that the effects were largest in this year.

[27] I choose the psychiatrist that individuals visited before they could have taken one of the three drugs to reduce a potential source of bias. Specifically, it is plausible that a patient would, in response to a change in health, seek out a certain psychiatrist because of his willingness to prescribe a certain treatment. I pair individuals who visited multiple psychiatrists with the one they consulted closest to the last day of 1993.

Table 6
OLS estimates of the effect of second-generation antipsychotics on Medicaid spending: 1998–2001

	log(total paid$_{97Q4-98}$)			log(total paid$_{99}$)			log(total paid$_{00}$)			log(total paid$_{01}$)		
	1	2	3	4	5	6	7	8	9	10	11	12
AnyRZS$_t$	0.877	0.648	0.665	0.971	0.808	0.818	1.055	0.909	0.906	1.076	0.961	0.951
	(.030)	(.021)	(.021)	(.029)	(.023)	(.023)	(.028)	(.024)	(.024)	(.029)	(.024)	(.024)
log(total paid$_{96Q4-97Q3}$)		0.730	0.691		0.627	0.570		0.566	0.499		0.537	0.474
		(.008)	(.011)		(.009)	(.013)		(.010)	(.014)		(.010)	(.014)
Medicare fraction$_t$	−0.379	−0.189	−0.230	−0.350	−0.200	−0.248	−0.312	−0.185	−0.234	−0.336	−0.214	−0.264
	(.030)	(.022)	(.021)	(.030)	(.024)	(.024)	(.030)	(.025)	(.025)	(.031)	(.026)	(.026)
Eligible months$_t$	0.112	0.138	0.128	0.134	0.160	0.151	0.126	0.145	0.139	0.131	0.145	0.139
	(.009)	(.006)	(.006)	(.011)	(.009)	(.008)	(.010)	(.009)	(.008)	(.011)	(.009)	
R-squared	0.153	0.576	0.593	0.181	0.489	0.511	0.209	0.456	0.477	0.222	0.449	0.473
Utilization controls?	No	No	Yes	No	No	Yes	No	No	Yes	No	No	Yes
#Observations	8002	8002	8002	7585	7585	7585	7292	7292	7292	6984	6984	6984
#No longer eligible	0	0	0	424	424	424	725	725	725	1032	1032	1032
#With zero spending	167	167	167	160	160	160	152	152	152	152	152	152
Median effect	6417	4902	5055	5648	5417	5520	6510	5997	5957	7363	7122	7011

Sample includes individuals eligible for Medicaid for 12 months from 1996Q4 to 1997Q3, with one or more (two or more if only outpatient) schizophrenia claims; in that year, with no claims for Risperdal, Zyprexa, or Seroquel during that 12-month period, and who are eligible for at least one month in 1997Q4–1998Q4. Dependent variable in each column is equal to the log of Medicaid spending in a certain year, with the first measure including spending for the five quarters from 1997Q4 to 1998Q4. All regressions also include 12 age × gender and four race dummy variables. Specifications in columns 3, 6, 9, and 12 include 15 controls for hospital, long-term care, outpatient, and prescription drug (antipsychotic and all other) utilization (with any, #days or claims, and #days or claims squared). The number of observations declines from one year to the next because individuals die, become ineligible for Medicaid, or have no spending.

identifier in 1993. Of the 9664 individuals diagnosed with schizophrenia and used in the Table 5 specifications, more than 47% have a paid claim to a psychiatrist with a provider ID.[28]

Using utilization data from 1993 for the sample of schizophrenia patients who visited a psychiatrist at least once, I start by predicting the probability that each individual would take a second-generation drug by estimating linear probability models of the following type:

$$\text{RZS}_{j,94} = \alpha + \beta X_{j,94} + \theta \text{SPEND}_{J,93} + \lambda \text{UTILIZATION}_{j,93} + \varepsilon_{j,94} \tag{5}$$

In this specification, the dependent variable is equal to one if the individual has one or more prescriptions for a second-generation antipsychotic in the year and zero otherwise. This specification includes the same demographic, spending, and utilization controls defined above. Using the results from this regression, I predict the probability that each individual took a second-generation drug in 1994. For each patient–psychiatrist pair, I then calculate the difference between the actual fraction of the psychiatrist's other patients who take the drug and the fraction one would have predicted based on their baseline characteristics. Specifically, I calculate the psychiatrist effect Z_{jk} for patient j as follows:

$$Z_{jk} = \frac{\left(\sum_{i=1}^{N_k} S_{i,k,94} - S_{j,k,94}\right) - \left(\sum_{i=1}^{N_k} \hat{S}_{i,k,94} - \hat{S}_{j,k,94}\right)}{N_k - 1} \tag{6}$$

with k indexing the psychiatrist for patient j and N_k equal to the total number of patients for psychiatrist k. In this equation, $S_{i,k,94}$ is set equal to one if patient i of doctor k takes a second-generation drug in 1994 and zero otherwise. The variable $\hat{S}_{i,k,94}$ represents patient i's predicted probability from regressions similar to (5) above. I exclude patient j's realized and predicted treatment from this calculation to avoid a mechanical relationship between j's treatment variable and the psychiatrist effect. This index is constructed so that psychiatrists with relatively high values for this variable are intensive users of the new drug treatments while their counterparts with low values tend not to use the new drug. It is important to emphasize that this psychiatrist effect controls for differences in patient characteristics, as much of the variation in the actual fraction taking the drug may simply be driven by differences across physicians in patient severity.

I next use this psychiatrist effect as an instrumental variable to predict treatment decisions for schizophrenia patients in 1994 and the subsequent three years. The identifying assumption of this approach is that, conditional on each patient's Medicaid spending, utilization, and other characteristics in 1993, psychiatrists only influence Medicaid spending in subsequent years through an effect on the use of second-generation drugs. Though some

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[28] These individuals do systematically differ from those patients without a visit, with average spending and utilization that is substantially higher. For example, more than 28% of the Medicaid recipients who visited a psychiatrist were hospitalized in 1993 with a primary diagnosis of schizophrenia while just 10% of their counterparts were hospitalized with a schizophrenia diagnosis during the same period. A large fraction of the remaining 53% did visit a psychiatrist but their provider did not have an identifier in the claims data. The reason for this is administrative, psychiatrists paid with Medicaid Short-Doyle funds are not identified, only the provider county is listed for these psychiatrists.

psychiatrists may be more intensive users of other types of medical care and this may be correlated with their propensity to use second-generation drugs, the pre-treatment controls for spending and utilization should at least to some extent control for this. The main advantage of using predicted rather than actual treatment as an explanatory variable is that it is unlikely to be driven by a change in an individual's own health.

If psychiatrists did not differ in their prescribing patterns, then Z_{jk} should not be significantly related with individual treatment decisions. But as the results presented in the first-stage row of the first four columns of Table 7 demonstrate, this psychiatrist effect is significantly positively related with individual-level treatment decisions, with t-statistics ranging from 7.3 to 14.0.[29] In these regressions, I include only the 77 psychiatrists with 15 or more patients in 1993.[30] Patients with psychiatrists who are intensive users of second-generation drugs, after controlling for the characteristics of the other patients, are significantly more likely to take Risperdal, Zyprexa, or Seroquel than their counterparts with low-intensity psychiatrists. Not surprisingly, the predictive power of this psychiatrist effect declines over time, with its coefficient falling from .822 in 1994 to .566 by 1997.

In the preceding rows of the same four columns of this table, I summarize the instrumental variable results from specifications that explain the log of Medicaid spending in each year as a function of predicted treatment and the 1993 spending and utilization measures. In every case, the estimated effects are positive, and these estimates are statistically significant in 1995 and 1996. The magnitude of the estimates and the implied median effects are similar to the ones from the corresponding OLS specifications though the standard errors using this method are substantially higher.

I replicate these results in the next four columns for the second part of the study period. Here, I take the last quarter of 1996 and the first three quarters of 1997 as the base period and pair patients with one of the 61 psychiatrists that has more than 15 patients during that period. Consistent with the OLS results, the estimated effects on Medicaid spending are larger during this high-diffusion period than the ones for the early period. Additionally the estimates increase over time, perhaps because the characteristics of the marginal patient or the intensity with which he/she is treated are changing over time. This seems plausible given that just 15% of the sample was taking a second-generation drug in 1996 whereas nearly 70% were by 2001. Once again, the IV estimates are similar to, but typically larger than, the corresponding OLS estimates.

Taken together, the OLS and IV specifications summarized in this section consistently demonstrate that the shift to second-generation antipsychotic drugs increased Medicaid spending.[31] The magnitude of the estimates increases over time, suggesting that the effect for the marginal patient varies as the drugs diffuse to a larger fraction of schizophrenia patients. Additional work is clearly needed to explore how the effect of second-generation

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[29] Standard errors are corrected to account for correlation in the error term within psychiatrist groups given that Z_{jk} is essentially varying at the psychiatrist level rather than at the individual patient level.

[30] This is actually a strong restriction because I am using a 20% sample and this essentially requires a psychiatrist to have 75 Medicaid patients in 1993 to be included in the estimation. More precision could no doubt be obtained with a 100% sample though the Department of Health Services unfortunately only makes a 20% sample available.

[31] In a companion set of results, not summarized here because of space limitations, IV estimates of the effect of the drugs on the prevalence of adverse side effects were imprecisely estimated and typically insignificant.

Table 7
IV estimates for the effect of RZS on Medicaid spending: 1994–2001

	log(total paid)							
	1994	1995	1996	1997	1998	1999	2000	2001
AnyRZS$_t$	0.351	0.854**	0.955*	0.667	1.116***	1.148***	2.235***	1.881**
	(.293)	(.366)	(.517)	(.434)	(.744)	(.396)	(.775)	(.744)
log(total paid$_{93}$)	0.697***	0.605***	0.491***	0.457***				
	(.023)	(.022)	(.026)	(.027)				
log(total paid$_{96Q4\text{-}97Q3}$)					0.655***	0.556***	0.453***	0.506***
					(.044)	(.038)	(.039)	(.048)
Medicare fraction$_t$	−0.187***	−0.318***	−0.23***	−0.105***	−0.261**	−0.251***	−0.268***	−0.264***
	(.050)	(.058)	(.065)	(.061)	(.050)	(.054)	(.068)	(.067)
Eligible months$_t$	0.150***	0.146***	0.181***	0.197***	0.122***	0.147***	0.099***	0.112***
	(.025)	(.026)	(.022)	(.046)	(.029)	(.028)	(.030)	(.047)
First-stage estimate	0.782***	0.545***	0.516***	0.520***	0.652***	0.481***	0.324***	0.335***
	(.056)	(.057)	(.063)	(.071)	(.078)	(.084)	(.087)	(.086)
#Observations	2295	2190	2088	1999	1561	1488	1430	1378
#Psychiatrists	77	77	77	77	61	61	61	61
Utilization controls?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Median effect	2480	3481	3232	4379	5666	5895	6984	8008

Sample for the 1994–97 regressions includes the individuals used in Table 5 with one or more visits to a psychiatrist in 1993 while the 1998–2001 sample includes the individuals used in Table 6 with one or more visits to a psychiatrist from 1996Q4 to 1997Q3. Additionally, the psychiatrist must have a provider ID and more than 15 patients from the sample in the base year. Dependent variable in each column is equal to the log of Medicaid spending in a certain year. The base year for the 1994–97 specifications is 1993, while for the 1998–2001 specifications, it is 1996Q4–1997Q3. First stage estimates for the physician effect are included. All regressions also include 12 age × gender interactions, four race dummy variables, and 15 variables to control for inpatient and outpatient care and for prescription drug utilization in the base year. Standard errors are clustered by psychiatrist. The number of observations declines from one year to the next because individuals die, become ineligible for Medicaid, or have no spending.

 * Statistical significance at 10% level.
 ** Statistical significance at 5% level.
*** Statistical significance at 1% level.

antipsychotics on health care spending varies across individuals and across drugs at a particular point-in-time.

7. Conclusion

During the last decade, government spending through the Medicaid program and in the U.S. generally on prescription drugs has increased at more than a 15% annual rate. Much of this increase was driven by a shift to new drugs, which tend to be more expensive than earlier drugs within the same therapeutic category. Previous research has suggested that new drugs may to some extent pay for themselves by reducing the need for other health care services. The findings presented in this paper, which uses three different identification strategies and a data set with more than 30,000 Medicaid-eligible schizophrenia patients, undermine this hypothesis for the one category of prescription drugs that accounts for more government spending than any other. Because of data limitations, the results for health outcomes are necessarily more speculative but suggest that while the drugs may have reduced the prevalence of extrapyramidal symptoms they have also increased the fraction of schizophrenia patients with diabetes. It is, therefore, not obvious that the net effect of the new treatments on health was sufficiently positive to justify the 610% increase in antipsychotic drug spending from 1993 to 2001.

If second-generation antipsychotics are not substantially better than the first-generation drugs that preceded them, what explains their much greater cost? Part of the explanation may stem from Medicaid's reimbursement formula, which essentially sets the price of a drug close to the non-Medicaid price. As the Medicaid market share increases, a profit-maximizing firm with patent protection would find it optimal to increase its price for non-Medicaid customers (Duggan and Scott-Morton, 2004). This is simply because the Medicaid program has a zero co-pay and thus a Medicaid recipient or the physician acting on the patient's behalf has little incentive to consider cost when choosing a treatment.

Whether the results presented here generalize to other categories of prescription drugs or to individuals with other types of health insurance is of course not obvious. The incentives for Medicaid recipients are not much different from those that exist in many private insurance plans, which often have a small co-pay that may differ slightly between brand and generic drugs. On the other hand, antipsychotics are very different from the typical drug category given that Medicaid accounts for the vast majority of spending on the drugs. But with the recent passage of a Medicare prescription drug benefit, the share of pharmaceutical spending accounted for by government programs will increase substantially in the upcoming years. Though drugs will be paid for differently under Medicare, Medicaid's experience with antipsychotics during the last decade may shed some light on what can occur when the government becomes the dominant purchaser for one category of prescription drugs.

Appendix A

See Table A.1

Table A.1
Series for Figs. 1–3

Year	Quarter	First	Current	Antipsychotic	Schizpaid
1993	1	0	0	1.88	12.72
1993	2	0	0	2.03	12.24
1993	3	0	0	2.08	13.69
1993	4	0	0	2.24	13.00
1994	1	584	584	2.26	14.10
1994	2	878	1342	2.97	13.33
1994	3	171	908	2.82	13.74
1994	4	205	1012	3.03	12.95
1995	1	206	1078	3.12	12.11
1995	2	228	1183	3.32	11.80
1995	3	195	1255	3.28	12.57
1995	4	201	1320	3.30	12.61
1996	1	227	1428	3.45	12.91
1996	2	253	1562	3.57	13.38
1996	3	204	1647	3.74	13.75
1996	4	335	1892	3.86	13.43
1997	1	400	2261	3.98	14.17
1997	2	404	2542	4.38	13.65
1997	3	457	2849	4.67	12.42
1997	4	1513	4459	5.89	13.82
1998	1	1154	5258	6.52	13.78
1998	2	1074	5950	7.39	13.98
1998	3	1045	6627	8.16	14.86
1998	4	902	7024	8.60	14.08
1999	1	905	7579	9.10	14.64
1999	2	840	8018	9.59	14.90
1999	3	839	8412	10.16	15.40
1999	4	643	8618	10.42	14.53
2000	1	776	9108	10.75	15.37
2000	2	637	9329	11.13	14.76
2000	3	685	9604	11.24	15.19

Table A.1 (*Continued*)

Year	Quarter	First	Current	Antipsychotic	Schizpaid
2000	4	621	9876	11.67	15.00
2001	1	625	10406	12.32	16.14
2001	2	574	10624	12.56	16.55
2001	3	476	10683	13.14	17.40
2001	4	467	10806	13.35	18.90

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