Online Appendix:

Common Practice: Spillovers from Medicare on Private Health Care

Michael Barnett, Andrew Olenski, and Adam Sacarny

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A Detailed Description of Patient Classification Algorithm

To develop an algorithm for classifying patients by clinical appropriateness, we studied the clinical literature and guidelines for antipsychotics (Maglione et al., 2011; Painter et al., 2017; Reus et al., 2016; American Geriatrics Society, 2019). The algorithm we ultimately elected classifies each patient into one of four mutually exclusive and exhaustive categories using diagnosis codes from the baseline and outcome periods (April 20, 2013 through December 31, 2017). When patients fit in multiple categories, they are assigned in cascading order to the highest-value one.

To make the approach as parsimonious as possible, the final algorithm was based on FDA approvals and an evidence summary table in Maglione et al. (2011), a systematic review of off-label prescribing of antipsychotics. Table A of that study displays the quality of evidence for each of a multitude of off-label uses. In the resulting algorithm, one category contains FDA approved uses and the remainder map to standards of evidence in Table A:

1. **Guideline-concordant** patients have a serious mental illness – bipolar disorder, schizophrenia, or major depression – for which quetiapine is approved by the FDA. If a patient has major depression but not bipolar disorder or schizophrenia, quetiapine is FDA approved for use alongside an antidepressant (called adjunctive therapy). For these patients, to match FDA approvals, the prescribing must overlap with an antidepressant. In the systematic review, these conditions are not listed because they are on-label, or in the case of major depression are listed as "moderate or high evidence of efficacy" with FDA approval.

2. **Intermediate evidence** patients have a condition for which the clinical evidence is mixed but has some support. We include patients with generalized anxiety disorder as well as those with major depression who are not concurrently receiving an antidepressant (called quetiapine monotherapy). In the systematic review, these conditions are listed as "moderate or high evidence of efficacy" without FDA approval.

3. **Low-value** candidates have conditions for which the evidence suggests that quetiapine has limited benefit or is even harmful. The most well known low-value condition is dementia, reflecting the guidelines which strongly discourage the use of antipsychotics in this population. We also include insomnia, post-traumatic stress disorder, obsessive-compulsive disorder,

personality disorders, eating disorders, and alcohol use disorder. The systematic review states these conditions as having "low or very low evidence of efficacy," "mixed results," or "low or very low evidence of inefficacy."

4. **Unknown** patients have no relevant diagnoses. We also include the small number of patients under age 18 in this category because pediatric guidelines for antipsychotics are distinct and study physicians rarely treat children and teenagers.

Appendix Table A8 provides a list of the ICD-9 and ICD-10 codes for each of these conditions.

For patients with major depression but not bipolar disorder or schizophrenia, the presence of antidepressants is pivotal for classification. In the prescriber-level analyses, we consider a quetiapine prescription to a major depression patient guideline-concordant if it overlapped with an antidepressant at the time it was dispensed and intermediate otherwise. In the patient-level analyses, we consider patients with major depression guideline-concordant if at least one of their quetiapine fills during the baseline period overlapped with an antidepressant on the day of dispense and classify them as intermediate otherwise. Overlap is determined using the date of service and days supply of the prescription fill.

While we pre-specified a classification algorithm, in practice we amended it in two ways to produce the above approach. First, the original algorithm did not consistently map between the systematic reviews and the guideline classifications. As a result, it mis-classified some indications: for example, prescribing to patients with obsessive compulsive disorder was erroneously considered to have "intermediate" support in the literature.[8] The updated algorithm uses a consistent classification. Second, we anticipated only using diagnosis codes from the baseline period in case diagnosis coding responded to the intervention. However, we found that most private insurance prescribing could not be classified with this approach due to short pre-intervention coverage durations and a lack of relevant diagnosis codes. We thus opted to include diagnosis codes from the outcome period. Despite both of these changes, our results are robust to the pre-specified approach (Appendix Table A9).

[8]Specifically, the pre-specified algorithm uses the following classification. Guideline-concordant: bipolar disorder, schizophrenia, major depression (irrespective of whether taken with antidepressant). Intermediate evidence: generalized anxiety disorder, depression (excluding major depression), obsessive-compulsive disorder, and personality disorder. Low-value: insomnia, PTSD, eating disorder, alcohol use disorder, and dementia.

B Construction of Baseline Patient Cohort

The baseline patient cohort consists of patients who received at least one quetiapine prescription from a study physician in the one year pre-intervention period (April 21, 2014 through April 20, 2015). Our initial dataset includes 12,418 patients meeting this criteria. The sample has three key restrictions. First, since patients periodically churn out of HCCI coverage and become unobserved in the data, they must still be enrolled in the month immediately prior to the intervention start, March 2015 (this excludes 2,546 patients). Second, we omit patients whose insurance type changes during the sample (e.g., private insurance to Medicare) or who maintain private insurance after age 64, since these patients are likely covered by both private insurance and Medicare (491 patients). Third, to ensure treatment status is clear, we exclude any patients who received a quetiapine prescription from more than one study prescriber during the year prior to the intervention (150 patients). These restrictions leave us with N=1,980 private insurance patients and N=7,384 Medicare patients.

C Measurement of Health Care Utilization and Spending

In addition to studying quetiapine prescribing to the baseline patient cohort, we also measure health care utilization (i.e. provider visits) and spending. We define several measures of utilization relevant to this patient population using three HCCI claims files: inpatient, outpatient, and physician. The inpatient and outpatient files contain institutional billing in their respective settings, while individual provider billing is contained in the physician file. We process claims from all three sources by reducing the these files to patient-provider-day level observations. Each patient-provider-day is considered one visit, so if a patient has multiple claims with the same provider on the same day, we only count these records as one encounter. Note that in HCCI data, claims and claim lines are already merged together.

We construct counts of inpatient, emergency department (ED), psychiatrist, and psychologist visits for each baseline patient in the post-intervention period (to use as outcomes) and pre-intervention period (to use as statistical controls). Our methodology for processing the data is as follows:

- **Inpatient stays**. We identify inpatient stays using the inpatient file and limiting to records

with a hospital type-of-bill code (codes beginning with 1 or 85). Further, we drop all records with zero allowed charges, missing DRGs, missing discharge status, or continuation discharge status (i.e. discharge status code 30). In the case that after removing these records the discharge date is not constant within a claim, we assign all records in the claim to the latest discharge date among them; in the extremely rare case that scrambled provider NPI is not constant within-claim, we pick the NPI in the first claim record. Finally, to remove duplicate claims and/or multiple encounters on the same day, we collapse together any records with the same patient, scrambled provider NPI, and discharge date. Each remaining record is considered to be one inpatient stay. We use this data to produce counts of the number of inpatient stays for each patient.

- **ED visits**. We identify ED visits using the outpatient file. We restrict to claims (i.e. claim IDs) that have at least one record with emergency department revenue centers (revenue center codes 450-459 or 981). Then we restrict to records with hospital or freestanding ED type-of-bill codes (codes beginning with 1, 85, or 78) and we drop records with zero allowed charges. In cases where the last date or scrambled NPI varies among records in the same claim, we mimic the approach used for inpatient stays and use the latest last date and first NPI among those records. Then, as with inpatient stays, we remove duplicate claims and/or multiple same-day encounters by collapsing together records with the same patient, scrambled provider NPI, and last date. Each remaining record is taken as one ED visit, and we use this data to generate the counts.

- **Psychiatrist or psychologist visits**. Visits with psychiatrists or psychologists are defined using the physician file. Only records with provider category 81 (psychiatrist) or 14 (psychologist) are loaded from this file. We exclude records with inpatient or ED place of service codes (codes 21, 23, 51, or 61), zero allowed charges, or missing scrambled NPI. To avoid double-counting visits that involve multiple claim lines or visits that are billed with multiple claims, we collapse together records with the same patient, scrambled provider NPI, and last date. If among records with the same patient-provider-date triple the provider is categorized as both a psychiatrist and a psychologist, we consider the provider a psychiatrist for all of those records. Each remaining record is taken as a visit with a psychiatrist or psychologist,

and we use these records to count encounters for the patients.

We also present measures of spending on health care services by service category using all four HCCI claims files: inpatient, outpatient, physician, and prescription drugs. Each measure corresponds to the given HCCI claims file and simply sums the insurer's allowed charges (which includes the patient's out of pocket obligation as well as the insurer's payment) for every patient record in the file with a date of service during the period. The measures involve no other processing of the source data.

D Detailed Description of Targeting Simulation

Here we describe in more detail the methodology of Section 7 in which we implement the original Medicare selection algorithm using HCCI data on Medicare and private insurance patients. For consistency with the original intervention, we closely match the algorithm that was originally run in Medicare, though in practice and by necessity our approach differs slightly. To match prior analyses in this manuscript, we omit prescribing to patients with no valid age and prescribing to privately insured patients 65 and up. We made four additional changes. First, if a patient filled multiple quetiapine scripts from the same doctor on the same day, CMS only included the fill with the longest duration, while we include all the fills; CMS previously found the two approaches were highly correlated ($\geq$95%). Second, CMS omitted long-term care pharmacies and patients but we include them because HCCI data does not identify them in its data during the analysis period. Third, CMS restricted its universe to PCPs with $\geq$10 quetiapine fills in a year but we relax the restriction to $\geq$1 fills due to lower prescribing volume in HCCI. Fourth, CMS excluded PCPs with a secondary specialty of psychiatry; we do not make this restriction because we only observe primary specialty.

We seek to identify 5,055 prescribers for each insurer (Medicare alone, private insurance alone, Medicare + private insurance). To ensure that when the algorithm is run it identifies the correct number of prescribers, we modify the outlier method described in the main text so that we can manipulate the threshold for outliers. Specifically, the new outlier threshold formula is:

$$T_{s,t,m} = Q^{75}_{s,t,m} + \kappa(Q^{75}_{s,t,m} - Q^{25}_{s,t,m}).$$

Where s indexes states, t indexes years, m indexes measures (quetiapine fills or days), $T_{s,t,m}$ is the threshold, and $Q^{p}_{s,t,m}$ is the pth percentile of measure m among prescribers in state s and year t. κ can be manipulated to raise or lower the threshold and thus the number of prescribers selected. In the original intervention, CMS searched κ to produce a sample of roughly 5,000 PCPs, picking $\kappa = 0.25$ (the method noted in the main text) which yielded a sufficiently close sample of $N = 5,055$. In practice, we search κ seeking to select 5,055 physicians. If there exists no value of κ that returns exactly 5,055 physicians, we choose the value that minimizes the absolute deviation from 5,055.

As in the CMS approach, to be selected, PCPs must be outliers relative to other prescribers in their state and year on four measures of quetiapine prescribing as given by the above formula: days supplied in 2013, days supplied in 2014, fills in 2013, and fills in 2014. The algorithm is run on just Medicare prescribing data, just private insurance prescribing data, and the combined Medicare and private insurance data. It yields three groups:

1. Outlier Medicare prescribers

2. Outlier private insurance prescribers

3. Outliers in combined Medicare and private insurance prescribing

In Figure 3 and Panels A and B of Appendix Table A7 we analyze and plot the distribution of quetiapine days prescribed by physicians in each of the three groups during the period 2013-2014. We compute the total days supplied to Medicare patients, private insurance patients, and Medicare+private insurance patients and compare the distributions across the providers in each of the groups. The main text also reports the overlap between the three groups as the share of prescribers in group g that are also in group g'.

Finally, using the three groups of providers and our point estimates of the percent effect of the intervention given in Table 2, we project the effect of intervening on each group of PCPs on national primary care quetiapine prescribing, reporting the results in Panel C of Appendix Table A7. Specifically, we estimate the reduction in quetiapine days supplied in the post-intervention period (April 21, 2015 – December 31, 2017) if an intervention were conducted in the given group of PCPs and divide it by the national volume of PCP prescribing that would have prevailed absent the

intervention. Because we are analyzing prescribing that occurred after CMS actually intervened, PCPs who were treated in the original CMS study have lower volume in this period than they would absent CMS's efforts. Many of these PCPs enter the numerator and denominator of the estimates, biasing each downward relative to the counterfactual in which no intervention had truly occurred. Thus we reweight any PCPs who were in the original study so that treated PCPs get no weight and control PCPs are proportionately upweighted.

The projected reductions are given by the following formula:

$$r_g^n = \frac{\hat{\rho}^n \sum_{i \in P_g} \omega_i^g y_i^n}{\sum_{i \in P_*} \omega_i^* y_i^n}, \; n \in \{\text{Private}, \text{Medicare}\}$$

Where n indexes insurers, i indexes PCPs, and g indexes the three outlier groups. In the numerator, $\hat{\rho}^n$ is the estimated percent effect of the intervention in insurer n, P_g is the set of PCPs in outlier group g, ω_i^g is the PCP's numerator weight, and y_i^n is the PCP's prescribing in the outcome period. In the denominator, P_* is the set of all PCP prescribers of quetiapine nationally and ω_i^* is the denominator weight. The weights are given by the following formulas:

$$\omega_i^g = \begin{cases} 1 & \text{if not in CMS study} \\ 0 & \text{if treated in CMS study} \\ \left(N_g^T + N_g^C\right)/N_g^C & \text{if control in CMS study} \end{cases} \quad \omega_i^* = \begin{cases} 1 & \text{if not in CMS study} \\ 0 & \text{if treated in CMS study} \\ \left(N_*^T + N_*^C\right)/N_*^C & \text{if control in CMS study} \end{cases}$$

Where N_g^T and N_g^C are the number of PCPs in group g who were in the treatment and control group respectively in the CMS study; N_*^T and N_*^C are the number of PCPs with any HCCI quetiapine prescribing who were in the treatment and control group in the CMS study. Given the randomization, the weights for control PCPs are approximately 2 in the numerator (ω_i^g) and denominator (ω_i^*).

These calculations yield projections for Medicare and private insurance. The projections for Medicare + private insurance combined are produced by adding the private and Medicare numerators, adding the private and Medicare denominators, and taking the ratio of the two sums.

E Additional Results from Analysis Plan

We pre-specified several additional analyses that we do not report in the main text. For completeness, we present and discuss them here. Appendix Table A9 reports additional outcomes for prescribers. First we report effects on new fills and refills using an alternative approach to the one used in the main text. In the approach here, a new fill is the first fill by a patient from the prescriber using a one year lookback period, and a refill is all other fills. While we pre-specified this approach, we found that churn in and out of private insurance coverage meant that many patients had incomplete lookback periods, leading to misclassification of refills as new fills. In the main text we take a different approach that uses the refill flag in the prescription dispense, which is reported by the pharmacy on the claim and is not subject to misclassification if the patient has an incomplete lookback period. Consistent with churn causing misclassification, we find smaller reductions in new fills here for private insurance than we do with the approach in the main text. Next, to get a sense of effects on the typical daily dose prescribed, we report effects on milligrams per day supply, dividing the former by the latter. This outcome is only defined for PCPs who prescribed some quetiapine in the outcome period (N=1,895 in private insurance and N=3,512 in Medicare). We do not detect an effect in private insurance but note a positive and significant effect in Medicare, consistent with prescribers curtailing relatively low-dose prescriptions due to the letter.

Subsequent rows of Appendix Table A9 report treatment effect estimates by quartiles of *ex ante* quetiapine prescribing volume (defined as the total of private insurance and Medicare prescribing). We counted prescribing during the 1 year pre-intervention period, a post-hoc modification from the analysis plan, which anticipated 9 months, because we sought to match our other analyses which generally used a one year pre-intervention period. Because a large number of study PCPs did not prescribe any quetiapine in HCCI data in the baseline period, quartile 1 contains all of them and is larger than one-fourth of the sample; these PCPs are missing from quartile 2, which is smaller than one-fourth. Across the quartiles absolute effect estimates are always negative and they expand in magnitude at higher quartiles for both private insurance and Medicare prescribing. Effects are only statistically significant for Medicare prescribing for quartiles 3 and 4. Percent effect estimates peak at quartile 2 for private insurance and quartile 3 for Medicare.

The final rows of the table display effects on prescribing to patients in the four appropriateness

groups but use the pre-specified algorithm to classify patients. That algorithm had imperfect fidelity with systematic reviews on quetiapine prescribing, and the main text reports findings using an updated and corrected algorithm. The original algorithm also only uses diagnoses reported prior to the start of the intervention, hampering its ability to classify the appropriateness of prescribing (it leaves over half of private insurance prescribing and about half of Medicare prescribing in the unknown appropriateness category). Still, the results are robust to the pre-specified approach: we find significant reductions in guideline-concordant prescribing in private insurance and significant reductions in guideline-concordant and low-value prescribing (and unknown appropriateness prescribing) in Medicare. We discuss the original and updated algorithms in detail in Appendix A.

Appendix Table A10 reports the remaining pre-specified patient outcomes. The first three outcomes are alternative definitions of quetiapine receipt. As expected, the fills measure is similar in percent terms to the days measure reported in the main text; fills differs only because it ignores the days supply on fills, counting those with a short or long supply of medication equally. Effects on quetiapine cost are noisily measured, a pattern we also observed at the prescriber level. While effects on this outcome were not statistically significant, the confidence intervals on the percent effects easily include the point estimates of the effects on days supply. A similar pattern occurs for quetiapine milligrams where effects are negative, insignificant, and more noisily measured than effects on days supply.

The next two measures are indicators for discontinuation in 2016Q4, i.e. the patient had no dispenses during this time, and dose reduction in 2016Q4, i.e. the patient received a lower dose in milligrams per day during this quarter as compared to the quarter before the intervention. The rate of dose reduction is lower than discontinuation because many patients already did not receive quetiapine during the last quarter before the intervention and so their dose could not be further reduced. Point estimates on these outcomes are all positive indicating less quetiapine receipt, but only reach statistical significance for dose reduction for Medicare patients.

We further pre-specified tests of whether patients were substituted to quetiapine alternatives. The next three outcomes report these tests for benzodiazepines, non-benzodiazepine insomnia drugs, and antidepressants, and do not detect any changes.

The subsequent four outcomes measure hospital encounters for substance use disorder (defined as visits with a principal diagnosis in AHRQ Clinical Classification Software categories 660 or 661)

and for mental health reasons (principal diagnosis in Clinical Classification Software categories 650-652, 655-659, 662, 663, or 670), looking separately at ED visits and inpatient stays (Agency for Healthcare Research and Quality, 2017, 2019). Of the 8 estimates, we only detect a statistically significant effect (a reduction) on ED visits for mental health reasons for Medicare patients.

Next, given that differential disenrollment between treatment and control would lead to potentially spurious findings of treatment effects, we conducted a simple test of whether treatment or control patients remained enrolled in coverage at the same rate. By December 2016, only about half of private insurance patients and two-thirds are Medicare patients remained covered. We did not detect a difference in enrollment rates between treatment and control patients in either insurer group, however.

The final rows of the table report effects dividing the outcome of quetiapine days received into three mutually exclusive and exhaustive sources: the patient's baseline prescriber to whom they were attributed, other prescribers who did not have psychiatric specialization, and other prescribers who had psychiatric specialization. The effects on receipt from the three sources sum to approximately the days supply treatment effect in Table 3, but do not exactly sum to it because the baseline control is different in each regression (the control is the patient's quetiapine receipt from the given source during the baseline period). The results show that in an accounting sense, for both private insurance and Medicare patients, the bulk of the cutback comes from the baseline prescriber with some compounding reductions from other prescribers. None of these effects is significant at the 5% level, and only the reduction from the baseline prescriber for Medicare patients is significant at the 10% level.

Appendix Figures

Department of Health & Human Services
7500 Security Boulevard, Mail Stop AR-18-50
Baltimore, Maryland 21244-1850

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES
CENTER FOR PROGRAM INTEGRITY

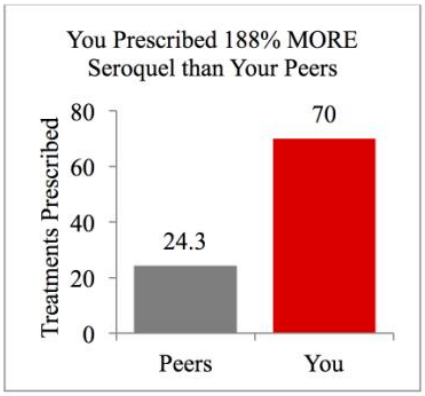
April 20, 2015

Pat Q. Provider MD
1234 Main St
Columbia, MD 21045
NPI: 1234567890 / Specialty: General Care Practitioner

Re: Your Seroquel prescribing is under review by the Center for Program Integrity.

Dear Dr. Provider,

The figure to the right displays your prescribing of Seroquel treatments (Seroquel, Seroquel XR, or generic quetiapine) compared to other general care practitioners in Maryland.



As can be seen, **you prescribed far more treatments – 188% more – than similar prescribers within your state.** In turn, you have been flagged as a markedly unusual prescriber, subject to review by the Center for Program Integrity.

We recognize that some flagged practitioners have appropriate reasons for this pattern. However, we have seen that other practitioners may drift into prescribing patterns that would be considered medically unjustified or abusive. Abusive prescribing can lead to extensive audits and even revocation of Medicare billing privileges.

We hope that you will use this information to see if your high prescribing level is consistent with the latest standards of care. To assist in your monitoring efforts, CMS will periodically send you letters with our most recent information about your Seroquel prescribing. **We may contact you at a later date to ask what steps, if any, you have taken in response to our communications.**

Read on for more information about the methodology used to analyze your prescribing behavior and to learn what actions to take next.

Sincerely,

[redacted]
Investigations and Audit Group

Figure A1 – Sample Intervention Letter

Appendix Tables

Table A1

Effects on Additional Prescribing Volume Measures

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Insurer	Private Insurance			Medicare			P-Val, %
Outcome	Control Mean	Treatment Effect	Percent Effect	Control Mean	Treatment Effect	Percent Effect	Effects Equal
Fills	6.1	-0.7	-11.6%	30.2	-4.9	-16.2%	[0.438]
		(0.3)	(5.3%)		(1.0)	(3.2%)	
New Fills*	2.53	-0.45	-17.8%	11.24	-2.26	-20.2%	[0.754]
		(0.15)	(5.9%)		(0.58)	(5.1%)	
Refills*	3.61	-0.26	-7.3%	18.99	-2.79	-14.7%	[0.268]
		(0.22)	(6.0%)		(0.66)	(3.5%)	
Cost	403.1	-44.9	-11.1%	1,417.8	-188.2	-13.3%	[0.859]
		(44.0)	(10.9%)		(80.1)	(5.7%)	
ln(Cost+1)† #		-0.217			-0.189		[0.031]
		(0.058)			(0.065)		
Total Milligrams	35,199.4	-4,995.3	-14.2%	140,263.2	-14,330.0	-10.2%	[0.547]
		(2,095.0)	(6.0%)		(5,019.0)	(3.6%)	
Days (2015-2016)	135.3	-16.9	-12.5%	658.2	-108.1	-16.4%	[0.451]
		(6.5)	(4.8%)		(16.5)	(2.5%)	
Days (eligible in December 2017)† ‡	115.9	-14.2	-12.2%	831.1	-152.7	-18.4%	[0.373]
		(7.7)	(6.6%)		(26.9)	(3.2%)	
Unique Patients (2015)	0.43	-0.05	-11.5%	1.62	-0.22	-13.3%	[0.736]
		(0.02)	(4.9%)		(0.04)	(2.2%)	
Unique Patients (2016)	0.61	-0.07	-12.2%	2.12	-0.44	-21.0%	[0.166]
		(0.04)	(5.9%)		(0.06)	(2.8%)	
Unique Patients (2017)	0.52	-0.06	-11.2%	2.25	-0.40	-17.7%	[0.396]
		(0.04)	(7.1%)		(0.08)	(3.4%)	

N=5,055. Notes: Table reports estimates for prescriber-level outcomes for private insurance (columns 1-3) and Medicare (columns 4-6). Each row presents an alternative measure of quetiapine prescribing volume during the outcome period (April 21, 2015 through December 31, 2017). See text for more detail. Columns 1 and 4 report the mean outcome for control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (1). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for private insurance and Medicare are equal. Robust standard errors in parentheses. P-values in brackets.

* Identified using the refill flag on the claim. The analysis plan pre-specified using whether the fill was the first for the patient-prescriber in the last year. This approach tended to mis-classify fills because patients frequently churned off coverage. Appendix E reports those results for completeness.

† Outcome not pre-specified.

Because the outcome is logged, these treatment effect estimates can be multiplied by 100 and interpreted as the log-point effect of the intervention on the cost of quetiapine covered.

‡ Days supplied to patients still enrolled (and, for private insurance, still under age 65) in December 2017.

Table A2

Summary Statistics of Baseline Patients

	(1)	(2)	(3)	(4)
Patient Cohort	Private Insurance		Medicare	
Characteristic	Control	Treatment	Control	Treatment
Age Band (Years)				
0-17	1.6%	1.9%		
18-25	9.5%	7.5%		
25-34	12.5%	15.9%	0.6%	0.9%
35-44	20.9%	21.4%	3.2%	3.0%
45-54	27.1%	28.0%	10.2%	11.6%
55-64	28.2%	25.3%	18.7%	18.4%
65-74			25.6%	24.5%
75-84			24.3%	23.0%
85+			17.4%	18.3%
Dual (Medicare-Medicaid) Eligible*	N/A	N/A	25.0%	27.0%
Female	58.1%	57.3%	62.7%	64.0%
Days of Quetiapine, Baseline Period	164.2 (141.1)	152.4 (135.1)	233.3 (161.9)	234.8 (159.4)
Appropriateness for Quetiapine				
Guideline-Concordant	51.1%	50.0%	57.6%	57.6%
Intermediate Evidence	11.9%	11.8%	7.5%	7.5%
Low-Value	16.0%	17.0%	20.8%	20.7%
Unknown	20.9%	21.2%	14.0%	14.2%
Enrolled December 2015	76.0%	74.0%	84.1%	83.8%
Enrolled December 2016	48.9%	51.5%	65.3%	66.0%
Months Enrolled, Outcome Period	18.8 (11.8)	18.9 (11.9)	23.4 (11.6)	23.6 (11.6)
N	974	1,006	3,837	3,547
P-value, omnibus test of equality	0.230		0.697	

Notes: This table reports summary statistics of the baseline patients of the study prescribers. Columns 1 and 2 consider baseline patients covered by private insurance who received quetiapine from one control arm prescriber and one treatment arm prescriber, respectively. Columns 3 and 4 consider baseline patients on Medicare Advantage. Binary variables displayed as percentages and continuous variables displayed as means (standard deviations). See text for more details on how patients are classified into appropriateness categories.

* Among the 69.5% of Medicare patients for whom dual status was observed.

Table A3

List of Drugs Included in Each Category

Drug Category	Drugs Included
Quetiapine	Quetiapine
Atypical Antipsychotics (Excluding Quetiapine)	Aripiprazole, Asenapine, Brexiprazole, Cariprazine, Clozapine, Iloperidone, Lurasidone, Olanzapine, Paliperidone, Pimavanserin, Risperidone, Ziprasidone
First-generation Antipsychotics	Chlorpromazine, Fluphenazine, Haloperidol, Loxapine, Molindone, Perphenazine, Pimozide, Thioridazine, Thiothixene, Trifluoperazine
Antidepressants	Amitriptyline, Amoxapine, Bupropion, Citalopram, Clomipramine, Desipramine, Desvenlafaxine, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Imipramine, Isocarboxazid, Maprotiline, Milnacipran, Mirtazapine, Nefazodone, Nortriptyline, Paroxetine, Phenelzine, Protriptyline, Selegiline, Sertraline, Tranylcypromine, Trazodone, Trimipramine, Venlafaxine, Vilazodone
Benzodiazepines	Alprazolam, Chlordiazepoxide, Clobazam, Clonazepam, Clorazepate, Diazepam, Estazolam, Flunitrazepam, Flurazepam, Halazepam, Lorazepam, Midazolam, Oxazepam, Prazepam, Quazepam, Temazepam, Triazolam
Insomnia (Excluding Benzodiazepines)	Doxepin, Eszopiclone, Ramelteon, Suvorexant, Tasimelteon, Zaleplon, Zolpidem

We used the following sources:
Antipsychotics: all included in 2016 CMS data, https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Part-D-Prescriber.html
Antidepressants: https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ad-adult-dosingchart.pdf
Benzodiazepines: https://www.cdc.gov/drugoverdose/resources/data.html
Insomnia: Non-benzodiazepine, non-barbituate prescription sleep aids according to https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm101557.htm

Table A4

Effects on Prescribing of Substitute or Alternative Medications

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Insurer	Private Insurance			Medicare			P-Val, %
	Control	Treatment	Percent	Control	Treatment	Percent	Effects
Medication	Mean	Effect	Effect	Mean	Effect	Effect	Equal
Other Atypical	171.3	-4.0	-2.3%	782.8	-18.4	-2.3%	[0.995]
Antipsychotics		(8.7)	(5.1%)		(25.7)	(3.3%)	
First-Gen	6.9	0.6	8.3%	124.9	-10.3	-8.2%	[0.404]
Antipsychotics		(1.3)	(19.2%)		(7.3)	(5.8%)	
Benzodiazepines	2,367.6	28.6	1.2%	5,881.6	41.9	0.7%	[0.851]
		(54.8)	(2.3%)		(131.4)	(2.2%)	
Antidepressants	6,011.7	270.3	4.5%	13,883.3	232.2	1.7%	[0.181]
		(107.4)	(1.8%)		(243.1)	(1.8%)	
Insomnia (excl.	1,073.2	17.2	1.6%	1,128.3	-2.0	-0.2%	[0.577]
Benzo.)		(26.6)	(2.5%)		(28.9)	(2.6%)	

N=5,055. Notes: Table reports estimates for prescriber-level outcomes for private insurance (columns 1-3) and Medicare (columns 4-6). Each row presents prescribing of a potential substitute or alternative drug class during the outcome period (April 21, 2015 through December 31, 2017). See text for more detail. Columns 1 and 4 report the mean outcome for control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (1). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for private insurance and Medicare are equal. Robust standard errors in parentheses. P-values in brackets.

Table A5

Effects on Prescribing by Patient Age or Appropriateness

Insurer	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Private Insurance			Medicare			
Group	Control Mean	Treatment Effect	Percent Effect	Control Mean	Treatment Effect	Percent Effect	P-Val, % Effects Equal
Prescribing to Patients in Specified Age Bin							
0-17	2.0	0.7	37.6%				
		(1.1)	(55.8%)				
18-24	9.1	0.4	4.7%				
		(1.7)	(18.5%)				
25-34	19.3	0.0	0.1%	4.4	1.8	40.3%	[0.216]
		(2.6)	(13.4%)		(1.3)	(30.0%)	
35-44	39.7	-1.6	-4.0%	28.8	-2.1	-7.5%	[0.820]
		(4.1)	(10.2%)		(3.4)	(11.6%)	
45-54	60.9	-6.5	-10.6%	98.3	-12.5	-12.7%	[0.824]
		(4.7)	(7.8%)		(6.2)	(6.3%)	
55-64	78.4	-17.8	-22.7%	209.3	-31.0	-14.8%	[0.310]
		(5.3)	(6.8%)		(9.9)	(4.7%)	
65+				753.6	-143.8	-19.1%	
					(24.2)	(3.2%)	
Prescribing to Patients in Specified Appropriateness Group							
Guideline-Concordant	104.4	-17.7	-17.0%	638.2	-111.0	-17.4%	[0.950]
		(6.7)	(6.4%)		(21.5)	(3.4%)	
with insomnia†	44.0	-11.2	-25.5%	224.7	-51.5	-22.9%	[0.802]
		(4.2)	(9.5%)		(10.4)	(4.6%)	
without insomnia†	60.4	-6.8	-11.3%	413.5	-61.9	-15.0%	[0.669]
		(4.8)	(8.0%)		(16.3)	(3.9%)	
Intermediate Evidence	29.1	-0.4	-1.2%	103.4	-17.9	-17.3%	[0.149]
		(2.9)	(10.1%)		(5.9)	(5.7%)	
Low Value / Inappropriate	29.1	-4.0	-13.9%	200.5	-33.7	-16.8%	[0.773]
		(2.8)	(9.7%)		(9.5)	(4.7%)	
Unknown	46.8	-3.0	-6.5%	152.3	-27.3	-17.9%	[0.254]
		(4.3)	(9.2%)		(8.4)	(5.5%)	

N=5,055. Notes: Table reports estimates for prescriber-level outcomes for private insurance (columns 1-3) and Medicare (columns 4-6). Each row counts quetiapine prescribing in days supply to patients in the specified age bin or appropriateness group during the outcome period (April 21, 2015 through December 31, 2017). See text for descriptions of the appropriateness groups and the algorithm used to classify patients. Private insurance patients age 65+ are omitted here (and throughout the study) because their status as Medicare patients is uncertain. Columns 1 and 4 report the mean outcome for control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (1). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for private insurance and Medicare are equal. Robust standard errors in parentheses. P-values in brackets.

† Outcome not pre-specified.

Table A6

Effects on Baseline Patients (Continuously Enrolled Subsample)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Patient Cohort	Private Insurance (N=610)			Medicare (N=3,684)			P-Val, %
Outcome	Control Mean	Treatment Effect	Percent Effect	Control Mean	Treatment Effect	Percent Effect	Effects Equal
Quetiapine Days Received	481.5	-67.5	-14.0%	632.6	-37.3	-5.9%	[0.195]
		(28.4)	(5.9%)		(14.3)	(2.3%)	
Antipsychotics Days Received	547.6	-80.8	-14.8%	711.2	-34.4	-4.8%	[0.100]
		(31.3)	(5.7%)		(15.1)	(2.1%)	
Inpatient Stays	0.64	-0.17	-27.1%	0.95	0.06	5.8%	[0.106]
		(0.12)	(19.4%)		(0.06)	(5.8%)	
ED Visits	1.63	-0.03	-1.5%	2.21	0.09	4.3%	[0.713]
		(0.22)	(13.7%)		(0.18)	(8.0%)	
Psychiatrist Visits	1.86	-0.35	-18.8%	1.64	0.10	6.3%	[0.223]
		(0.34)	(18.4%)		(0.15)	(9.1%)	
Psychologist Visits	0.54	0.43	80.3%	1.23	-0.07	-5.4%	[0.219]
		(0.33)	(61.9%)		(0.39)	(31.6%)	

Notes: Table repeats the pre-specified outcomes of Table 3 on the subsample of baseline patients who were continuously enrolled during the outcome period. We omit subgroup analyses by appropriateness due to small sample sizes.

The table reports estimates for outcomes for privately insured baseline patients (columns 1-3) and baseline patients on Medicare (columns 4-6). See text for more details on the construction of the baseline patient cohorts. Each measure counts health care use during the outcome period (April 21, 2015 through December 31, 2017). Columns 1 and 4 report the mean outcome for baseline patients of control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (2). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for the private insurance and Medicare cohorts are equal. Robust standard errors clustered at the baseline prescriber level in parentheses. P-values in brackets.

Table A7

Prescribing of Outlier PCPs in Targeting Simulations and Projected Effects

Prescriber Group	(1) Medicare Outliers	(2) Private Ins. Outliers	(3) Medicare + Private Outliers
A. No Quetiapine Prescribing, 2013-2014, %			
in Medicare	0.0	56.2	9.6
in Private Insurance	71.9	0.0	50.9
in Medicare+Private Combined	0.0	0.0	0.0
B. Quetiapine Days Supplied, 2013-2014, average			
in Medicare	1,580.8	287.3	1,441.0
in Private Insurance	105.2	639.9	334.3
in Medicare+Private Combined	1,686.0	927.2	1,775.3
C. Projected National Change in Primary Care Quetiapine Days from Intervening on Outliers, %			
in Medicare	-4.67	-1.39	-4.42
in Private Insurance	-1.13	-3.43	-2.24
in Medicare+Private Combined	-3.88	-1.84	-3.93
N	5,076	5,055	5,075

Notes: Table reports statistics or projections for physicians in each group. Groups are defined as physicians who are outliers in prescribing to Medicare patients (column 1), to privately insured patients (column 2), and to Medicare and private insurance combined (column 3). Panel A reports the percent of prescribers with no prescribing in the given insurer in 2013-2014, the period used by the algorithm to identify outliers. Panel B reports the average level of quetiapine days supplied during the 2013-2014 period. Finally, Panel C reports the projected national percent reduction in quetiapine days supplied by all PCPs in the given insurer during the outcome period (April 2015 to end-2017) if the entire outlier population were treated with letters. All calculations done using HCCI data only. See text for more details.

Table A8

List of Diagnosis Codes by Condition

Condition	ICD-9	ICD-10
Guideline-Concordant Conditions		
Bipolar Disorder	Multi-Level CCS Code 5.8.1	F30.10-F30.13, F30.2, F30.3, F30.4, F30.8, F30.9, F31.0, F31.10-F31.13, F31.2, F31.30, F31.31, F31.32, F31.4, F31.5, F31.60-F31.64, F31.70-F31.78, F31.81, F31.89, F31.9, F33.8, F34.81, F34.89, F34.9, F39
Schizophrenia	Multi-Level CCS Code 5.10	Multi-Level CCS Code 5.10
Guideline-Concordant or Intermediate Value Depending on Presence of Antidepressant		
Major Depression	293.83, 296.2X, 296.3X	F06.30, F32.9, F32.0, F32.1, F32.2, F32.3, F32.4, F32.5, F33.9, F33.0, F33.1, F33.2, F33.3, F33.41, F33.42
Intermediate Value Condition		
Generalized Anxiety Disorder	300.02	F41.1
Low-Value Conditions		
Dementia / Alzheimer's	331.0, 331.1, 331.11, 331.19, 331.2, 331.7, 290.0, 290.10-290.12, 290.20, 290.21, 290.3, 290.40-290.43, 294.0, 294.1, 294.10, 294.11, 294.20, 294.21, 294.8, 797, 290.13	F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F04, F05, F06.1, F06.8, G13.8, G30.0, G30.1, G30.8, G30.9, G31.1, G31.2, G31.01, G31.09, G94, R41.81, R54
Insomnia	327.0, 327.01, 327.02, 327.09, 307.41, 307.42, 291.82, 292.85, 780.51, 780.52	F10.182, F10.282, F10.982, F11.182, F11.282, F11.982, F13.182, F13.282, F13.982, F14.182, F14.282, F14.982, F15.182, F15.282, F15.982, F19.182, F19.282, F19.982, F51.02, F51.09, F51.01, F51.03, G47.01, F51.04, F51.05, G47.30, G47.00
PTSD	309.81	F43.10, F43.12
Obsessive-Compulsive Disorder	300.3, 301.4	F42.2, F42.3, F42.8, F42.9, F60.5
Personality Disorder	301.X, 301.XX	F21, F34.0, F34.1, F60.0-F60.7, F60.9, F60.81, F60.89, F68.10, F68.11, F68.12, F68.13, F69
Eating Disorder	Multi-Level CCS Code 5.15.2	F50.00, F50.9, F50.2, F98.3, F98.21, F50.89, F50.81, F50.82, F50.89, F98.29
Alcohol Use Disorder	Multi-Level CCS Code 5.11	Multi-Level CCS Code 5.11
Additional Intermediate Value Condition (only used in pre-specified algorithm)		
Depression (Ex. Major)	311, 300.4, 309.0, 309.1. 309.28, 298.0	F34.1, F43.21, F43.23, F32.9

Notes: When possible, we deferred to AHRQ Clinical Classification Software (CCS) groups. When the appropriate CCS group was a level 2 category, we used the ICD-9 and 10 codes from that group. Because level 3 categories are not yet available for ICD-10, when the group was a level 3 category (bipolar disorder, eating disorders), we used the given ICD-9 codes and found the relevant ICD-10 codes using equivalency mapping tables. ICD-9 and 10 codes for Dementia/Alzheimer's and Personality Disorder were taken from the Chronic Conditions Warehouse. For the other conditions, we sought out relevant academic literature and performed internet searches; this process typically identified ICD-9 codes which we then mapped to ICD-10 codes using equivalency tables.

Table A9

Additional Prescriber-Level Outcomes from Analysis Plan

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Insurer	Private Insurance			Medicare			P-Val, %
	Control	Treatment	Percent	Control	Treatment	Percent	Effects
Outcome	Mean	Effect	Effect	Mean	Effect	Effect	Equal
New Fills	1.0	-0.1	-8.6%	3.2	-0.7	-22.4%	[0.071]
(Lookback)		(0.1)	(7.0%)		(0.1)	(3.5%)	
Refills	5.1	-0.6	-12.2%	27.1	-4.3	-15.9%	[0.564]
(Lookback)		(0.3)	(5.7%)		(0.9)	(3.4%)	
MG /	145.5	-0.6	-0.4%	125.3	11.5	9.2%	[0.031]
Days Supply*		(5.3)	(3.6%)		(3.6)	(2.9%)	
Quetiapine Days by Quartiles of Ex Ante (1-Year Baseline Period) Private + Medicare Prescribing							
Quartile 1	38.2	-4.3	-11.4%	159.7	-25.1	-15.7%	[0.819]
(N=1,778)		(6.4)	(16.8%)		(17.5)	(10.9%)	
Quartile 2	115.7	-19.8	-17.1%	500.1	-69.7	-13.9%	[0.847]
(N=782)		(17.8)	(15.4%)		(42.4)	(8.5%)	
Quartile 3	187.3	-25.0	-13.3%	960.8	-202.6	-21.1%	[0.438]
(N=1,245)		(17.2)	(9.2%)		(50.8)	(5.3%)	
Quartile 4	521.3	-52.9	-10.2%	2,859.8	-457.3	-16.0%	[0.421]
(N=1,250)		(35.8)	(6.9%)		(104.0)	(3.6%)	
Quetiapine Days to Patients in Specified Appropriateness Group, Pre-Specified Approach[§]							
Guideline-	39.2	-7.4	-18.9%	297.9	-51.4	-17.2%	[0.858]
Concordant		(3.4)	(8.7%)		(11.3)	(3.8%)	
Intermediate	29.7	-4.8	-16.1%	145.4	-11.2	-7.7%	[0.454]
Evidence		(3.0)	(10.1%)		(7.4)	(5.1%)	
Low Value /	14.0	-0.5	-3.5%	126.3	-19.4	-15.4%	[0.453]
Inappropriate		(2.1)	(14.9%)		(7.2)	(5.7%)	
Unknown	126.6	-8.1	-6.4%	524.9	-117.9	-22.5%	[0.039]
		(8.8)	(6.9%)		(24.4)	(4.7%)	

N=5,055. Notes: Table reports estimates for prescriber-level outcomes for private insurance (columns 1-3) and Medicare (columns 4-6) that were defined in the analysis plan but were not otherwise reported in the main text. Each row presents prescribing of a different quetiapine measure during the outcome period (April 21, 2015 through December 31, 2017). See appendix and analysis plan for more details. Columns 1 and 4 report the mean outcome for control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (1). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for private insurance and Medicare are equal. Robust standard errors in parentheses. P-values in brackets.

* N=1,895 for private insurance and N=3,512 for Medicare because this outcome is only defined for physicians with quetiapine prescribing in the outcome period.

[§] Uses the pre-specified approach to assign patients to appropriateness groups rather than the preferred (post-hoc) approach. See appendix for more details on how the approaches differ.

Table A10

Additional Patient-Level Outcomes from Analysis Plan

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Patient Group	Private Insurance (N=1,980)			Medicare (N=7,384)			P-Val, %
	Control	Treatment	Percent	Control	Treatment	Percent	Effects
Outcome	Mean	Effect	Effect	Mean	Effect	Effect	Equal
Quetiapine Fills	7.3	-0.7	-9.6%	11.7	-0.8	-6.9%	[0.665]
		(0.4)	(5.5%)		(0.3)	(2.6%)	
Quetiapine Cost	794.9	-88.7	-11.2%	711.8	-1.2	-0.2%	[0.423]
		(93.5)	(11.8%)		(48.8)	(6.9%)	
Quetiapine MG	54,019.6	-5,936.7	-11.0%	68,052.3	-1,044.5	-1.5%	[0.206]
		(3,662.3)	(6.8%)		(2,225.3)	(3.3%)	
Indicator for Discontinued 2016Q4	0.76	0.00	0.1%	0.62	0.02	3.2%	[0.316]
		(0.02)	(2.5%)		(0.01)	(1.9%)	
Indicator for Dose Reduced 2016Q4	0.50	0.02	4.0%	0.50	0.03	5.8%	[0.731]
		(0.02)	(4.6%)		(0.01)	(2.6%)	
Benzodiazepine Days	162.5	0.8	0.5%	239.4	1.4	0.6%	[0.992]
		(10.3)	(6.3%)		(6.9)	(2.9%)	
Non-Benzodiazepine Insomnia Drug Days	62.8	-0.8	-1.3%	42.3	3.2	7.7%	[0.449]
		(6.0)	(9.6%)		(2.9)	(6.9%)	
Antidepressants Days	318.4	2.6	0.8%	522.6	4.8	0.9%	[0.987]
		(16.9)	(5.3%)		(11.8)	(2.3%)	
ED Visits for Substance Use Disorder	0.04	0.01	22.2%	0.03	-0.01	-19.8%	[0.369]
		(0.01)	(36.3%)		(0.01)	(29.7%)	
ED Visits for Mental Health Reasons	0.04	0.01	26.5%	0.07	-0.05	-78.3%	[0.038]
		(0.01)	(35.2%)		(0.02)	(36.2%)	
Inpatient Stays for Substance Use Disorder	0.07	0.02	33.7%	0.02	0.00	6.1%	[0.528]
		(0.03)	(34.6%)		(0.00)	(26.2%)	
Inpatient Stays for Mental Health Reasons	0.04	0.01	14.6%	0.07	0.00	2.6%	[0.727]
		(0.01)	(31.1%)		(0.01)	(15.4%)	
Enrolled December 2016*	0.49	0.03		0.65	0.01		
		p=0.264			p=0.595		
Quetiapine Days by Source of Receipt							
Baseline Prescriber	188.5	-17.4	-9.2%	296.5	-17.0	-5.7%	[0.599]
		(11.3)	(6.0%)		(8.9)	(3.0%)	
Non-Psych Prescribers (ex Baseline)	56.4	-4.5	-8.1%	120.2	-3.0	-2.5%	[0.662]
		(6.7)	(11.8%)		(6.1)	(5.1%)	
Psych Prescribers (ex Baseline)	15.7	-1.9	-12.1%	24.3	-2.1	-8.7%	[0.892]
		(3.7)	(23.5%)		(2.6)	(10.7%)	

Notes: Table reports estimates for outcomes for privately insured baseline patients (columns 1-3) and baseline patients on Medicare (columns 4-6) that were defined in the analysis plan but were not otherwise reported in the main text. See text for more details on the construction of the baseline patient cohorts. See appendix and analysis plan for more details on the outcomes. Each measure counts health care use during the outcome period (April 21, 2015 through December 31, 2017) unless otherwise stated. Columns 1 and 4 report the mean outcome for baseline patients of control prescribers. Columns 2 and 5 report the treatment effect estimate from equation (2). Columns 3 and 6 divide the treatment effect by the control mean to produce a percent effect. Column 7 reports the p-value from a test that the percent effects for the private insurance and Medicare cohorts are equal. Robust standard errors clustered at the baseline prescriber level in parentheses. P-values in brackets.

* Reports simple difference in means and p-value of test of equality of means between treatment and control, p-value of test clustered at baseline prescriber level.