

Do New Prescription Drugs Pay for Themselves?

The Case of Second-Generation Antipsychotics

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Abstract

During the last several years, spending on prescription drugs in the U.S. increased at a 15% annual rate, with the \$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 need for hospitalizations and other costly 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.

1. Introduction

From 1996 to 2002, spending on prescription drugs in the U.S. grew at a 15% annual rate, with the \$178 billion in 2002 expenditures accounting for more than 11% of all health care spending in that year. Given this rapid expenditure growth, prescription drugs accounted for a disproportionate share of the increase in overall health care spending, which grew by a more modest 7% per year during this same period. The growth in pharmaceutical spending was primarily 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 within the same therapeutic category (NIHCM, 2002).

The growth in pharmaceutical spending has been similarly rapid within the federal-state Medicaid program, with Medicaid spending on prescription drugs increasing from \$12.3 billion in 1996 to \$29.6 billion in 2002.¹ State governments have differed in their response to the increase in spending, 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. While the stated goal of these policies has been to control Medicaid costs, the projections suggest that Medicaid pharmaceutical spending will increase by more than 14% per year from 2002 to 2004 (Kaiser, 2004).

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 choose an expensive drug over a much cheaper alternative even if he/she

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

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 total health care spending that would result if a patient were to choose one treatment over the other (Lichtenberg, 1996, 2001). For example, the more expensive prescription drug may deliver health benefits that reduce his/her need for hospitalizations or other costly health care services, potentially offsetting the cost difference between the two treatments. When considering the optimal policy, it would therefore be useful to know the effect of each possible treatment on both health care spending and health outcomes for potential patients. If more expensive drugs consistently pay for themselves or deliver health benefits that are sufficiently large to pass a cost-benefit test, then policies that discourage the use of expensive drugs may reduce social welfare.

In this paper, I investigate the effect of new prescription drugs on total Medicaid spending, health care utilization, and health outcomes. This question is inherently difficult given that drug treatment is not randomly assigned and there are approximately 25,000 drug-dosage combinations covered by the Medicaid program 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 \$3.73 billion on these drugs during the 2002 calendar year.

There have been substantial changes in the pharmacological treatment of psychotic illnesses during the past decade. Three drugs that were approved by the FDA and entered the market in the mid-1990s are now the most commonly prescribed treatments for individuals with psychotic illness. Risperdal, Zyprexa, and Seroquel are substantially more expensive than the first generation drugs that preceded them and were numbers one, two, and four, respectively, among all prescription drugs in terms of total 2002 Medicaid spending. These new antipsychotic medications were initially found to have fewer

² This 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. See Manning et al (1987) and Eichner (1997) for estimates of the effect of health insurance co-pays on health care utilization.

adverse extrapyramidal side effects (EPS) than the first-generation antipsychotics (Kerwin, 1994; Leucht et al, 1999) but recent studies suggest that the new drugs may increase the prevalence of diabetes and related illnesses (Casey and Zorn, 2001; Lindenmayer et al, 2001; Sernyak et al, 2002; Meyer, 2001).

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. While focusing on Medicaid alone prevents me from exploring whether the causal effects of interest vary by individuals' insurance status, the fact that approximately 75% of antipsychotic prescriptions are written for beneficiaries of this program suggests that this group is the most natural one to consider first. Additionally, there does not exist similarly detailed data for as long a time period for individuals with other types of insurance.

I construct the initial analysis sample by selecting the 37,369 individuals diagnosed with schizophrenia at some point between 1993 and 2001. 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 second-generation drugs. While antipsychotics are used to treat other mental illnesses, schizophrenia is the condition for which these drugs are most commonly prescribed, with the individuals in the analysis sample accounting for 60% of antipsychotic prescriptions in the full sample of more than 2.9 million Medicaid recipients.

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 drugs. 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 challenge for this study is that the Medicaid data will provide an incomplete picture of health for individuals with schizophrenia. To the extent that the drugs may influence dimensions of

health or quality-of-life that are not observable in the data, the estimated effects for health outcomes will necessarily be somewhat more speculative. Following previous research, I focus on the prevalence of adverse side effects when investigating whether the new drugs have improved health outcomes.

The 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 drugs 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 modest decline in the measured prevalence of tardive dyskinesia and other extrapyramidal symptoms but also with an increase in the prevalence of diabetes and related illnesses.

Of course, a trend analysis for just one geographic area suffers from the difficulty that factors other than antipsychotic treatments are changing over time, and these other changes may themselves be influencing the outcome variables of interest. To control for these potentially confounding factors, I next exploit variation across geographic areas in the rate at which second-generation drugs penetrate each market. 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 second-generation antipsychotics. 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 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 are consistent with those described above, suggesting that the shift to the new drugs has led to a substantial increase in Medicaid spending and an increase in the prevalence of diabetes.

Taken together, the findings presented in this paper suggest that the new antipsychotic drug treatments, which are approximately ten times more expensive than the first-generation drugs that preceded them, did not reduce spending on other types of medical care. This finding undermines the hypothesis that the new drugs to some extent “paid for themselves.” The findings for health outcomes are less clear-cut because there appear to be both positive (fewer extrapyramidal symptoms) and negative (higher prevalence of diabetes) effects of the drugs. Perhaps more importantly, the claims data do not provide full information on health or quality of life. Individuals may have experienced some improvement in cognitive functioning, for example, but this would not necessarily show up in Medicaid claims data. But coupled with the results from a recent study using much more detailed health and quality-of-life measures (Rosenheck et al, 2003), it is not obvious that the new drugs deliver benefits that are sufficient to justify the 610% increase in spending on antipsychotic drugs from 1993 to 2001.

Two questions remain given the results presented in this paper. First, if the net impact of second-generation antipsychotics on health is modest and there is little effect on other health care spending, why are Risperdal, Zyprexa, and Seroquel so expensive? One potential explanation is that the reimbursement formula used by Medicaid to determine the price for each drug may not work well when Medicaid accounts for 75% of the market.³ A pharmaceutical firm would, all else equal, charge a higher price for its product as the Medicaid market share increases because its customers will be price-inelastic (Scott-

³ The Medicaid formula sets its price equal to 90 – 95 percent of the average wholesale price, with this ratio varying across states (Kaiser, 2002).

Morton, 1998). Interestingly, the one therapeutic category (HIV antivirals) with an average price above the one for antipsychotics is the only other one with a Medicaid market share in excess of 50%.⁴

The second question is – do the results generalize to other categories of prescription drugs? As Lichtenberg (2001) notes, the effect of new drugs may vary substantially across therapeutic categories, and thus it is certainly possible that new drugs in other categories significantly lower total health care spending. Antipsychotics are clearly different from other categories of drugs because they are purchased almost exclusively by Medicaid, the Department of Veterans’ Affairs (DVA), and other government programs with zero co-pays. But the incentives in Medicaid are not much different from those in a typical private insurance plan, where co-pays are typically modest. Additionally, with the passage of the Medicare prescription drug benefit, it may soon be the case that government programs account for the majority of prescriptions in other therapeutic categories as well.

2. Background and Previous Research

Schizophrenia is a chronic and debilitating mental illness that afflicts nearly 2 million individuals in the U.S. It is characterized by a range of symptoms, including delusions, hallucinations, cognitive impairments, apathy, 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, thioridazine, or some other “first-generation” antipsychotic for the treatment of schizophrenia, though the adverse side effects commonly associated with these drugs prevented some patients from taking them. The most notable ones included muscle spasms, tremors, tardive dyskinesia, and other extrapyramidal side effects.

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; Melter et al, 1999). Though Clozaril was found to have serious side effects of its own that limited its use

⁴ Average prices for HIV antiviral and antipsychotic prescriptions were equal to \$404 and \$168, respectively, in 2001. The average price for all other drugs was equal to just \$48 (NIHCM, 2002).

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.

A. Previous Research

A number of previous studies have investigated the relationship between the use of second-generation antipsychotics and health care costs or utilization measures such as hospitalization rates. 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.⁵ An even larger body of research has examined the effect of second-generation antipsychotics on the prevalence of adverse side effects, including diabetes, abnormal weight gain, hyperlipidemia, and extrapyramidal symptoms (Gianfrancesco et al, 2002; Koro et al, 2002; Lund et al, 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 can lead to abnormal weight gain, diabetes, and hyperlipidemia.

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 federal DVA and randomized each person to the haloperidol or Zyprexa treatment groups. A wide set of outcome measures were considered, including cognitive functioning, quality of life, adverse side effects,

⁵ A related set of research has estimated price indices for the treatment of schizophrenia. For example, Frank et al (2003) use Medicaid data from two counties in the state of Florida to examine whether costs (the authors consider mental health costs only rather than total costs) for individuals with schizophrenia have changed after controlling for treatment decisions. This is of course a different question from the one posed here because changes in average costs conditional on a certain treatment can differ substantially from changes in average (unconditional) costs. Suppose, for example, that spending for schizophrenia patients with no treatment equals X , while for those with a certain treatment it equals $2X$, and that these potential outcomes do not vary across individuals or over time. If in period t the fraction of individuals taking the treatment is equal to 10% and this increases to 50% in the subsequent period, average costs would increase from $1.1X$ to $1.5X$ but average costs conditional on treatment would not have changed.

and health care spending. Individuals were followed for up to one year, with outcome measures obtained at 1.5, 3, 6, 9, and 12 months. 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 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, with this potentially increasing their risk for diabetes and related illnesses.

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 economics⁶ 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.

Second, most randomized studies have relatively small sample sizes with which it is difficult to obtain sufficient precision for a skewed outcome variable such as health care expenditures. The main reason for this is cost – randomized studies are very expensive to administer – and thus randomized studies that consider costs often have wide confidence intervals. A third limitation of most randomized studies is their focus on just two drugs. In 1993, before Risperdal, Zyprexa, or Seroquel were yet available, haloperidol was the most commonly prescribed antipsychotic. However, there were several other drugs that were used to treat schizophrenia, with some being prescribed almost as frequently as haloperidol. Thus among schizophrenia patients in this base year, a comparison of Zyprexa and haloperidol is most relevant for those who were taking haloperidol but perhaps not relevant for those

⁶ See, for example, many of the studies that estimate the return to schooling summarized in Card (2003).

taking a different first-generation drug. Similarly, Zyprexa accounts for less than half of second-generation prescriptions, and thus even if haloperidol is better than Zyprexa for certain patients, it is possible that they would choose Risperdal or Seroquel over haloperidol.

An additional limitation of randomized studies is that they are often tightly controlled. It is possible that individuals are much less likely to adhere to a certain 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 and final limitation with the randomized trials 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 forties who had recently been hospitalized were considered. Given that the effect of the drugs may vary with demographic characteristics and by prior utilization of medical care, it is important to consider individuals from other groups as well. Perhaps more importantly, individuals can choose not to participate in randomized trials. While the Rosenheck study successfully enrolled 309 individuals, there were 969 patients who refused to participate and another 561 whose clinicians would not allow them to. If the individuals who enroll in a randomized study are substantially different from those who choose not to participate then the estimates may not apply for this other group.⁷

B. Medicaid and the Market for Antipsychotic Drugs

From 1996 to 2002, Medicaid spending in the U.S. on prescription drugs increased by 141% from \$12.3 billion to \$29.6 billion. Growth in this service category far outpaced Medicaid spending on all other health care services, which increased by just 29% from \$164 billion to \$212 billion during this same period. Recent research suggests that the growth in pharmaceutical spending may have lowered total health care spending below what it otherwise would have been, as new prescription drugs may improve health and thus lower spending on other types of medical care (Lichtenberg, 1996, 2001).

⁷ One final issue with previous studies (both randomized and other) on costs, utilization, or the prevalence of adverse side effects is that a large number were funded by one of the three pharmaceutical companies that produce the new second-generation drugs. See, for example, Basson et al (2001), Casey (2000), Davidson (2001), Emsley (1999), Feifel (2000), Gomez et al (2000), Kornegay et al (2002), Malla et al (2001), McCombs et al (1999), Rascati et al (2003), and Rosenheck et al (2003).

The Food and Drug Administration classifies each drug that it approves into one of twenty major classes. Table 1 provides information on total Medicaid spending in the U.S. for each of these classes in 1996 and 2002. In both years, spending for drugs used to treat central nervous system (CNS) disorders was greater than for any other therapeutic category and Medicaid spending on just this one category of prescription drugs now exceeds all spending by the federal government on job training programs, which stood at \$6.7 billion in 2002 (Department of Labor, 2003).

Within the CNS therapeutic category, the two classes of drugs that account for the majority of prescriptions are antidepressants and antipsychotics. This first group includes drugs used to treat various forms of depression while drugs used to treat schizophrenia, bipolar disorder, and dementia are in the latter group. As Table 2 shows, these two categories accounted for more than 80% of the \$7.34 billion in Medicaid spending on CNS drugs in the U.S. in 2002. During the 1996-2002 period, real Medicaid spending on antipsychotic drugs grew at a 25% annual rate, with most of this expenditure growth explained by the increase from \$61 to \$171 in the average price of an antipsychotic prescription.

Although the number of antidepressant prescriptions filled for Medicaid recipients exceeded the corresponding number of antipsychotics, Table 3 demonstrates that the Medicaid market share is substantially greater for this latter category. In this table, I list the top three drugs for each of the two classes in 2002. Among antidepressants, Medicaid accounts for roughly 20% of total U.S. revenues, while the corresponding share for antipsychotics is close to 75%. Additionally, the top three selling antipsychotics were numbers one, two, and four in terms of total Medicaid spending among all prescription drugs in 2002⁸ and accounted for 88% of all Medicaid spending on antipsychotic drugs. Given that Medicaid accounts for the vast majority of antipsychotic prescriptions, the current study's focus on beneficiaries of this program is not as limiting as it might otherwise be.

3. The Medicaid Sample and the Diffusion of Second-Generation Antipsychotic Drugs

A. The Medicaid Claims and Eligibility Data

⁸ Number three was the antiulcerant Prevacid at \$670 million and number five was the cholesterol-reducing drug Lipitor at \$539 million.

To estimate the effect of second-generation antipsychotic drugs on health care spending, utilization, 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 sample of California residents with at least one month of Medicaid eligibility between January of 1993 and December of 2001. 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. 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 twelve months during the year and also contains month-by-month information on the individual's aid code, which indicates 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 Part A or Part 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 indicates whether each recipient is enrolled in a managed care plan and if so provides the plan number. Though the utilization data will be incomplete for most managed care recipients, a file with capitation rates by Medicaid aid code, plan number, and month can be used to calculate Medicaid managed care spending for them (Duggan, 2004).

In a typical year, the Medicaid claims data for the 20 percent sample contain more than 30 million claims. These include every fee-for-service payment made to hospitals, physicians, long-term care facilities, pharmacies, and other health care providers for 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 ten-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.

B. 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 schizophrenia. The data uses the ICD-9 classification system, and thus a diagnosis code that begins with the three digits 295 represents this mental illness. Prescription drug claims do not have a diagnosis code though virtually all of the inpatient and outpatient claims do. 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 percent 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 4 lists the ten most commonly prescribed antipsychotics in the full Medicaid sample in 1993 and in 2001,¹⁰ with the table providing both the number of prescriptions and the average amount spent per prescription. The number of units does vary across prescriptions, though the most common prescription provides a one-month supply. As the table shows, haloperidol was the most commonly prescribed antipsychotic in 1993, though it accounted for just slightly more than 20% of all antipsychotic

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

¹⁰ In 1993 approximately 59% of these prescriptions are written for individuals in the schizophrenia sample while in 2001 that number is slightly higher at 62%.

prescriptions in this base year. Eight years later the top selling drugs were Zyprexa and Risperdal, with Seroquel just slightly behind the second-generation drug Clozaril. These three new 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. Each of these three drugs was substantially more expensive than haloperidol and other first-generation drugs, and thus the shift to these drugs largely explains the fivefold increase in the average cost of an antipsychotic prescription during this period.

C. Defining the Causal Effect of Second-Generation Drugs

Before proceeding to the empirical analyses, it is useful to first define the causal effects of interest for this section and the subsequent ones. Define for schizophrenia 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 focuses attention on the difference across these three categories rather than within each category (or within a drug as the effect would likely vary with dosage). Additionally, it assumes that drug treatment in period t affects outcomes in period t but not in future periods. 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.

With these two simplifications in hand, the effect of a second-generation drug relative to no drug treatment for individual j in period t is equal to $\Delta_{jt0} = Y_{jt2} - Y_{jt0}$ and the corresponding effect relative to a first generation drug is simply $\Delta_{jt1} = Y_{jt2} - Y_{jt1}$. Both causal parameters are indexed by j and t to capture the fact that the effect may vary across individuals or within the same individual over time. These two parameters can be incorporated into the following equation for Y_{jkt} as follows:

$$(1) Y_{jt} = \alpha + \beta X_{jt} + \Delta_{jt0} * Second_{jt} + (\Delta_{jt0} - \Delta_{jt1}) * First_{jt} + \mu_j + \theta_t + \varepsilon_{jt}$$

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 decisions are not random. Individuals who take a second-generation drug are likely to differ in both observed and unobserved ways from their counterparts who take a first-generation drug or no drug at all.

The subsequent three sections aim to empirically estimate the effect of the shift to second-generation drugs on Medicaid spending, health care utilization, and health outcomes for individuals diagnosed with schizophrenia. No one of these methods is free from potential biases, though the fact that each one points in the same direction strengthens the findings.

4. Time-Series Trends in Spending, Utilization, and Health Outcomes

In 1993, no Medicaid-eligible schizophrenia patients in the state of California were taking Risperdal, Zyprexa, or Seroquel but by 2001 nearly 70% were. This shift coincided with a substantial increase in Medicaid antipsychotic drug spending. In this section, I summarize trends in average measures of Medicaid spending, utilization, and health for Medicaid recipients diagnosed with schizophrenia during this nine-year period. In doing this, I investigate whether these trends appear to be affected by sharp changes in the use of these three second-generation drugs. Each column of Table 5 includes average annual measures for more than 30 variables for those Medicaid recipients with one or more schizophrenia claims during each year. The number diagnosed with schizophrenia at least once during the year ranges from a low of 12,114 in 1994 to a high of 14,083 in 2001.

An obvious first concern with any examination of simple time-series trends is that the characteristics of individuals diagnosed with schizophrenia may change over time. The first six rows provide average characteristics for Medicaid recipients diagnosed with schizophrenia in each year. As is clear from the table, these averages remain fairly stable over time, though there are modest changes. For example, the fraction of schizophrenia patients who are male increases from 53.4% in 1993 to 56.5% by 2001, while the average age increases from 43.5 to 44.4 during this same period. Additionally, the

fraction of schizophrenia patients in the Medicaid sample who are dually eligible for Medicare falls from 44.0% in 1993 to 38.3% by 2001, with more than half of this decline occurring from 1993 to 1994. And finally, the fraction of individuals who are enrolled in a managed care plan during the year increases from 1.2% in 1993 to 6.7% by 2001. Utilization data will be partially incomplete for Medicaid recipients in a managed care plan, though 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 during the nine-year study period.

A. A Discontinuous Change in the Use of Second-Generation Antipsychotics

Figure 1A and Appendix Table 1 provide information on the number of individuals taking one of the three major second-generation drugs for the first time in each quarter.¹¹ The first prescription for Risperdal in the Medicaid data was written 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 Risperdal patients declines substantially in the next quarter, and hovers around 200 from the third quarter of 1994 through the third quarter of 1996. Thus the number of individuals in the schizophrenia sample with one or more Risperdal prescriptions in each quarter increases only gradually during this period (Figure 1B) 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 Risperdal or Zyprexa for the first time, with this number increasing to 457 by the third quarter of 1997. And as Figure 1B 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, however, occurs in the fourth quarter of 1997. As Figure 1A and Appendix Table 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

¹¹ A person can appear in this table only once – thus if he/she takes Risperdal in 1994 and Zyprexa in 1997, only the first of these would show up in this table.

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.

B. Did Other Health Care Spending Decline?

This sharp and substantial break in trend in the use of these novel antipsychotic treatments provides an excellent opportunity to gauge the short-term effect of second-generation drugs on several outcome variables of interest. If second-generation drugs do significantly reduce the number of hospitalizations, physician visits, or other health care services used by schizophrenia patients, one would expect to see a decline in spending on schizophrenia services in the fourth quarter of 1997 or shortly thereafter. Figure 2 compares quarterly data for total spending on antipsychotic drugs in the Medicaid sample with total spending for all inpatient and outpatient care with a primary diagnosis of schizophrenia.

But 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. Of course other treatment patterns or prices may have been changing in this same quarter, but the fact that there is no detectable change in spending on schizophrenia-related services undermines the hypothesis that the second-generation antipsychotics could plausibly have paid for themselves.

An alternative way to examine this issue is to compare the change in spending on antipsychotic drugs during the study period 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 schizophrenia sample increased by 610% - from \$1.88 million to \$13.35 million,¹² with this growth almost entirely driven by the shift to the three new antipsychotic drugs. The

¹² This 610% increase is somewhat larger than the increase implied by Table 2. The reason for this is that while Figure 2 includes spending on antipsychotic drugs in year *t* for individuals diagnosed with schizophrenia in some

\$11.47 million increase is just slightly smaller than the \$12.72 million in total schizophrenia spending in the first quarter of 1993. Thus to a first approximation the drugs would have needed to lower schizophrenia spending by 90% to be cost-neutral. Of course there are important limitations to this calculation¹³ but it helps to show how large the effect on utilization would need to be for these drugs to actually have lowered Medicaid spending.

A wider set of outcome variables is summarized in Table 5, though because of space limitations only annual measures are included here. Rows (7) through (12) provide average spending by category for Medicaid recipients diagnosed with schizophrenia in each year. In 1993, prescription drugs accounted for just 13.5% of total Medicaid expenditures, with this share increasing substantially to 32.7% by 2001. Schizophrenia services accounted for approximately half of total inpatient and outpatient spending for individuals diagnosed with schizophrenia in 1993, with the remaining spending almost equally divided between other mental disorders and services that were not for mental health.

Consistent with the quarterly data for schizophrenia spending described above, there is no apparent 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 total 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 to 2001 period. This strongly suggests that the diffusion of second-generation antipsychotics, which accelerated 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 among Medicaid recipients diagnosed with schizophrenia. As row (17) demonstrates, nearly 70% of

other year (but not year t), the summary statistics for each year in Table 2 only include information for individuals with a schizophrenia diagnosis in that year.

¹³ For example, it excludes spending on other types of medical care and ignores the changes in schizophrenia spending that would have occurred in the absence of these new drugs.

schizophrenia patients 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 76.7% of schizophrenia patients taking one or more antipsychotic prescriptions in 1993 and this number increasing to 86.7% by the end of the study period (with two-thirds of the increase occurring from 1993 to 1994). 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 among individuals diagnosed with schizophrenia has not changed 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, with this fraction increasing slightly to 38% by 2001. Similarly, the average number of inpatient days remained virtually unchanged, declining slightly from 26.7 to 26.5. Similar trends emerge if one instead 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 several different side effects that previous studies suggest may be affected by the use of second-generation antipsychotics. To estimate the prevalence of diabetes, for example, I simply calculate the fraction of individuals with one or more inpatient or outpatient claims with a primary diagnosis of this illness. This approach is admittedly imperfect, as some individuals may have a certain illness but it may not be diagnosed by a doctor or – even if it is diagnosed – the doctor may not code it on a claim. To the extent that the magnitude of this measurement error does not vary over time then these outcome variables should not provide a misleading picture, though it is worth keeping this in mind when examining trends here and interpreting the empirical results in the next sections.

A number of recent studies suggest that second-generation drugs may increase the prevalence of diabetes, hyperlipidemia, abnormal weight gain, and related illnesses (Casey and Zorn, 2001; Lindenmayer et al, 2001; Sernyak et al, 2002; Meyer, 2001). The trends summarized in Table 5 suggest that the prevalence of the first two illnesses has increased substantially during the study period.¹⁴ In the case of hyperlipidemia the increase appears to be more rapid in the early part of the period when the diffusion of the second-generation drugs was gradual, suggesting that the utilization of these drugs is not the driving factor behind the observed increase. In the case of diabetes the opposite is true. From 1993 to 1998 there is a 1.0% increase in the measured prevalence of diabetes but this trend accelerates during the next three years, increasing by approximately 2.6%. As rows (28) through (30) show, the measured prevalence of tardive dyskinesia and other extrapyramidal symptoms declines substantially beginning from 1997 to 1998. Consistent with the results from previous research, this suggests that the second-generation drugs did lower the prevalence of these adverse side effects.

The final three rows summarize exit rates from the Medicaid program for individuals diagnosed with schizophrenia. The first two columns summarize the fraction of individuals diagnosed with schizophrenia during the year who die 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 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.¹⁵

Taken together, the trends summarized in this section provide suggestive evidence regarding the effect of second-generation antipsychotic drugs. Of course, there are limitations to time-series analyses, as other treatment patterns may be changing over time and the characteristics of individuals diagnosed

¹⁴ The diagnosis codes used for each of these side effects are as follows: diabetes (250, 362, 3572, 6480, 36641), hyperlipidemia (272), abnormal weight gain (783, 278), tardive dyskinesia (33382), parkinsonian symptoms (332), and other EPS (333 excluding 33382). In the regressions that follow in the next two sections I group the first three conditions together into one variable (i.e. Any Diabetes, Hyperlipidemia, or Abnormal Weight Gain) and do the same for the latter three variables (Any EPS).

¹⁵ See Berndt et al (1998) for an estimate of the effect of anti-depressants on workplace performance.

with schizophrenia may also be changing. But the fact that there is virtually no change in average spending on other types of medical care following the discontinuous increases in the fraction taking a second-generation drug undermines the hypothesis that these new drugs paid for themselves.

5. Variation across Geographic Areas in the Diffusion of Second-Generation Antipsychotics

One important limitation of the analysis from the preceding section is that other factors may have been changing at precisely the same time that spending on second-generation drugs exhibited a sharp increase. If these other factors also influence Medicaid spending or other outcome variables of interest then an examination of trends in average outcomes for Medicaid recipients diagnosed with schizophrenia could provide a misleading picture of the effect of these new drug treatments. In an effort to control for this potential source of bias, the current section exploits variation across geographic areas in the rate at which the new antipsychotic treatments diffused. If these potentially confounding factors are changing similarly across areas or changes in them are unrelated to the rate at which the drugs diffuse to new areas, then this strategy will provide a more accurate picture of the effect of second-generation antipsychotics.

As previous researchers have noted, there exist substantial differences across geographic areas in the use of more expensive 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 antipsychotic treatments penetrated relatively rapidly have significantly different changes in outcome variables of interest from other areas while estimating specifications of the following type:

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

In this equation, z indexes geographic areas and t indexes time periods, while ΔY , ΔX , and ΔSecond represent average changes in the outcome variable, other explanatory variables, and the use of second-generation 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 second-generation antipsychotics.

If the variation in the use of second-generation antipsychotics 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_{jt} 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.¹⁶ I include the 70 areas with 50 or more Medicaid schizophrenia patients in 1993 and then follow these same patients for the subsequent eight years, pairing them with their 1993 zip code in every case. 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 initial zip code because future residential decisions could be influenced by changes in treatment or in health.¹⁷

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 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.

¹⁶ The county of Los Angeles, for example, includes more than 35% of all Medicaid patients living in one of the state's 58 counties, though the results presented below are similar if I use the county as the unit of observation.

¹⁷ For example, an individual might be admitted to an intermediate or long-term care facility.

Much of it may be driven by differences in the *level* of health across areas, but by including zip code-specific fixed effects in the regressions below I control for time-invariant differences across geographic areas. Additionally, I include zip code-specific time trends in one-half of the specifications, which allows me to control for the possibility that spending, utilization, or health is trending differentially across areas.

In Table 6 I summarize the results from specifications analogous to (2) with average outcomes defined at the four-digit zipcode-year level. Each specification explores whether increases in the use of second-generation drugs are significantly related with changes in spending, utilization, or health. Each specification controls for changes in the fraction of schizophrenia patients who are dually eligible for Medicare, the average number of eligible months, and the fraction of the initial sample that is still observed in the data. These specifications also include zip code and year fixed effects and control for changes in the age, gender, and race of individuals in each area from one year to the next. These average demographic characteristics could change if, for example, certain groups were differentially likely to die or become ineligible for Medicaid (thus appearing in year t but not in year $t+\tau$) than others.

As the results for the first specification demonstrate, increases in the use of second-generation drugs are significantly positively related with total Medicaid spending. In this specification the dependent variable is the change in the log of average Medicaid spending. The results suggest that a 10 percentage point increase in the use of antipsychotic drugs is associated with a 4.7% increase in average Medicaid spending. The estimate is virtually identical when I include zipcode-specific time trends. The next two specifications summarize the relationship with average Medicaid spending, and suggest that this increases by approximately \$500 in response to a ten percentage point increase in the use of Risperdal, Zyprexa, or Seroquel. This would translate into an effect of approximately \$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, 2003). The estimate is approximately 20% lower than the midpoint of their confidence interval, perhaps partly because they focus only on the most expensive of the three drugs (Zyprexa) while my specifications consider all three.

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 significantly 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 0.96% increase in the fraction of schizophrenia patients who are hospitalized. If properly estimated, this estimate implies that the second-generation drugs increase rather than reduce the utilization of other types of medical care.

One obvious concern with this estimate is that it may be driven by an omitted third factor that is influencing both the probability of hospitalization and the probability of initiating treatment with a second-generation drug. For example, individuals may switch to a new drug following a hospitalization, which was itself caused by a change in their demand for medical care. To gauge the potential importance of this source of bias, I determine the date that each individual first took a second-generation drug (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:

$$(3) ANYIP_{jt} = \sum_{t=T-1}^{T+N} PRE_{jt} + FIRST_{jt} + \sum_{t=T+1}^{T+N} POST_{jt} + \alpha_j + \varepsilon_{jt}$$

In this regression, $ANYIP_{jt}$ is an indicator variable that is equal to one if individual j stayed one or more nights 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. This regression also includes an individual fixed effect to control for differences across individuals in the average use of inpatient care.

In the specifications summarized in Table 7, the unit of observation is the person-day. I use utilization data for the fifty days before and the fifty 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 2283913 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 percentage points more likely to be in the hospital a few 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 .096 estimate from the zipcode-year regression is primarily driven by the increase in inpatient care preceding the first prescription for a second-generation drug. But the fact that the two estimates are almost identical also suggests that – for the remaining 90.8% of individuals who were not hospitalized just days before their first prescription – there was no decline in the likelihood of being hospitalized. Consistent with the time series results presented above, this finding suggests that the new antipsychotic drugs have not lowered the utilization of inpatient care.

In the next four specifications of Table 6, I investigate whether the increase in the use of second-generation drugs was associated with a change in the measured prevalence of certain side effects that have been linked to first or second-generation antipsychotics in previous research. For example, a number of studies have suggested the shift from first-generation drugs like haloperidol to second-generation drugs like Zyprexa has lowered the prevalence of extrapyramidal side effects. I investigate whether this is the case in columns 7 and 8 of Table 6. In this regression, the dependent variable is equal to the fraction of schizophrenia patients in the four-digit zipcode with one or more Medicaid claims that has a primary diagnosis of tardive dyskinesia, Parkinsonian symptoms, or some other extrapyramidal side effect.¹⁸ In

¹⁸ An alternative way to measure the prevalence of extrapyramidal side effects from this data would be to examine whether an individual is also taking one of the drugs used to treat EPS. The problem with this type of measure is

both cases the coefficient estimates on the %*Any R,Z,S* variable are negative, though neither is statistically significant. This is not surprising given the low mean of the dependent variable (.018) – even with the large number of observations there is not enough power to obtain adequate precision. But the direction of the estimates does suggest that the second-generation drugs have led to a modest reduction in the prevalence of the adverse side effects commonly associated with first-generation drugs.

In the final two specifications I investigate whether the increased utilization of second-generation drugs has been associated with a change in the fraction of schizophrenia patients diagnosed with diabetes, hyperlipidemia, or abnormal weight gain. The estimates summarized in columns 9 and 10 suggest that areas in which the drugs were taken up relatively rapidly did have much greater increases in the fraction of schizophrenia patients with one or more of these illnesses. Thus while the drugs may improve health by reducing the prevalence of extrapyramidal symptoms such as tardive dyskinesia, it appears that they also lower health by increasing individuals' risk for diabetes and related illnesses. Whether on average this represents an improvement or a decline in health is not obvious. If physicians are accurately inferring the short and long-term effects of the drugs and aim to maximize the well-being of their patients, then the sharp increase in the use of second-generation drugs does suggest that they do – on net – improve health.

Taken together, the results summarized in this section suggest that the shift to second-generation antipsychotics during the past decade has substantially increased Medicaid spending, has not reduced the use of other health care services, and has increased the prevalence of diabetes and related illnesses. The evidence for an effect on tardive dyskinesia and other extrapyramidal side effects is somewhat more speculative with the statistically insignificant point estimates suggesting a modest decline.

6. Individual-Level Estimates of the Effect of Second-Generation Antipsychotics

One limitation with the results from the previous section that use aggregate zipcode-level data is that some of the differential use of these drugs across geographic areas appears to be driven by a change

that it would fail to distinguish between individuals taking the drug in response to symptoms as opposed to those taking the drug in order to prevent symptoms. The five drugs that account for virtually all of this EPS treatment are benzotropine mesylate, trihephenidyl hydrochloride, amantadine, propranolol, and diphenhydramine. The fraction of schizophrenia patients taking one or more of these drugs declines from 63.1% in 1993 to 48.0% in 2001.

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 % *Any R,Z,S* 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 antipsychotics. I use this variation to estimate the effect of second-generation drugs for the marginal patient – individuals who would take the drugs with certain psychiatrists but not with others. Additionally, I explore whether the marginal effect of second-generation antipsychotics varies over time as the drugs diffuse to an increasing fraction of Medicaid-eligible schizophrenia patients.

I 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 Figures 1A and 1B. But beginning in the fourth quarter of 1997, the diffusion of second-generation drugs accelerated, with more individuals taking these drugs for the first time in the subsequent nine months than in the preceding forty-five. This increase was likely driven by legislation enacted in 1997 that lifted prior authorization restrictions on second-generation antipsychotics. This legislative change made it easier for psychiatrists and other physicians to prescribe these new drugs.

A. OLS Estimates of the Effect of Second-Generation Antipsychotics on Medicaid Spending

I begin by estimating 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 $t+\tau$:

$$(4) SPEND_{j,t+\tau} = \alpha + \beta X_{j,t+\tau} + \theta SPEND_{jt} + \gamma SECOND_{jt} + \lambda UTILIZATION_{jt} + \varepsilon_{jt}$$

In this equation, the variable $SECOND_{jt}$ is defined to equal one if individual j has one or more Risperdal, Zyprexa, or Seroquel claims in period t and zero otherwise. The parameter of interest is γ , which

represents the effect of the new antipsychotic treatments on Medicaid spending. Though this effect may vary across individuals or within a person over time, I begin with the baseline case of a common treatment effect. As emphasized above, the challenge for reliable estimation of this parameter is the endogeneity of treatment – individuals who take the drug are likely to differ in unobservable ways from those who do not.

Table 8 summarizes the results from several specifications analogous to (4). The sample consists of the 9664 individuals diagnosed with schizophrenia in 1993, eligible for Medicaid throughout that baseline year, and who are eligible for Medicaid for at least part of the year in 1994. I exclude the 685 individuals from the sample with one or more months of managed care eligibility during the period up through and including the third quarter of 1997 because the utilization data may be incomplete for them. Following previous work (Manning, 1998) I use the log of Medicaid spending as the dependent variable in these specifications given that health care expenditures are quite skewed to the right.¹⁹ Given that less than 2% of schizophrenia patients from 1993 have zero spending in a subsequent year while they are eligible for Medicaid, the fact that these observations are not included in the estimation should not be too problematic for the analysis.²⁰ Twelve age-gender interactions and four race indicator variables are included in every regression.

The first three specifications examine the relationship between the use of the second-generation antipsychotic drug Risperdal (Zyprexa and Seroquel were not yet available) and the log of Medicaid spending in 1994. The first column summarizes the results from a specification that controls for the number of months each individual was eligible for Medicaid in 1994 and the fraction of those months that were also covered by Medicare. This specification does not include any controls for prior Medicaid spending or health care utilization. The statistically significant estimate of .926 on the *Any R,Z,S*

¹⁹ This transformation produces a distribution that is much closer to the standard normal distribution. For example, in 1994 average Medicaid spending for individuals in this sample is equal to \$7943 while the median is substantially lower at just \$3224. These two statistics are much closer for log Medicaid spending at 8.124 and 8.107, respectively. Similarly, the 5th and 95th percentiles for the log of spending are 1.62 and 1.55 standard deviations from the mean, versus 0.64 and 1.87 standard deviation distances, respectively, for the level of spending.

²⁰ If anything, this would bias down the estimated effect of the new drugs on spending, as it would drop individuals with zero spending, all of whom would be in the control (no second-generation drug) group.

coefficient suggests that the use of these drugs is associated with an increase of approximately \$5400 for an individual with average (log) Medicaid spending in 1993. This is similar to the estimates presented in the previous section that used variation across geographic areas in the diffusion of the new drugs.

In the second specification I include a control for each individual's (log) Medicaid spending in the base year. This variable is highly significant in the regression and its inclusion reduces the point estimate for γ by more than 35%. The statistically significant estimate of .595 for the *Any R,Z,S* coefficient suggests that the use of Risperdal in 1994 was associated with an increase of approximately \$2900 in Medicaid spending for an individual with average (log) Medicaid spending in 1993. The inclusion of 15 measures of health care utilization²¹ from 1993 in the third specification reduces the point estimate a bit further to .550, with this estimate corresponding to an increase of \$2638 in Medicaid spending, which is less than half the value implied by the first specification.²² The small standard errors on this estimate suggest that it is quite precisely estimated, with the 95% confidence interval ranging from \$2240 to \$3063 for the person with average (log) spending in 1993.

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 three specifications 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 been taking second-generation drugs. Consistent with the results for 1994, the inclusion of 1993 Medicaid spending substantially lowers the point estimate for γ in each year, with the measures of utilization leading to somewhat smaller reductions in this estimate. The magnitude of the estimate is generally increasing over

²¹ 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.

²² Frank et al (2003) estimate regressions similar to the one summarized in the first column when estimating price indices for schizophrenia care in two Florida counties from 1994 to 2000. Their specifications focus on spending for mental health services only and do not include controls for baseline spending and utilization as the specifications in columns two and three do.

time, suggesting that the effect of second-generation drugs may change as the drugs diffuse to a systematically different group of patients within the initial cohort diagnosed in 1993.

In Table 9 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 twelve 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 8 for the four years from 1998 through 2001. Because it includes expenditure data for the last quarter of 1997, the spending data for 1998 includes five quarters of information.

Consistent with the results from the previous table, the findings here suggest that the use of second-generation drugs is associated with a substantial increase in Medicaid spending, with the estimates declining in every case when pre-treatment spending and utilization data are included. Interestingly, the estimated effects are substantially larger in this case than for the earlier period. For example, the estimate of 0.820 in the specification with all of the control variables for 1999 spending suggests that taking a second-generation drug is associated with a \$4824 increase in expenditures for the individual with average (log) Medicaid spending in the base year, with the 95 percent confidence interval ranging from a low of \$4437 to a high of \$5230.

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. As Table 7 demonstrated, individuals may be hospitalized on day d and then shift to a second-generation drug on day $d+1$ or shortly after that, with this change in drug treatment potentially being driven by a change in the individual's health (or simply an attempt to find a better treatment). Aggregating the data to a full year and including utilization data from a base year, it is not possible for me to rule out this type of endogeneity. 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.

B. Variation across Psychiatrists in the Use of Second-Generation Antipsychotics

As previous researchers have noted, there is substantial variation across doctors in prescribing patterns even after controlling for differences in patient mix (Hellerstein, 1996). In this section I aim to exploit this variation when estimating the effect of second-generation antipsychotic drugs on Medicaid spending, health care utilization, and observable measures of health. I begin by pairing each Medicaid-eligible individual diagnosed with schizophrenia during the 1993 calendar year with the psychiatrist they visited during that base year. I pair individuals who visited multiple psychiatrists with the one they consulted closest to the last day of 1993. I choose the psychiatrist that individuals visited before they could possibly have taken a second-generation drug to reduce a potential source of bias. For example, it is plausible that Medicaid recipients would, in response to a change in health, seek out a certain psychiatrist because of his willingness to prescribe the new drug treatments.

By constructing the sample in this way, I end up excluding those schizophrenia patients who did not visit a psychiatrist in 1993. As Table 10 demonstrates, almost half of the Medicaid recipients who were included in the Table 8 specifications have a paid claim to a psychiatrist with a provider ID.²³ 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 with a primary diagnosis of schizophrenia at least once during the year while just 10% of their counterparts were hospitalized for this mental illness during this same period.

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:

$$(5) \text{SECOND}_{j,94} = \alpha + \beta X_{j,94} + \theta \text{SPEND}_{j,93} + \gamma \text{SECOND}_{j,93} + \lambda \text{UTILIZATION}_{j,93} + \varepsilon_{j,94}$$

²³ A large fraction of the remaining patients also visit a psychiatrist but their provider does not have an identifier in the Medicaid claims data. The reason for this is administrative – those psychiatrists paid with Medicaid Short-Doyle funds do not have provider identifiers in the claims data (only the provider county is listed for these providers) while those paid directly with Medicaid funds do.

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 controls for each patient’s gender, age, and race, along with detailed information about his/her utilization of medical care in a baseline year. As the first column of Table 11 demonstrates, measures of pre-treatment utilization are significantly related to the probability that individuals take a second-generation drug in 1994, the first year that they are available. For example, patients with relatively many antipsychotic claims or outpatient claims are significantly more likely to take a second-generation drug than those with few claims of either type.

Using the results from this regression, I predict the probability that each individual takes 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 pre-treatment characteristics. Specifically, I calculate the psychiatrist effect Z_{jk} for patient j as follows:

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

with k indexing the psychiatrist for patient j and N_k equal to the total number of patients for psychiatrist k . 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 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 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 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 columns (2) through (5) of Table 11 demonstrate, this psychiatrist effect is significantly positively related with individual-level treatment decisions, with t-statistics ranging from 8.2 to 15.0. In these regressions I include only those psychiatrists with 15 or more patients in 1993.²⁴ 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 next four columns of Table 11, 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 is similar to the OLS estimates though the standard errors using this method are substantially higher.

I replicate these results in the nine specifications summarized in Table 12 for the second part of the study 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. For example, the point estimate of 1.047 in 1999 suggests that Medicaid spending increased by \$7021 for an individual with average (log)

²⁴ 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 DHS unfortunately only makes a 20% sample available.

Medicaid spending in the base year. The estimates for 2000 and 2001 Medicaid spending are even larger, suggesting that the marginal effect of the second-generation drugs may vary over time as the drugs diffuse to a different set of patients. Unfortunately the standard errors are much higher for these final two years and thus compatible with a wide range of estimates.

In Tables 13 and 14 I summarize IV results for the effect of second-generation drugs on the probability that an individual has one or more claims with a primary diagnosis of diabetes or extrapyramidal symptoms during the high-diffusion period from 1998-2001. I include only those individuals who do not have a claim for this each type of condition in the baseline period, though the results are similar if I instead include all schizophrenia patients. Consistent with the earlier results, these findings suggest that the drugs have increased the prevalence of diabetes and related illnesses, though the results are statistically significant in just one of the four years. The findings for extrapyramidal symptoms are small and statistically insignificant in every case.

Taken together, the OLS and IV specifications summarized in this section suggest that the shift to second-generation antipsychotic drugs led to a substantial increase in Medicaid spending. Additionally, 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. Consistent with the earlier two sets of results, the new drugs appear not to have paid for themselves.

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 other drugs within the same therapeutic category. Previous research has suggested that new drugs may pay for themselves by reducing the need for hospitalizations and other costly 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. More generally, the findings are consistent with

those from a recent randomized study (Rosenheck, 2003), suggesting that one can reliably estimate the causal effect of health care treatments on health care spending from observational data with careful use of appropriate empirical methods.

The findings presented here also suggest that, while there may be some modest health benefits associated with the new drugs, the shift to Risperdal, Zyprexa, and Seroquel has led to a significant increase in the prevalence of diabetes. It is important to stress once again that some health and quality-of-life effects may not be observed in the claims data. But given that the main benefit of Risperdal, Zyprexa, and Seroquel relative to the first-generation drugs that preceded them was considered to be the reduction in extrapyramidal symptoms, the small estimates presented in this paper and in other recent studies suggest that the benefits of the new drugs have not been sufficiently large to justify the 610% increase in spending on them from 1993 to 2001.

If the drugs are not substantially better than the ones 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. 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. This pricing rule may also have important dynamic effects, as pharmaceutical firms may alter their R&D expenditures in response to the Medicaid reimbursement rule and the fraction of potential customers who are likely to be insured by this program. Indeed, recent research suggests that one must carefully consider these dynamic effects when considering the effect of alternative policies (Finkelstein, 2003).

Whether the results presented here generalize to other categories of prescription drugs 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 much different from the typical drug category given

that Medicaid, the DVA, and other government programs account for the vast majority of spending on the drugs.

But with the introduction of a Medicare prescription drug benefit and recent increases in the Medicaid rolls, the share of pharmaceutical spending accounted for by Medicare, Medicaid, and other government programs seems destined to 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 a category of prescription drugs. Additional research that estimates the effect of government programs on pharmaceutical pricing, innovation, health care spending, and health is clearly needed in this rapidly changing policy environment.

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Figure 1A: # Taking Second-Generation Antipsychotic for First Time

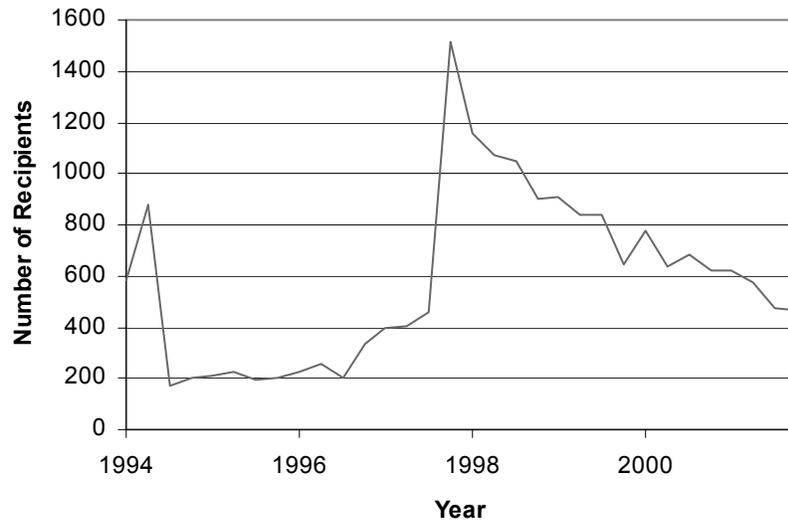


Figure 1B: # in Medicaid Sample taking Risperdal, Zyprexa, or Seroquel

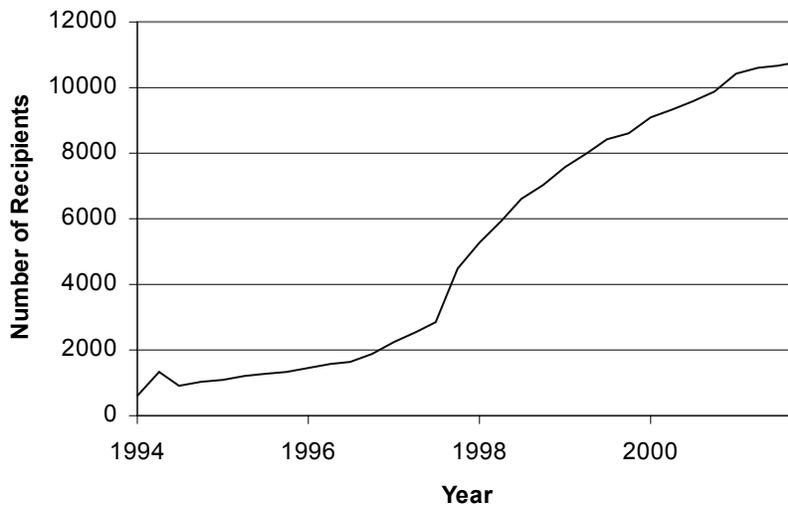


Figure 2: Antipsychotic and Schizophrenia Spending

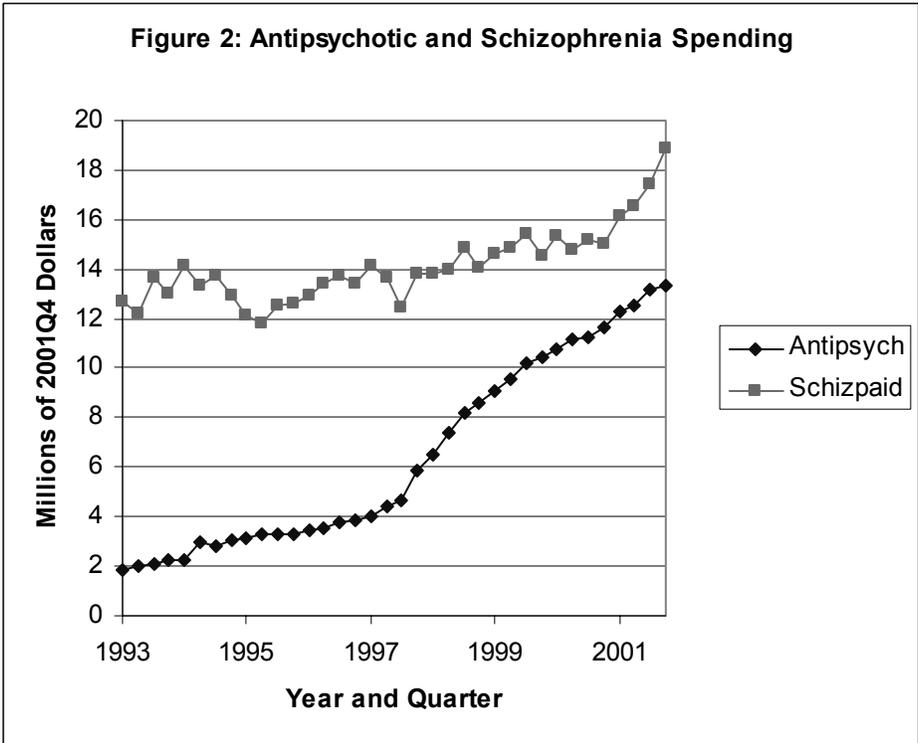


Table 1: Medicaid Prescription Drug Spending by Therapeutic Category: 1996 and 2002

	Expenditures (in millions)		Prescriptions (in millions)		Avg. Cost	
	1996	2002	1996	2002	1996	2002
Central Nervous System	\$1,991	\$7,340	44.9	85.4	\$44	\$86
Cardiovascular-Renal	\$1,622	\$3,105	51.4	94.2	\$32	\$33
Antimicrobials	\$1,534	\$3,216	38.1	48.8	\$40	\$66
Gastrointestinals	\$1,369	\$2,479	19.1	28.4	\$72	\$87
Hormones	\$869	\$2,612	27.6	49.8	\$31	\$52
Respiratory Tract	\$818	\$2,437	29.9	56.3	\$27	\$43
Relief of Pain	\$762	\$2,915	33.1	54.1	\$23	\$54
Neurologics	\$671	\$1,992	18.4	33.6	\$37	\$59
Metabolics / Nutrients	\$469	\$1,696	13.4	30.7	\$35	\$55
Hematologics	\$350	\$1,150	6.1	10.3	\$57	\$111
Skin / Mucous Membr.	\$280	\$386	10.4	10.4	\$27	\$37
Oncolytics	\$251	\$567	3.4	4.3	\$73	\$132
Immunologics	\$156	\$563	0.3	0.8	\$457	\$741
Ophthalmics	\$151	\$364	5.9	8.7	\$25	\$42
Miscellaneous	\$99	\$378	1.5	2.4	\$67	\$157
Otics	\$97	\$172	6.0	7.6	\$16	\$23
Anti-Parasitics	\$39	\$60	1.9	2.3	\$21	\$26
Anesthetics	\$22	\$50	0.5	0.9	\$43	\$59
Antidotes	\$13	\$27	0.1	0.2	\$132	\$117
Radiopharm	\$0	\$3	0.0	0.1	\$23	\$45
Missing	\$1,154	\$1,112	70.9	53.6	\$16	\$21
Total (with double-counting)	\$12,719	\$32,624	382.9	582.9	\$33	\$56
Total (no double-counting)	\$12,296	\$29,628	366.9	521.7	\$34	\$53

Dollars on spending and number of prescriptions by drug were obtained from the Center for Medicare and Medicaid Services State Drug Utilization Data. The therapeutic category for each drug was obtained from the FDA's National Drug Code directory. In some cases, a drug was not listed in the FDA files - these drugs are in the "Missing" category. Dollar values are inflation-adjusted to 2001 dollars.

Table 2: Medicaid Utilization for Central Nervous System Drugs: 1996 and 2002

CNS Category	Expenditures (millions)		Prescriptions (millions)		Average Cost	
	1996	2002	1996	2002	1996	2002
Anti-Psychotic Drugs	\$819	\$3,734	13.3	21.8	\$61	\$171
Anti-Depressants	\$766	\$2,202	15.8	33.8	\$48	\$65
All Other CNS	\$471	\$1,404	17.8	29.8	\$26	\$47

Data were obtained from the Center for Medicare and Medicaid Services and the FDA.

Table 3: 2002 Medicaid Mkt. Share for Top Antipsychotic & Antidepressant Drugs

Drug	Antipsychotics			Drug	Antidepressants		
	Scripts	Revenue	Mkt Share		Scripts	Revenue	Mkt. Share
Zyprexa	5.78	\$1,669	79.5%	Paxil	5.38	\$455	20.1%
Risperdal	6.15	\$1,047	84.0%	Zoloft	5.39	\$425	19.2%
Seroquel	3.01	\$553	73.0%	Wellbutrin	2.20	\$198	14.3%

Number of Medicaid prescriptions in millions and amount of Medicaid revenue in millions of 2001 dollars.

Table 4: Top Ten Antipsychotic Drugs in 1993 and 2001

1993					
Drug Name	Prescriptions		Spending in \$1000		Avg Price
	# Scripts	% of Total	Total Paid	% of Total	
Haloperidol	66018	20.5%	\$1,515	12.4%	\$23
Thioridazine	47832	14.9%	\$579	4.8%	\$12
Clozapine	41616	12.9%	\$4,374	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%	\$1,584	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%	\$12,179	100.0%	\$38

2001					
Drug Name	Prescriptions		Spending in \$1000		Avg. Price
	# Scripts	% of Total	Total Paid	% of Total	
Zyprexa	113919	24.9%	\$41,120	47.6%	\$361
Risperdal	108969	23.8%	\$23,049	26.7%	\$212
Clozapine	50211	11.0%	\$6,494	7.5%	\$129
Seroquel	42785	9.3%	\$10,253	11.9%	\$240
Haloperidol	35480	7.7%	\$1,419	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%	\$2,170	2.5%	\$56
Total	458246	100.0%	\$86,337	100.0%	\$188

Table summarizes Medicaid spending and number of prescriptions in the CA Medicaid sample for the top ten antipsychotic drugs in 1993 and 2001.

Table 5: 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) Avg. Antipsychotic RX Paid	586	791	893	937	1174	1867	2294	2562	2854
(8) Avg. Other RX Paid	671	686	654	775	925	1070	1259	1491	1760
(9) Avg. Schizophrenia IP/OP Paid	4049	4458	3973	3931	3834	4250	4504	4467	4898
(10) Avg. Other Mental Hlth IP/OP Paid	1811	1886	1573	1593	1560	1649	1680	1739	1970
(11) Avg. All Other IP/OP Paid	2187	2070	2122	2266	2401	2346	2590	2456	2621
(12) Avg. 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) % Any R,Z,S	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) % 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 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.

Table 6: Area-Level Estimates of the Effect of Second-Generation Antipsychotics

	Δ Log(TotalPaid)		Δ TotalPaid		Δ % Hospitalized		Δ %EPS Claim		Δ % w/Diab,etc. Claim	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Δ % Any R,Z,S	0.466 (.124)	0.512 (.139)	4869 (1149)	5610 (1273)	0.096 (.054)	0.115 (.061)	-0.008 (.017)	-0.024 (.019)	0.073 (.041)	0.080 (.047)
Δ % Medicare	-0.910 (.373)	-0.827 (.417)	-7747 (3445)	-6889 (3824)	0.124 (.162)	-0.027 (.188)	0.007 (.052)	0.005 (.058)	0.040 (.126)	0.130 (.143)
Δ Avg. Months	0.112 (.027)	0.101 (.029)	1053 (245)	915 (266)	0.014 (.012)	0.006 (.013)	0.008 (.004)	0.009 (.004)	0.033 (.009)	0.032 (.010)
Δ % Remaining	0.083 (.313)	-0.184 (.364)	208 (2894)	-3178 (3334)	0.020 (.136)	-.142 (.159)	-0.014 (.042)	-0.009 (.049)	0.110 (.102)	0.099 (.121)
Year Effects?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zip Effects?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zip Trends?	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
R-squared	0.334	0.404	0.412	0.481	0.334	0.404	0.167	0.250	0.214	0.267
Number Obs.	560	560	560	560	560	560	560	560	560	560

Dependent variables in each specification represent 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 include only those four-digit zip codes with more than 50 people in 1993. % Any R,Z,S equals one at the individual level if person has 1 or more R,Z, and/or S scripts in the year and zero otherwise. Regressions are weighted by zip code's share of observations in each year. Specifications include year and zip code fixed effects and control for changes in age*gender distribution and for changes in race distribution. Specifications summarized in the even-numbered columns include zip code - specific time trends.

Table 7: Utilization Immediately Before & 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	0.0720 (.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 DAY2 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 Observations	2283913	2283913
Person Effects?	Yes	Yes
R-squared	0.616	0.147

Specifications include 101 person-day observations for each of the 22613 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.

Table 8: Cross-Sectional Estimates of the Effect of 2nd 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)
Any Second Gen. Drug _t	0.926 (.046)	0.595 (.033)	0.550 (.033)	0.924 (.047)	0.661 (.038)	0.618 (.038)	0.924 (.043)	0.700 (.036)	0.659 (.036)	1.017 (.037)	0.795 (.033)	0.757 (.032)
Log (Total Paid ₉₃)		0.738 (.008)	0.684 (.011)		0.649 (.009)	0.583 (.012)		0.568 (.010)	0.487 (.013)		0.512 (.010)	0.429 (.013)
Medicare Fraction _t	-0.469 (.031)	-0.144 (.023)	-0.193 (.023)	-0.540 (.032)	-0.286 (.026)	-0.336 (.026)	-0.402 (.032)	-0.193 (.027)	-0.250 (.027)	-0.312 (.031)	-0.124 (.027)	-0.174 (.028)
Eligible Months _t	0.130 (.011)	0.165 (.008)	0.160 (.008)	0.114 (.010)	0.147 (.008)	0.141 (.008)	0.145 (.010)	0.162 (.009)	0.158 (.009)	0.199 (.016)	0.225 (.014)	0.224 (.014)
Any Schz IP Stay ₉₃			-0.205 (.038)			-0.184 (.044)			-0.193 (.046)			-0.169 (.047)
# Schz IP Days ₉₃			-0.003 (.002)			-0.005 (.002)			-0.002 (.002)			0.000 (.002)
# Schz IP Days ² ₉₃			1.5E-5 (7.5E-6)			7.3E-6 (8.5E-6)			-3.0E-6 (1.1E-5)			-7.6E-6 (1.1E-5)
Any OP Schz Claims ₉₃			0.012 (.077)			-0.060 (.090)			-0.136 (.097)			-0.018 (.100)
# OP Schz Claims ₉₃			0.0035 (.0005)			0.0023 (.0006)			0.0026 (.0006)			0.0022 (.0006)
# OP Schz Claims ² ₉₃			-8.4E-6 (1.9E-6)			-4.0E-6 (2.2E-6)			-5.1E-6 (2.2E-6)			-5.4E-6 (2.3E-6)
Any Antipsychotic ₉₃			0.059 (.032)			0.013 (.037)			0.004 (.039)			0.003 (.040)
Antipsychotic Claims ₉₃			0.0067 (.0019)			0.0133 (.0022)			0.0156 (.0023)			0.0137 (.0023)
Antipsych. Claims ² ₉₃			-3.0E-5 (2.2E-5)			-7.4E-5 (2.5E-5)			-1.1E-4 (2.6E-5)			-8.7E-5 (2.7E-5)
R-squared	0.092	0.523	0.541	0.098	0.419	0.443	0.105	0.362	0.389	0.132	0.345	0.371
# Observations		9492			9053			8642			8216	
μ,σ of Dep. Variable		(8.12,1.44)			(8.09,1.46)			(8.22,1.42)			(8.02,1.39)	

Sample includes individuals eligible for Medicaid for 12 months in 1993, with one or more (two or more if only outpatient) schizophrenia claims in that year, and who are eligible for at least one month in 1994. 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 also include 12 age*gender and 4 race dummy variables. Specifications in columns 3, 6, 9, and 12 also control for LTC utilization and use of other prescription drugs (with any, # days or claims, and # days or claims squared). The number of observations declines from one year to the next because individuals die or become ineligible for Medicaid.

Table 9: Cross-Sectional Estimates of the Effect of 2nd 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)
Any Second Gen. Drug _t	0.880 (.030)	0.652 (.021)	0.668 (.021)	0.974 (.029)	0.811 (.023)	0.820 (.023)	1.055 (.028)	0.909 (.024)	0.906 (.024)	1.078 (.029)	0.964 (.024)	0.953 (.024)
Log (Total Paid _{96Q4-97Q3})		0.728 (.008)	0.688 (.011)		0.626 (.009)	0.567 (.013)		0.566 (.010)	0.497 (.014)		0.537 (.010)	0.470 (.014)
Medicare Fraction _t	-0.376 (.030)	-0.188 (.021)	-0.228 (.021)	-0.351 (.030)	-0.201 (.024)	-0.248 (.024)	-0.313 (.030)	-0.184 (.025)	-0.233 (.025)	-0.347 (.031)	-0.221 (.026)	-0.270 (.026)
Eligible Months _t	0.113 (.009)	0.138 (.006)	0.129 (.006)	0.135 (.011)	0.161 (.009)	0.151 (.008)	0.126 (.010)	0.145 (.009)	0.139 (.008)	0.131 (.011)	0.145 (.009)	0.139 (.009)
Any Schz IP Stay _{96Q4-97Q3}			-0.211 (.036)			-0.196 (.041)			-0.113 (.044)			-0.134 (.044)
# Schz IP Days _{96Q4-97Q3}			-0.0039 (.0016)			-0.0027 (.0017)			-0.0035 (.0018)			-0.0018 (.0019)
# Schz IP Days _{96Q4-97Q3} ²			9.1E-6 (5.8E-6)			9.1E-6 (6.5E-6)			8.4E-6 (6.8E-6)			4.3E-6 (6.8E-6)
Any OP Schz Claims _{96Q4-97Q3}			-0.111 (.080)			-0.033 (.093)			-0.020 (.101)			-0.016 (.106)
# OP Schz Claims _{96Q4-97Q3}			8.7E-4 (4.1E-4)			5.8E-4 (4.6E-4)			9.8E-4 (4.9E-4)			-5.8E-5 (5.0E-4)
# OP Schz Claims _{96Q4-97Q3} ²			-9.7E-7 (1.3E-6)			-8.7E-7 (1.4E-6)			-2.0E-6 (1.5E-6)			4.2E-7 (1.5E-6)
Any Antipsychotic _{96Q4-97Q3}			0.061 (.032)			-0.010 (.036)			-0.014 (.038)			0.012 (.039)
Antipsychotic Claims _{96Q4-97Q3}			0.0079 (.0017)			0.0129 (.0018)			0.0133 (.0019)			0.0137 (.0020)
Antipsych. Claims _{96Q4-97Q3} ²			-3.2E-5 (1.7E-5)			-7.9E-5 (1.9E-5)			-8.1E-5 (2.0E-5)			-7.9E-5 (2.1E-5)
R-squared	0.156	0.576	0.593	0.183	0.490	0.511	0.209	0.456	0.477	0.225	0.450	0.474
# Observations		8002			7585			7292			6984	
μ,σ of Dep. Variable		(8.65,1.34)*			(8.59,1.34)			(8.68,1.35)			(8.83,1.34)	

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 to 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 include 12 age*gender and 4 race dummy variables. Specificatons in columns 3, 6, 9, and 12 also control for LTC utilization and use of other prescription drugs (with any, # days or claims, and # days or claims squared). The number of observations declines from one year to the next because individuals die or become ineligible for Medicaid.

Table 10: Summary Statistics for Sample Individuals Who Visit vs. Do Not Visit a Psychiatrist

1993 Utilization Measures	1993 Psychiatrist Visit?		96Q4-97Q3 Utiliz. Measures	96Q4-97Q3 Psych. Visit?	
	Yes	No		Yes	No
Number Observations	4574	5090	Number Observations	3633	4536
Total Medicaid Spending	9371	6842	Total Medicaid Spending	9870	7305
Log(Medicaid Spending)	8.30	8.09	Log(Medicaid Spending)	8.50	8.24
Any Schiz. Hospital Stay?	28.4%	11.0%	Any Schiz. Hospital Stay?	24.1%	11.5%
Schizophrenia Hospital Days	6.58	1.80	Schizophrenia Hospital Days	4.97	2.64
Any Schiz. LTC Stay?	4.0%	3.0%	Any Schiz. LTC Stay?	3.6%	2.1%
Schizophrenia LTC Days	9.30	7.39	Schizophrenia LTC Days	9.93	5.84
Any Antipsychotic?	84.9%	77.9%	Any Antipsychotic?	89.0%	79.7%
Antipsychotic Claims	15.2	9.8	Antipsychotic Claims	15.6	10.9
Any Other Prescription Drugs	96.9%	92.0%	Any Other Prescription Drugs	97.0%	92.5%
Other Presc. Drug Claims	33.5	23.3	Other Presc. Drug Claims	33.8	24.6
Any Outpatient Schiz Claims	100.0%	96.0%	Any Outpatient Schiz Claims	100.0%	96.8%
% Months Medicare	49.5%	45.1%	% Months Medicare	47.9%	43.1%
Age	44.9	44.0	Age	46.8	45.2
Male	54.3%	53.5%	Male	55.6%	55.3%
Male YOB 1970-76	1.7%	2.5%	Male YOB 1970-79	3.9%	4.6%
Male YOB 1960-69	13.1%	14.4%	Male YOB 1960-69	13.8%	15.8%
Male YOB 1950-59	19.4%	19.3%	Male YOB 1950-59	19.7%	19.4%
Male YOB 1940-49	11.1%	10.4%	Male YOB 1940-49	10.7%	9.8%
Male YOB 1930-39	5.3%	3.9%	Male YOB 1930-39	5.0%	3.4%
Male YOB 1900-29	3.7%	3.0%	Male YOB 1900-29	2.5%	2.3%
Female YOB 1970-76	1.1%	1.1%	Female YOB 1970-79	1.5%	2.3%
Female YOB 1960-69	6.1%	6.5%	Female YOB 1960-69	7.4%	8.2%
Female YOB 1950-59	11.9%	12.5%	Female YOB 1950-59	11.8%	12.6%
Female YOB 1940-49	10.5%	10.6%	Female YOB 1940-49	10.0%	10.3%
Female YOB 1930-39	7.2%	7.2%	Female YOB 1930-39	7.0%	5.7%
Female YOB 1900-29	9.0%	8.6%	Female YOB 1900-29	6.8%	5.6%
White	59.9%	56.9%	White	56.6%	52.6%
Hispanic or Asian	8.0%	10.4%	Hispanic or Asian	10.1%	14.7%
Black	18.4%	17.5%	Black	20.6%	18.2%
Missing Race	13.7%	15.2%	Missing Race	12.7%	14.6%

Table provides average characteristics for individuals in the Table 8 and Table 9 samples. Splits into two groups - those who visit versus those who do not visit a psychiatrist with a provider identifier in the baseline year.

Table 11: IV Estimates of the Effect of 2nd-Generation Antipsychotics on Medicaid Spending: 1994-1997

	Any New Antipsychotic _t					Log(Total Paid _t)			
	1994	1994	1995	1996	1997Q1-3	1994	1995	1996	1997Q1-3
Any Second Gen. Drug _t						0.320 (.290)	0.715 (.368)	0.956 (.485)	0.602 (.379)
Physician Effect ₉₄		0.822 (.055)	0.593 (.056)	0.564 (.061)	0.566 (.069)				
Medicare Fraction _t	0.045 (.012)	0.021 (.016)	0.008 (.016)	0.003 (.018)	0.038 (.020)	-0.180 (.052)	-0.306 (.061)	-.220 (.067)	-0.131 (.067)
Eligible Months _t	0.013 (.003)	0.009 (.005)	0.015 (.005)	0.012 (.006)	0.024 (.010)	0.145 (.028)	0.153 (.026)	0.184 (.023)	0.217 (.051)
Log (Total Paid ₉₃)	-0.007 (.005)	-0.010 (.007)	-0.010 (.008)	-0.009 (.008)	-.001 (.009)	0.697 (.023)	0.603 (.022)	0.505 (.027)	0.457 (.028)
Any Schz IP Stay ₉₃	0.030 (.018)	0.060 (.025)	0.045 (.025)	0.085 (.028)	0.100 (.031)	-0.077 (.087)	-0.108 (.119)	-0.263 (.108)	-0.316 (.098)
# Schz IP Days ₉₃	0.0020 (.001)	0.0012 (.0012)	0.0022 (.0012)	0.0002 (.0013)	0.0006 (.0015)	-0.0060 (.003)	-0.0076 (.0049)	-0.0018 (.0040)	0.0071 (.0044)
# Schz IP Days ² ₉₃	-1.1E-5 (7.3E-6)	-3.9E-6 (8.6E-6)	-8.6E-6 (8.7E-6)	1.3E-6 (9.5E-6)	-7.0E-7 (1.1E-5)	3.9E-5 (1.7E-5)	9.7E-6 (3.9E-5)	-1.2E-6 (2.5E-5)	-5.1E-5 (3.1E-5)
# OP Schz Claims ₉₃	9.5E-4 (2.5E-4)	0.0010 (3.5E-4)	0.0011 (3.6E-4)	0.0015 (3.9E-4)	0.0009 (4.4E-4)	0.0019 (.0010)	0.0020 (.0011)	0.0005 (.0012)	0.0012 (.0013)
# OP Schz Claims ² ₉₃	-9.9E-7 (8.7E-7)	-2.5E-6 (1.3E-6)	-3.1E-6 (1.3E-6)	-3.5E-6 (1.4E-6)	2.5E-6 (1.5E-6)	-3.4E-6 (2.7E-6)	-4.5E-6 (2.8E-6)	-2.3E-7 (2.9E-6)	-2.6E-6 (3.7E-6)
Any Antipsychotic ₉₃	0.0034 (.0172)	-0.0049 (.0242)	0.0129 (.0247)	0.0216 (.0271)	-.0007 (.0305)	0.0225 (.0777)	0.1021 (.0779)	0.0598 (.0801)	-.012 (.095)
Antipsychotic Claims ₉₃	0.0053 (.0009)	0.0066 (.0012)	0.0046 (.0012)	0.0051 (.0013)	0.0083 (.0015)	0.0119 (.0037)	0.0090 (.0045)	0.0110 (.0049)	0.0118 (.0063)
Antipsych. Claims ² ₉₃	-5.0E-5 (9.8E-6)	-6.6E-5 (1.4E-5)	-4.3E-5 (1.4E-5)	-5.8E-5 (1.5E-5)	-8.6E-5 (1.7E-5)	-9.6E-5 (3.5E-5)	-4.2E-5 (4.3E-5)	-6.4E-5 (4.8E-5)	-7.7E-5 (6.2E-5)
R-squared	0.071	0.147	0.111	0.105	0.115	-	-	-	-
# Observations	4574	2295	2195	2094	2004	2295	2195	2094	2004
μ,σ of Dep. Variable	(.14,.35)	(.14,.35)	(.13,.34)	(.15,.36)	(.20,.40)	(8.33,1.40)	(8.28,1.41)	(8.43,1.37)	(8.24,1.35)

Sample includes individuals eligible for Medicaid for 12 months in 1993, with one or more (two or more if only outpatient) schizophrenia claims in that year, with one or more visits to a psychiatrist with a provider ID and 15 or more patients in 1993, and who are eligible for at least one month in 1994. Dependent variable in the first five columns is an indicator variable that equals one if a person took the drug in the year and zero otherwise (with columns 2 through 5 including the results from first stage regression for columns 6 through 9). The dependent variable for the IV specifications summarized in the next four columns 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 also include 12 age*gender and 4 race dummy variables. Specifications also control for LTC utilization and use of other prescription drugs (with any, # days or claims, and # days or claims squared). The number of observations declines from one year to the next because individuals die or become ineligible for Medicaid. Patients for 77 different psychiatrists are included in the specifications summarized in columns 2 through 9.

Table 12: IV Estimates of the Effect of 2nd-Gen. Antipsychotics on Medicaid Spending: 1997Q4-2001

	Any New Antipsychotic _t					Log(Total Paid _t)			
	97Q4-98	97Q4-98	1999	2000	2001	97Q4-98	1999	2000	2001
Any Second Gen. Drug _t						1.105 (.272)	1.047 (.433)	1.990 (.806)	1.690 (.822)
Physician Effect ₉₈		0.632 (.084)	0.459 (.090)	0.314 (.093)	0.310 (.093)				
Log (Total Paid _{96Q4-97Q3})	0.031 (.008)	0.020 (.013)	0.005 (.014)	0.005 (.015)	-0.022 (.015)	0.639 (.052)	0.546 (.039)	0.441 (.041)	0.487 (.046)
R-squared	0.076	0.105	0.075	0.070	0.082	-	-	-	-
# Observations	3633	1561	1488	1430	1378	1561	1488	1430	1378
μ,σ of Dep. Variable	(.36,.48)	(.35,.48)	(.44,.50)	(.49,.50)	(.55,.50)	(8.84,1.32)	(8.78,1.31)	(8.85,1.32)	(8.99,1.36)

Table 13: IV Estimates of the Effect of 2nd-Generation Antipsychotics on Diabetes: 1997Q4-2001

	Any New Antipsychotic _t					Any Diabetes Claim _t			
	97Q4-98	97Q4-98	1999	2000	2001	97Q4-98	1999	2000	2001
Any Second Gen. Drug _t						0.193 (.099)	0.189 (.144)	0.121 (.183)	0.293 (.219)
Physician Effect ₉₈		0.655 (.093)	0.444 (.100)	0.311 (.104)	0.297 (.106)				
Log (Total Paid _{96Q4-97Q3})	0.031 (.008)	0.019 (.014)	0.013 (.015)	0.010 (.016)	-0.018 (.016)	0.005 (.009)	0.016 (.012)	0.022 (.012)	0.025 (.013)
R-squared	0.076	0.119	0.088	0.090	0.088	-	-	-	-
# Observations	3633	1243	1202	1154	1102	1243	1202	1154	1102

Table 14: IV Estimates of the Effect of 2nd-Generation Antipsychotics on EPS: 1997Q4-2001

	Any New Antipsychotic _t					Any Diabetes Claim _t			
	97Q4-98	97Q4-98	1999	2000	2001	97Q4-98	1999	2000	2001
Any Second Gen. Drug _t						0.012 (.036)	0.009 (.040)	-0.029 (.052)	0.025 (.092)
Physician Effect ₉₈		0.620 (.086)	0.438 (.091)	0.304 (.094)	0.287 (.095)				
Log (Total Paid _{96Q4-97Q3})	0.031 (.008)	0.020 (.013)	0.009 (.014)	0.009 (.015)	-0.019 (.015)	0.005 (.002)	0.004 (.004)	0.005 (.003)	0.004 (.005)
R-squared	0.076	0.106	0.081	0.081	0.092	-	-	-	-
# Observations	3633	1506	1452	1398	1336	1506	1452	1398	1336

Sample in Tables 12 through 14 includes individuals eligible for Medicaid for 12 months from 10/96 until 9/97, with one or more (two or more if only outpatient) schizophrenia claims in that year, with one or more visits to a psychiatrist with a provider ID and 15 or more patients in that year, and who are eligible for at least one month from 10/97 until 9/98. Dependent variable in the first five columns is an indicator variable that equals one if a person took the drug in the relevant year and zero otherwise (with columns 2 through 5 including the results from first stage regression for columns 6 through 9). The dependent variable for the IV specifications summarized in the next four columns of Table 12 is equal to the log of Medicaid spending in a certain year, with the first measure including spending for the last quarter of 1997 and all four quarters of 1998. The next two tables have indicator variables that equal one if an individual has a diabetes claim and an EPS claim, respectively. All regressions also include include 12 age*gender, 4 race dummy variables, and the 15 utilization measures used in the earlier regressions. The number of observations declines from one year to the next because individuals die or become ineligible for Medicaid. Patients for 61 different psychiatrists are included in the specifications summarized in columns 2 through 9. Tables 13 and 14 exclude individuals diagnosed with diabetes (and related illnesses) and extrapyramidal symptoms, respectively, in the baseline year.

Appendix Table 1: Series for Figures 1A, 1B, and 2

Year	Quarter	First	Current	Antipsych	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
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