Common Practice: Spillovers from Medicare on Private Health Care*

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January 26, 2022

Abstract

Efforts to raise the productivity of the U.S. health care system have proceeded slowly. One potential explanation is the fragmentation of payment across insurers. Each insurer's efforts to improve care could influence how doctors practice medicine for other insurers, leading to unvalued externalities. We study these externalities by examining the unintended private insurance spillovers of a public insurer's intervention. In 2015, Medicare randomized warning letters to doctors to curtail overuse of antipsychotics. Even though the letters did not mention private insurance, they reduced prescribing to privately insured patients by 12%. The reduction to Medicare patients was 17%, and we cannot reject one-for-one spillovers. If private insurers conducted a similar intervention with their own limited information, they would stem half as much prescribing as a social planner able and willing to better target the intervention. Our findings establish that insurers can affect health care well outside their direct purview, raising the question of how to match their private objectives with their scope of influence.

JEL Classification: H44, I13, I18

Keywords: physician practice styles; prescribing; spillovers; antipsychotics; common agency

*We thank Loren Baker, Sarah Berkson, Janet Currie, Amy Finkelstein, Tal Gross, Kate Ho, Amanda Kowalski, Neale Mahoney, Maxim Pinkovskiy, Brad Shapiro, several anonymous referees, and participants in presentations at the Columbia Health Economics and Policy Seminar, Columbia HPM Lunch Seminar, Princeton University Center for Health and Wellbeing, ASSA/AEA HERO sessions, and AHRQ for their helpful comments. We gratefully acknowledge support from the Laura and John Arnold Foundation (all), National Institute on Aging K23 AG058806-01 (Barnett), and National Science Foundation Graduate Research Fellowship (Olenski). We acknowledge the assistance of the Health Care Cost Institute and its data contributors, Aetna, Humana, and UnitedHealthcare, in providing the claims data analyzed in this study. The authors report no relevant financial conflicts of interest; Barnett and Sacarny assisted the Centers for Medicare and Medicaid Services in conducting the original trial this research analyzes, but were not compensated for this work. This research was approved by the Institutional Review Boards of Columbia University and the National Bureau of Economic Research.

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1 Introduction

Productivity-raising innovations in the U.S. health care system have often proceeded slowly. Classic examples of delayed adoption include low-cost, evidence-based treatments such as aspirin and beta-blockers; health information technology in the form of electronic medical records; and reforms to health payment mechanisms that favor value over volume (Cutler, 2011; Lee, McCullough and Town, 2013; Skinner and Staiger, 2015). One potential root of this phenomenon is the fragmented system that pays for care. Health care providers contract with an array of government and private insurers. When insurers try to raise the performance of health care providers, their efforts may have externalities that accrue to other insurers. For example, if one insurer tries to change how physicians treat its beneficiaries, those physicians may change how they treat all patients (Baker, 2003; Glied and Graff Zivin, 2002). As a result, fragmentation may yield weak incentives for insurers to invest in improving performance relative to the socially optimal level (Glazer and McGuire, 2002; Frandsen, Powell and Rebitzer, 2019). The extent to which such externalities occur in practice remains an open question.

This study provides evidence on how physicians behave when contracting with multiple health insurers. We show that one insurer's investment to improve quality of care generated large, unintended spillovers onto the health care covered by other insurers. Our research exploits a randomized controlled trial conducted by Medicare, the largest insurer in the U.S., which sent warning letters to doctors who heavily prescribed the most popular antipsychotic medication, quetiapine. Using data on private insurance patients covered by three of the five largest insurers in the U.S., we consider the external effects of these letters. These patients were neither mentioned in nor the focus of the Medicare letter.

We show that Medicare's investment in stemming use of antipsychotics also reduced their use outside Medicare. Following the intervention, treated doctors rapidly curtailed their prescribing of the antipsychotic in Medicare *and* private insurance compared to doctors in the control group (Figure 1). Treated physicians cut back by 17% in Medicare and 12% in private insurance. The direct and spillover effects are both unusually large compared to most physician quality improvement interventions; for example, a systematic review of audit and feedback interventions found a median effect of 1.3% (Ivers et al., 2012). We cannot reject that the spillover effect had the same magnitude

as the direct effect.

We next probe the mechanisms underlying the spillover. We explore whether the intervention encouraged physicians to consult the medical literature and update their beliefs about the returns to antipsychotics. Changes in beliefs could result in spillover effects if physicians draw upon these primitives when they treat all of their patients. Our findings are inconsistent with this mechanism: physicians did not cut back on other antipsychotics that have essentially the same guidelines but were not mentioned in the letter, they failed to tailor quetiapine cutbacks to patients who were observably poor candidates for antipsychotics, and they did not avoid reductions for patients who were observably better matched to quetiapine than other antipsychotics.

We note two alternative mechanisms with more support in the data. First, the letters could have imposed "moral costs" (c.f. Levitt and List, 2007) by highlighting prescribers' deviation from social or professional norms. If physicians consider the totality of their prescribing across insurers, they could cut back in private insurance, too. Second, letters could have changed expectations about Medicare penalties like audits and investigations. Spillovers on private insurance would then occur if physicians were unable or unwilling to tailor their treatment decisions by insurer. Indeed, we show that cutbacks in private insurance were concentrated on older "Medicare-like" patients, suggesting doctors may have tailored cutbacks to a correlate of Medicare, age, rather than Medicare itself. Physicians may have also believed (albeit incorrectly) that Medicare could observe their activity in private insurance and changed their behavior accordingly.

Taken together, the mechanisms we rule in imply that insurers have the power to affect how physicians practice medicine more generally. This power may be strongest when physicians treat similar patients in other insurers and when the intervening insurer can impose strong penalties, as large and public insurers like Medicare do.

Rich data on patient health outcomes provides evidence on the welfare impacts of the intervention and its spillovers. We consider whether the resource savings from reduced prescribing were offset by patient harms. We fail to detect adverse effects on patients in the form of emergency department visits and hospital stays. Doctors may have prescribed poorly to begin with, and their cutbacks could rectify prescribing that did not benefit patients in the first place. Alternatively, doctors could have used private information to appropriately cut back prescribing to patients who appeared to be good candidates to the econometrician.

Finally, as a window into how the fragmented payment system under-incentivizes similar interventions with spillovers, we simulate hypothetical interventions conducted by private insurers, Medicare, and a merged social planner with access to both datasets. The simulations use Medicare's approach to identify outliers, contact the same number of prescribers, and assume the same effects on prescribing as those estimated in the current study; we only vary the data used to select outliers. They show that private insurers would stem half as much prescribing as a social planner that observed all data and targeted the overall outliers. Private insurers' limited information on outside prescribing, as well as their objectives that ignore patients on other plans, reduce the social return on the intervention.

Our study builds on a theoretical and empirical literature on physician-insurer contracting in a principal-agent framework (e.g. Pauly, 1980). A key variant of this model considers physicians contracting with multiple insurers at once, an approach derived from the common agency model of Bernheim and Whinston (1986). Glazer and McGuire (2002) and Frandsen, Powell and Rebitzer (2019) set out conditions under which insurer principals can free ride on each other or fail to coordinate in contracting with health care provider agents. The result is the under-provision of performance-improving investments. A similar failure of insurers to coordinate could also drive the high administrative costs in the U.S. (Cutler and Ly, 2011).

The Medicare intervention provides a unique opportunity to study common agency in health care empirically. First, it was targeted at prescribing covered by Medicare – the letter did not mention private insurance prescribing, and Medicare did not track or have access to such data. Thus, changes in private insurance prescribing did not trivially derive from Medicare using its leverage to influence health care covered by other insurers. Second, the direct effects of the intervention on Medicare prescribing were large. It is therefore *a priori* reasonable that the intervention led to detectable spillovers. Large direct effects make it more plausible that a detected spillover is real and that a failure to detect a spillover reflects a true null.

To our knowledge, this study is the first to use a randomized intervention to show that one insurer's actions to change physician practice styles can affect the health care that physicians provide to patients covered by other insurers. The randomized treatment in the current study eliminates concerns about endogeneity. This feature is particularly useful for evaluating spillovers. When identification is questionable, an effect on a second-order outcome like a spillover could represent a

failure to address endogeneity rather than a true external impact.

Earlier literature on managed care plans generally found spillovers, but the non-random growth of managed care threatened causal inference (Baker, 2003). In the cross-section, Glied and Graff Zivin (2002) show that physicians who treat more managed care patients utilize a more judicious practice style for all patients. Two quasi-experimental studies have looked at cross-insurer spillovers, though not for doctors. Baicker, Chernew and Robbins (2013) find that Medicare managed care lowers the intensity of hospital treatment for the privately insured while Grabowski, Gruber and Angelelli (2008) show that nursing homes provide common levels of quality across self-pay and Medicaid patients. An adjacent literature has studied the effects of one insurer's payment changes on other insurers. Private insurers mimic Medicare's payment systems and relative prices for services (Clemens, Gottlieb and Molnár, 2015; Clemens and Gottlieb, 2017); a randomized Medicare hospital payment reform to lower costs of hip and knee replacements had similar effects on the private Medicare Advantage program, which was not a part of this reform (Einav et al., 2020; Wilcock et al., 2020). Appointment availability and utilization in one insurer depends on the payment rates of others, suggesting that spillovers can operate through demand channels (Garthwaite, 2012; Glied and Hong, 2018; Richards and Tello-Trillo, 2019).

Our findings speak to the nature of physician practice styles, and we view the intervention as a shock to practice styles over psychiatric prescribing. The extant literature has yet to demonstrate how physicians tailor treatment practices to insurers. We contribute by showing that the intervention changed practice styles in Medicare and private insurance together. This finding has broad implications for the health care system and efforts to change the practice of medicine because large practice style variations are essentially ubiquitous across treatment decisions made by physicians, even those that seem straightforward *ex ante* (Phelps and Mooney, 1993; Skinner, 2011; Skinner and Staiger, 2015). Contexts with variations include primary care (Fadlon and Van Parys, 2020), depression treatment (Currie and MacLeod, 2020), test ordering (Abaluck et al., 2016; Mullainathan and Obermeyer, 2019), heart attack treatment (Currie, MacLeod and Van Parys, 2016; Molitor, 2018), and use of caesarean sections (Epstein and Nicholson, 2009; Currie and MacLeod, 2017). Berndt et al. (2015) find that psychiatrists tend to concentrate their prescribing on one or a handful of antipsychotics. Physician beliefs, including beliefs with little support in clinical evidence, are strong predictors of spending variations across regions (Finkelstein, Gentzkow and Williams, 2018;

Cutler et al., 2019).

2 Background

The complexity and uncertainty around the use of antipsychotics make these drugs excellent objects of study for understanding physician practice styles. Quetiapine, the focus of this study, is the most commonly used antipsychotic medication in the U.S. (Gallini, Donohue and Huskamp, 2013). Antipsychotics like quetiapine are widely used to treat serious mental illness, and quetiapine is FDA-approved for schizophrenia, bipolar disorder, and, when alongside an antidepressant, major depression (Food and Drug Administration, 2020*b*,*a*). Physicians should have strong priors that quetiapine is effective for these conditions given the array of randomized trials and meta-analyses demonstrating reductions, often dramatic, in symptoms for these patients (Maglione et al., 2011; Leucht et al., 2012).

Quetiapine's main alternatives are other antipsychotics which fall into two classes: second-generation or "atypical" antipsychotics, including quetiapine; and older first-generation or "typical" medications (Alexander et al., 2011). Trials of antipsychotics have generally demonstrated comparable benefits across medications (Meltzer, 2013). However, there are meaningful differences in the side effects of these medications, making the match of patient to side effect profile the central task in selecting an antipsychotic. For example, a physician might prefer quetiapine for patients with insomnia because it leads to more pronounced sedation than other antipsychotics (Jibson, 2019).

Key to antipsychotic prescribing practice styles is how physicians use the drugs outside their FDA-approved indications (off-label prescribing). This prescribing is legal and happens across numerous pharmaceuticals. In some cases it is supported by strong clinical evidence, like β blockers for heart failure or anti-VEGF medications for macular degeneration (Largent, 2009; Rosenfeld et al., 2018); in other cases there is little evidence backing the uses, like antibiotics for the cold and flu or most psychiatric medications for patients with dementia (Alsan et al., 2015; Maust et al., 2018, 2020). AstraZeneca was fined for illegally marketing quetiapine for off-label indications but it is hard to attribute present-day patterns to that activity. Off-label use of antipsychotics long predates the introduction of quetiapine (Borson and Doane, 1997; Kales et al., 2011), it is not clear that the marketing effectively raised off-label prescribing (Shapiro, 2018), and the intervention began over 8

years after the marketing ended (U.S. Department of Justice, 2010).

Trials have extensively studied antipsychotics for off-label indications, yielding evidence for some common uses while providing less support for others. For two indications, generalized anxiety disorder and major depression (when used without an antidepressant), off-label prescribing has some benefits according to trials. The FDA failed to approve these labelings for quetiapine because its side effects are more severe than alternative medications (Food and Drug Administration, 2009). We expect physicians' beliefs on the value of quetiapine to be less clearly positive for these conditions compared to those with FDA approvals.

For other indications, quetiapine and other antipsychotics have small or even negative expected benefits. Their use in patients with dementia has been heavily studied and found to elevate the risk of death and numerous other adverse effects, prompting warnings from major medical specialty societies and the federal government (Reus et al., 2016; Maglione et al., 2011; American Geriatrics Society, 2019; OIG, HHS, 2011; Government Accountability Office, 2015). Despite the broad recognition that this use is harmful, the lack of any approved pharmaceutical for symptoms of dementia and the continued use of these drugs in this context suggests variations in beliefs across physicians. Other common off-label uses with little support in trials include insomnia, alcohol use disorder, and post-traumatic stress disorder (PTSD) (Maglione et al., 2011).

3 Intervention

The intervention was conducted by Centers for Medicare and Medicaid Services (CMS), the U.S. Office of Evaluation Sciences, and academic researchers. It was part of a larger program to test interventions informed by behavioral science to make prescribing safer in the Medicare program (Sacarny, Yokum and Agrawal, 2017).

This collaboration sought to test whether augmenting a peer comparison message with language about negative consequences and penalties for prescribers could improve the quality of Medicare prescribing. Randomized evaluations have found that letters that emphasize penalties raise tax payment, but there is less evidence on using this language in health care (Castro and Scartascini, 2015; Fellner, Sausgruber and Traxler, 2013). CMS chose high prescribers of quetiapine as the target following a report by a federal oversight agency that found high rates of questionable antipsychotic

prescribing in Medicare and case reports of patients abusing and reselling these drugs (Government Accountability Office, 2015; Klein-Schwartz, Schwartz and Anderson, 2014; Cubała and Springer, 2014).

3.1 Selection of Physicians

The study population was primary care physicians (PCPs, defined as physicians with a specialty of general practice, family practice, or internal medicine without additional specialization in psychiatry (National Uniform Claim Committee, 2021)) who were persistent outliers in prescribing quetiapine relative to other PCPs in the same state.[1] PCPs were chosen because they supplied a high volume of a powerful psychiatric medication yet lacked intensive psychiatric training. AstraZeneca was also fined for marketing quetiapine to PCPs (U.S. Department of Justice, 2010). PCPs play a key role in quetiapine prescribing in Medicare – in our data, in the year prior to this intervention, they supplied 52% of all quetiapine in Medicare but only 28% in private insurance.

CMS analyzed Medicare quetiapine prescribing from PCPs in 2013 and 2014. Those with fewer than 10 quetiapine dispenses in the year were removed. CMS identified outliers based on two volume measures: 1) the number of quetiapine prescriptions filled and 2) the number of quetiapine days across the fills. Outlier thresholds for each state-year-measure were calculated as the 75th percentile plus 0.25 times the interquartile range of physicians falling into the cell (Tukey, 1977). A physician had to clear the thresholds for both measures in 2013 and 2014. N=5,055 physicians became the study population.

The calculations did not adjust for differences in physicians' patient populations and they omitted prescriptions to long-term care patients, where overuse is likely most severe and most prone to lead to welfare losses. While these factors may have deteriorated the targeting of the intervention, a corollary is that study physicians tended to treat patients who were observably appropriate *as well as* questionable candidates for quetiapine – permitting the econometrician to study effects on both populations. We include all quetiapine prescribing in our analyses.

[1] For more details on the selection process, see the online supplement in Sacarny et al. (2018).

3.2 Intervention

The treatment letter combined a peer comparison emphasizing social and professional norms with penalty-focused language emphasizing the adverse consequences for physicians determined to be improper prescribers (Appendix Figure A1). It stated that the physician was responsible for many more quetiapine prescriptions than other PCPs in the same state. A bar graph displayed the physician's Medicare prescribing level in red and compared it to that of her average peer. The subject line stated that the physician's quetiapine prescribing was "under review by the Center for Program Integrity" – the division of CMS responsible for stemming fraud, waste, and abuse in Medicare. The body discussed the consequences of medically unjustified prescribing, like restrictions on receiving Medicare payments. It also indicated that physicians could expect to receive future communications from CMS. The placebo intervention was a letter and pamphlet discussing an unrelated Medicare provider enrollment regulation.

A random 50% of the 5,055 physicians were allocated to the treatment group and the remainder were allocated to the control group. CMS sent the treatment and placebo letters to the respective study groups in April 2015. The treatment group was also sent follow-up letters with updated prescribing data in August and October 2015. The control group was sent a clarification notice in June 2015 to address questions about the placebo message. Neither message to the control group mentioned quetiapine or antipsychotics.

3.3 Prior Findings from Medicare Data

Two prior clinical studies have analyzed the effects of these letters on Medicare prescribing but have not considered spillovers to patients outside Medicare. The intervention caused PCPs to become much less intensive prescribers of quetiapine in Medicare and led to no detected patient harms (Sacarny et al., 2018). It had no detectable peer effects on prescribers who worked with study PCPs (Sacarny, Olenski and Barnett, 2019). In this study, we access prescribing covered by the three HCCI insurers to focus on private insurance patients who were not tracked in the earlier works. When we study Medicare outcomes, our findings closely track the earlier publications.

4 Data and Methods

4.1 Data

Study data comes from HCCI, a repository of claims from three of the five largest health insurers in the U.S.: Aetna, Humana, and UnitedHealthCare (Health Care Cost Institute, 2021). It includes patients with Medicare Advantage, the managed care program in Medicare, and patients with private insurance, including the employer-sponsored and individual insurance markets. The availability of Medicare Advantage claims (which are tracked by CMS) and private insurance claims (which are not) allows us to capture direct and spillover effects side-by-side. The 2017 data includes 27.2 million privately insured lives with prescription drug coverage and 7.1 million Medicare covered lives with drug coverage.

The analyses use data from 2013-2017. Unless otherwise stated, we measure all outcomes from the day after letters were mailed through the end of the data period, April 21, 2015 through December 31, 2017.[2] We track prescribing using pharmacy claims and link records to the IBM Micromedex RED BOOK database (IBM Micromedex, 2021). Data on inpatient, outpatient, and physician encounters provides diagnosis codes to classify the appropriateness of prescribing. We also use this data to assess health care utilization. We remove private insurance patients age 65 and up since they are likely covered by Medicare.

4.2 Analytic Framework

Our main analyses are at the level of the physician and take the form:

$$y_i^n = \alpha^n + \beta^n \cdot TREAT_i + X_i^n \Gamma^n + \varepsilon_i^n \tag{1}$$

where i indexes physicians and $n \in \{P, M\}$ indexes private insurance or Medicare, respectively. y_i^n denotes an outcome of interest, $TREAT_i$ indicates assignment of the physician to the treatment group, and X_i^n is a set of statistical controls. Due to the random assignment, there is no need for controls to identify the treatment effect. However, covariates can improve precision when they

[2]We pre-specified that the outcome period would end on December 31, 2016, but later received 2017 data and modified the outcome period to include it. The effect on prescribing was essentially identical with the shorter outcome period (Appendix Table A1).

have explanatory power and thus reduce residual variation in the regression. Given the strong autocorrelation in prescribing volume, we pre-specified the inclusion of one control, the lagged outcome, in all analyses.

For each outcome we estimate separate regressions for private insurance and Medicare. We convert estimates of β^n to percent effects by dividing them by the mean for the control group. To assess the magnitude of spillovers, we use seemingly unrelated regression (SUR) to test equality of the percent effects between the two regressions.

An additional set of analyses tracks a cohort of baseline patients who received quetiapine from study physicians in the year prior to the intervention and takes the form:

$$y_j = \alpha^n + \beta^n \cdot TREAT_{i(j)} + X^n_{i(j)}\Gamma^n + Z_j\Delta^n + \epsilon_j \quad j \in J^n \tag{2}$$

where j indexes patients, $i(j)$ is the physician from which patient j received quetiapine in the baseline period, X^n_i denotes physician-level statistical controls, and Z_j denotes patient-level controls. We run separate regressions for privately insured patients ($j \in J^C$) and patients insured under Medicare ($j \in J^M$). We pre-specified two controls: the patient's lagged outcome and the physician's lagged outcome. In patient analyses, we cluster standard errors at the physician level to match the level of randomization. To test for equality in percent effects for private insurance and Medicare patients, we estimate equation 2 fully interacted with patient insurance source.

We pre-registered this study on the AEA Social Science Registry (AEARCTR-0003209) and archived a pre-specified analysis plan prior to viewing any HCCI data. We note deviations from the analysis plan in the text. This manuscript presents all pre-specified outcomes.

4.3 Classifying the Appropriateness of Prescribing

To provide a sense of how physicians responded to the letter and the implications for welfare, we consider patients' observable appropriateness for antipsychotics. We develop a classification methodology based on clinical literature (Maglione et al., 2011; Painter et al., 2017; Reus et al., 2016; American Geriatrics Society, 2019). We use diagnoses from the baseline and outcome periods to classify patients. Appendix Section A provides more detail on our approach.

The algorithm classifies patients into four mutually exclusive and exhaustive categories. Patients

who match multiple categories are assigned to the one listed first. *Guideline-concordant* patients appear to be receiving quetiapine consistent with FDA approvals. They have bipolar disorder, schizophrenia, or, if they are also taking an antidepressant, major depression. *Intermediate evidence* patients have a condition that the drug may effectively treat, though it is not FDA-approved: generalized anxiety disorder or, if they are not taking an antidepressant, major depression. *Low-value* candidates appear to be receiving quetiapine for unapproved indications and it is unlikely to help or may be harmful: dementia (the key condition in Medicare), insomnia, PTSD, obsessive-compulsive disorder, personality disorders, eating disorders, or alcohol use disorder. *Unknown* patients have no diagnoses in the above categories or are under age 18 (pediatric guidelines differ).

4.4 Analysis Sample and Descriptive Statistics

Over 99% of study physicians had contact with the HCCI insurers in that they had at least one prescription of any drug covered during the one year pre-intervention period. Table 1 provides summary statistics. Pre-intervention outcomes were balanced between the treated and control groups (P=0.16).

While the physicians were high-volume quetiapine prescribers in the overall Medicare program by design, their volumes were often less extreme in the HCCI data. In the year prior to the intervention, 42% had no quetiapine prescribing to Medicare Advantage patients and 74% had no private insurance quetiapine prescribing. The low volume for some physicians reflects variations in the market share of the HCCI contributors in private insurance and Medicare Advantage as well as the lack of Original Medicare patients in the data.

Patient-level analyses use the sample of N=9,364 baseline patients of the physicians (its construction is described in Appendix Section B). Appendix Table A2 provides summary statistics. The private insurance patients tend to be younger than Medicare patients, but there is meaningful overlap in the age distributions. Off-label use of quetiapine is common in the privately insured sample: just half had diagnoses that matched FDA guidelines for prescribing (guideline-concordant).

The average out of pocket cost for a 30-day supply of quetiapine privately for insured baseline patients is $13.82, and the average total payment including the insurer payment is $90.29. By comparison, the average out of pocket cost and total payment for a physician office visit are $28.90 and $99.81, respectively.

5 Results

5.1 Effects on Prescribing Volume

Figure 1 presents an unadjusted time series of quetiapine prescribing by treatment and control physicians. The plot uses a log scale to display effects in percent terms to facilitate comparisons between Medicare and private insurance. Relative to control physicians, treatment physicians reduced private insurance and Medicare prescribing substantially after the letters were sent. Reductions persist through the end of the outcome period.

Table 2 reports estimates from equation (1) for the primary outcome, the days of quetiapine prescribed by the physician and filled by their patients. The intervention reduced quetiapine supplied to private insurance patients by 24.5 days on a control group mean of 209.5 days, or 11.7%. For Medicare, the reduction was 183.6 days on a control mean of 1,094.5 days, or 16.8%. We are unable to reject that these percent effects are equal – we cannot reject one-for-one spillovers (P=0.34). We find essentially the same percent effects on the number of patients per quarter, indicating that physicians cut back by reducing the size of their quetiapine patient panels.

The point estimate on quetiapine spending is $45, about half the cost of an office visit.[3] These findings are also highly robust to other prescribing measures (Appendix Table A1). Effects are larger when focusing on new prescriptions, reflecting that new fills require the physician to take action by writing a new script and could respond rapidly. Reductions were largest in percentage terms for physicians who did not prescribe at all in private insurance during the pre-intervention period.[4] We next consider prescribing of other medications (Appendix Table A3 lists them), where the effects are *ex ante* ambiguous: prescribing could rise if physicians game the quetiapine metric referenced in the letter and switch to similar drugs or decline if physicians glean new clinical information about antipsychotics in general. We fail to find any meaningful signs of such a shift when we evaluate prescribing of all antipsychotics together (Table 2) nor when we study prescribing of other antipsychotics directly (Appendix Table A4). We also failed to uncover a clear pattern of

[3]This effect is imprecisely measured in levels but is similar in percent terms to other prescribing outcomes. A post-hoc analysis of spending in logs was highly significant (P=0.002).

[4]This analysis was not pre-specified. An additional post-hoc analysis considered whether spillovers differed depending on a physician's ratio of Medicare to private insurance patients. We found similar spillover effects across terciles of this ratio, though estimates were very imprecise. We note these findings are close to our pre-specified analysis by subgroup of combined Medicare and private insurance prescribing, which revealed similar albeit imprecisely measured effects across the four volume quartiles (Appendix Table A9).

substitution toward other psychiatric medications.[5]

5.2 Effects on Prescribing to Patient Subgroups

To better describe the marginal prescription curtailed by the intervention, we next study effects on prescribing to patient age and appropriateness subgroups (Figure 2 and Appendix Table A5).

Age Study physicians tend to prescribe to older privately insured patients. Point estimates become monotonically more negative with patient age. Reductions are only statistically significant to privately insured patients age 55-64, the decade of life before Medicare take-up becomes nearly universal. We reject equal percent effects for patients age 0-44 and 55-64 in private insurance (P=0.03). Thus spillovers onto private insurance were concentrated on patients closest to the Medicare age range.

Appropriateness While the intervention significantly reduced private insurance prescribing to likely good (guideline-concordant) candidates, point estimates were similar for low-value candidates, though not significant. In Medicare, where more prescribing occurs and power is higher, the effects are nearly identical and statistically significant for the four appropriateness groups. Thus in percent terms, the intervention appears to curtail prescribing by similar magnitudes regardless of whether patients are observably indicated for quetiapine. In a post-hoc analysis we explored another aspect of appropriateness by studying guideline-concordant patients who were observably better matched to quetiapine than other antipsychotics because they also had an insomnia diagnosis. Patients with insomnia may benefit from quetiapine's sedating side effects. Yet we found that cutbacks to guideline-concordant patients with insomnia were, if anything, larger than to those patients without insomnia.

5.3 Effects on Patients

In order to evaluate effects on patient health, we estimate equation (2) for the baseline patients of study physicians (Table 3). We first evaluate total quetiapine received, including receipt from

[5] We detect a significant increase in antidepressants in private insurance, but find no significant changes otherwise. While substitution to antidepressants could benefit patients, the signal of this result is weakened by our failure to detect it in Medicare nor in the patient-level analyses (Appendix Table A10).

physicians outside the study to incorporate any potential substitution to other prescribers. Private insurance patients experienced a 9% decrease in receipt of quetiapine due to the letter (significant at the 10% level). Reductions occurred for guideline-concordant patients as well as likely low-value patients, but the effect was only significant at the 10% level for the former group. We detect no signs that patients moved to other antipsychotics.

Given the reduction in antipsychotic treatment and the presence of mental health conditions among the vast majority of baseline patients, their high rate of inpatient and emergency department encounters (1.4 visits for the average control patient) suggests that these outcomes might be useful to detect improper disruptions in care. Nonetheless, we find no statistically significant changes in these visits and the point estimates are small in absolute and percent terms. We also failed to detect substantive changes in use of mental health care, with increases in psychologist visits offset almost exactly by decreases in psychiatrist visits. A post-hoc analysis of patient spending outcomes yielded no detected effects for private insurance patients.

These analyses include patients who exit coverage during the outcome period by counting their health care use for the months in which it is observed. The findings are robust to focusing on the subsample of patients with continuous enrollment (Appendix Table A6).

6 Discussion

6.1 Mechanisms

We now explore the channels that drive the spillovers of the Medicare intervention on private insurance. One is updating over beliefs about appropriate prescribing. For example, the letters could have prompted physicians to consult medical literature or clinical guidelines. Yet cutbacks are not restricted to off-label use, do not occur for other antipsychotics with similar guidelines, and are if anything slightly stronger for patients who appear to be particularly good candidates for quetiapine relative to other antipsychotics. It is hard to reconcile these broad patterns with clinical evidence.

Two other channels have some support in the data. One is the activation of social or professional norms about prescribing. The letter's messaging focused heavily on the physician's behavior relative to peers, potentially raising the "moral costs" of departing from norms and prescribing heavily (c.f.

Levitt and List, 2007). Spillovers would occur if physicians consider the totality of their prescribing when evaluating whether they have deviated from norms. This channel also aligns with our finding of cutbacks concentrated on older privately insured patients, as a message from Medicare could signal norms most strongly for "Medicare-like" privately insured patients.

The other channel relates to the penalty-oriented messaging of the letter, which could have raised the implicit costs of prescribing by highlighting the potential for a CMS review. If physicians fail to distinguish between appropriate and inappropriate patients – as suggested by their high volume of prescribing to patients in both categories – expectations of broad penalties would lead to indiscriminate reductions in Medicare prescribing. The spillovers to private insurance could occur because physicians do not readily observe the patient's insurer or find it distasteful to vary practice styles on that basis. Indeed, the cutbacks to older privately insured patients could reflect a heuristic in which physicians target Medicare imperfectly by cutting back to all older patients. Physicians would still reduce prescribing to the privately insured because quetiapine is commonly prescribed to the under-65 Medicare population eligible via disability insurance (about one-third of Medicare prescribing in the study goes to patients under age 65).

The penalty oriented messaging also could have spilled over if physicians have anticipated that CMS would use private insurance data to evaluate their behavior or that this data would be revealed to CMS in the case of an audit. Cutbacks focused on older privately insured patients could result from physicians fearing that CMS would be most concerned about such prescribing.

Some alternative mechanisms make predictions that have less support in the data. For example, physicians may have believed that they would face an audit from private insurers if they did not reduce their prescribing. Yet in percent terms, reductions were even larger for physicians who did not prescribe any quetiapine in our private insurance data in the year prior to the intervention and thus had less to fear from such a review (Table 2). Another alternative is that physicians anticipate older privately insured patients will be joining Medicare soon and will be tracked by CMS. However, when we studied prescribing to patients who would not be aging onto Medicare soon because they remained privately insured and under the Medicare retirement age at the end of our outcome period, percent effects were similar though somewhat less precise (Appendix Table A1).

6.2 Welfare Impacts

A prior clinical evaluation of this intervention studied the effects on the universe of Medicare beneficiaries and found support that the intevention was welfare-improving given that the letters triggered a large reduction in prescribing of quetiapine in Medicare without any detected harms to patients (Sacarny et al., 2018).[6] The prior study did not observe private insurance spillovers, which could theoretically offset these welfare gains. The prescribing landscape in private insurance differs from Medicare in welfare-relevant ways. For example, just 2% of baseline privately insured patients had dementia, compared to 43% of baseline patients in Medicare. Stemming overuse of antipsychotics for dementia has been a key objective of CMS but is clearly a second-order concern for private insurers. In practice, physicians in the study still prescribed to likely off-label patients in private insurance with other conditions like insomnia and PTSD. As a result, the appropriateness of prescribing was ultimately similar by insurer. Taken together, there is little evidence that the welfare effects differ when accounting for the spillover onto private insurance.

6.3 Common Agency

Using the common agency framework of Bernheim and Whinston (1986) as a lens for physician-insurer contracting, Glazer and McGuire (2002) and Frandsen, Powell and Rebitzer (2019) argue that free-riding and coordination failures across insurers can explain low levels of performance-raising investments in health care. In the simplest model, a market failure occurs because some of the gains from one insurer implementing the optimal contract accrue to the other insurers. To date, there has been little empirical evidence on the key pattern these models assume: that efforts by one insurer to alter physician behavior affect the care reimbursed by other insurers.

Our finding of strong spillovers onto private insurance shows that the potential for free-riding on these interventions exists. While warning letters like the ones sent by CMS can have powerful effects on the practice of medicine, depending on the motivations and information available to

[6] A further advantage of the intervention is its low explicit cost, which mainly consists of mailing letters. While CMS has not provided cost estimates, they likely compare favorably to the savings in Medicare of $979 per treated prescriber reported in Sacarny et al. (2018). Costs are also likely small compared to savings in private insurance of $45 per treated prescriber (Appendix Table A1). Interventions may have additional implicit costs that must be taken into consideration, however. Physicians could have attention fatigue or adapting expectations, particularly if (potentially costly) actions mentioned in the letters like audits are not implemented. Insurers could face additional costs if conducting interventions make health care providers less willing to contract with them in the future.

insurers, there is little reason to expect they would be provided optimally in equilibrium. Private insurers that only sought to maximize the quality of care they reimbursed would fail to internalize the benefits (or harms) of interventions when determining how much of them to supply. When spillovers help competitor firms, private insurers would have even less incentive to conduct interventions. It is perhaps unsurprising that key examples of insurer cooperation are often led by CMS, like the Comprehensive Primary Care Plus program, which sought to harmonize performance-raising incentives across insurers (see e.g. CMS, 2021). An additional friction comes from the incomplete information available to health insurers. In general, insurers only observe the care that they cover. As a result, even a socially-minded insurer that valued the external effects of its interventions would be hampered in its efforts.

7 Targeting Simulation

We now simulate the effects of a similar intervention conducted by an insurer that does not observe, or does not care about, prescribing covered by other plans. The simulation (not pre-specified) studies three potential interventions: one performed by private insurers alone, one by Medicare alone, and one by a merged (social planner-like) entity. We hold constant the algorithm to select prescribers and the budget to intervene (i.e. number of prescribers contacted), but separately identify prescribers from private insurance, Medicare, and merged data. The exercise assumes that the effects of the intervention would match those of the CMS trial. It also takes the CMS outlier algorithm as the correct measure of prescribing quality; thus intervening on higher prescribers is sufficient to improve intervention targeting.

We show that private insurers' limited ability to observe prescribing covered by others deteriorates targeting and attenuates the economy-wide reductions in prescribing relative to Medicare and the social planner. Since our data does not distinguish contributing private insurers, we treat them as one merged entity. The typical private insurer will therefore be smaller and have access to data on an even smaller fraction of the market, making our findings, if anything, conservative.

We begin by modifying the CMS algorithm to apply to HCCI Medicare and private insurance prescribing in 2013 and 2014 (see Appendix Section D for a detailed description). We also update the outlier formula so the outlier threshold is adjustable and set it to match the sample size CMS

used as closely as possible in all simulated interventions. To ensure that our findings are not driven by these changes, the section focuses on outliers in HCCI data rather than the PCPs selected by CMS in the original intervention.

7.1 Characteristics of the Outliers

In the simulation, each insurer accounts only for the prescribing it covers when running the algorithm. Its outliers may not match up well with the outliers for the other insurer, nor with those selected when combining both insurers' data (which proxies for the socially optimal targeting). A Medicare intervention may be poorly targeted in private insurance or vice versa. Figure 3 and Panels A and B of Appendix Table A7 characterize the targeting by describing the three sets of outliers and their prescribing volume.

As expected, the outliers selected from one insurer's data have the highest prescribing volume for that insurer but often prescribe little or nothing to patients of the other insurer. In Panel A of Figure 3, Medicare-only outliers are shown prescribing more than fivefold the quetiapine to Medicare patients than outliers selected from private insurance data. Panel B shows the reversed pattern looking at prescribing to private insurance patients. The two sets of outliers had little overlap: only 9% of Medicare outliers were also private insurance outliers and vice versa.

The final panel of Figure 3 plots prescribing in Medicare and private insurance combined. By construction, the outliers selected from the combined data prescribe the most here on average – yet outliers selected from Medicare data alone prescribe nearly as much. In contrast, targeting combined prescribing with just private insurance data works relatively poorly. This finding reflects that Medicare prescribing volume is much higher than private insurance, making 76% of the Medicare outliers (but only 32% of private insurance outliers) also outliers in the combined data.

7.2 Foregone Reductions in Prescribing

We now explore how the difference in targeting deteriorates the effects of the intervention. In Panel C of Appendix Table A7 we project the volume of economy-wide primary care quetiapine prescribing curtailed by the intervention by assuming it has effects on Medicare and private insurance given by Table 2. That projection is scaled by an estimate of prescribing that would have occurred nationally absent the intervention.

Private insurers intervening on their own would forego substantial economy-wide reductions. Their intervention would reduce total prescribing by less than half the effect of the social planner's intervention. Thus, even if private insurers had found such an intervention worthwhile and conducted it at the same intensity (and with the same effect on prescribing) as CMS, they would have achieved substantially smaller reductions. Private insurance prescribing and total prescribing by PCPs are imperfectly correlated, so the PCPs targeted by private insurers differ substantially from those the social planner would choose.

Panel C also shows that a Medicare program conducting its own intervention would match the social planner's effect (3.9%) up to a rounding error. Though Medicare does not observe private insurance data in the simulation, its own information still provides a close approximation to the total because it covers roughly three-fourths of quetiapine prescribing in HCCI data. When a single insurer observes an accurate signal of aggregate behavior, its actions can more closely replicate those of the social planner.[7] Such a situation could still occur in competitive insurance markets if, for example, the insurers competed over the same pool of patients rather than specializing in different patient populations.

Insurers could also share data with each other, though competing firms may be reluctant to do so. A useful exception that implies the rule comes from a program by Blue Cross and Blue Shield (BCBS) insurers to direct patients to high-quality low-cost specialty care providers (BlueCross BlueShield, 2021). This program pools data across BCBS insurers and Medicare. It is notable that this cooperation occurs between the BCBS insurers, which are regionally distinct and thus compete less with one another. It also highlights that Medicare's public reporting can benefit other insurers.

8 Conclusion

This paper provides new, randomized evidence documenting spillovers from Medicare on private insurance by exploiting a trial of Medicare letters which sought to improve the quality of prescribing of the most commonly used antipsychotic medication, quetiapine. We find large effects on prescribing to privately insured patients and cannot rule out one-for-one spillovers. As mechanisms for these

[7] We also explored whether these findings were an artifact of identifying outliers with a short measurement period. Results were essentially unchanged using two-year measurement periods (2011-2012 and 2013-2014) rather than one-year periods. Medicare would nearly match the social planner's effect (3.5% vs. 3.6%) while private insurers would produce about half the reduction (1.8%).

spillovers, we find evidence consistent with moral cost and penalty effects of the letters.

These findings have broader implications for the causes and evolution of health care productivity in the U.S. The cross-insurer spillovers following this intervention show that insurers, and government insurers in particular, have the power and opportunity to improve health care that other entities pay for. Yet if insurers fail to internalize the full benefits of their interventions, those that are worthwhile are likely to be under-provided in equilibrium. Thus a key open question for policymakers is how to encourage these performance-raising investments when payment is fragmented across multiple, uncoordinated entities.

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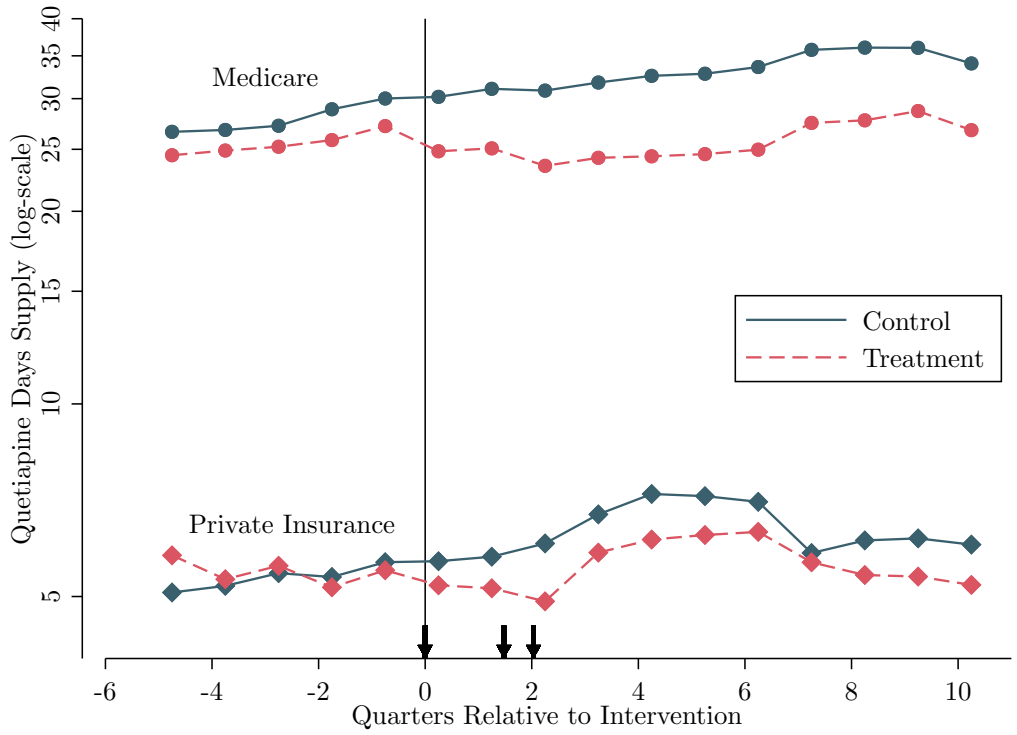
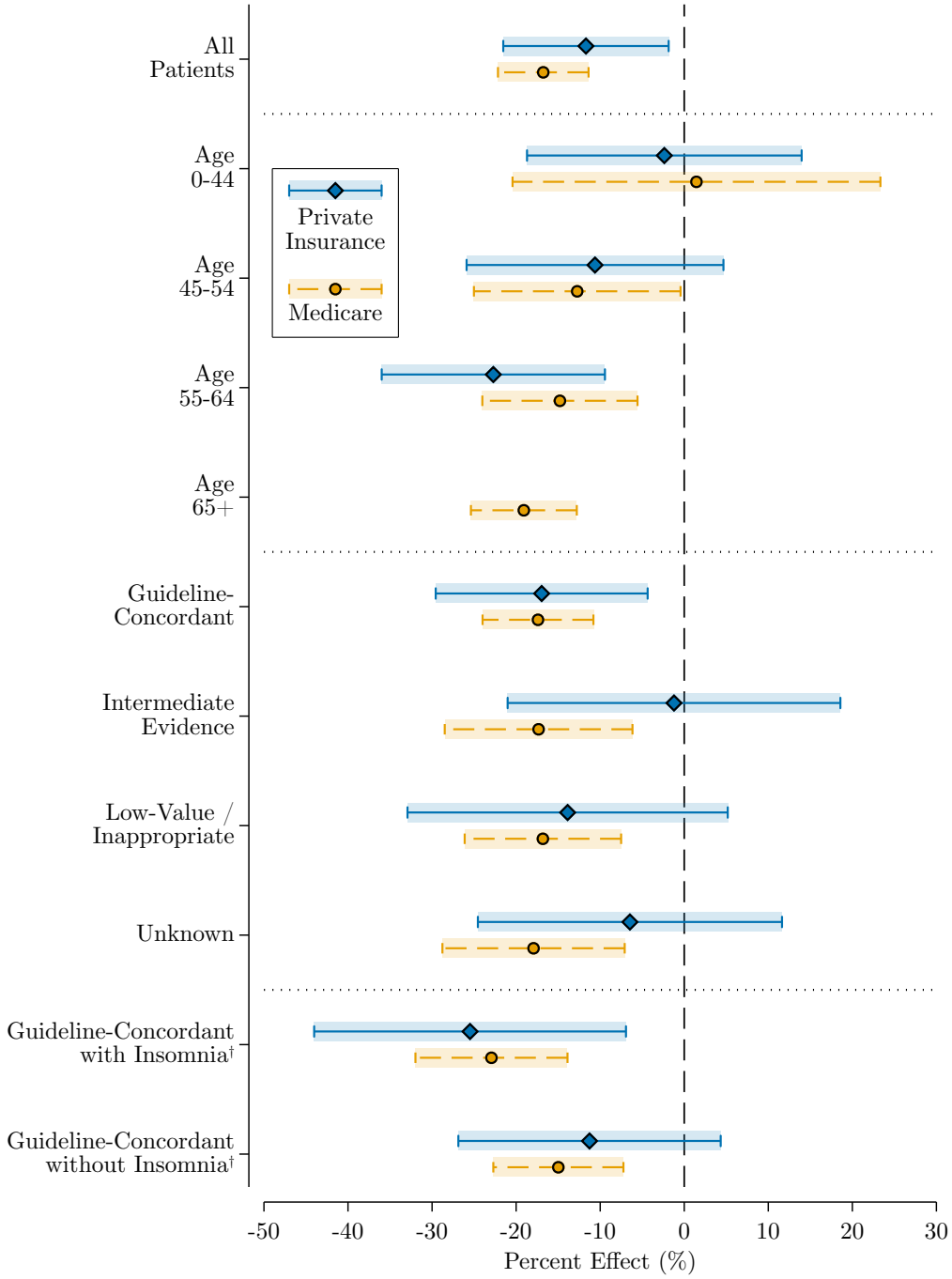
Figures

Figure 1 – Quarterly Prescribing over Sample Period



Notes: Figure plots the raw average days of quetiapine supplied by control (blue solid line) and treatment (red dashed line) study prescribers. The series in the upper half of the figure count prescribing in Medicare while the series in the lower half count prescribing in private insurance. The solid vertical line denotes the start of the intervention and the arrowheads indicate when the treatment letters were sent. The y-axis uses a log-scale to visualize differences in percent terms, given the large difference in prescribing volume to private insurance and Medicare patients. Trends in quetiapine supplied in private insurance partly reflect changes in covered lives in the data as well as the share of covered lives for which prescribing is observed. In particular, a decline in covered lives alongside a decline in the share of lives with prescribing data occurs in January 2017, corresponding to the drop in quetiapine supply in private insurance between quarters 6 and 7 in the figure.

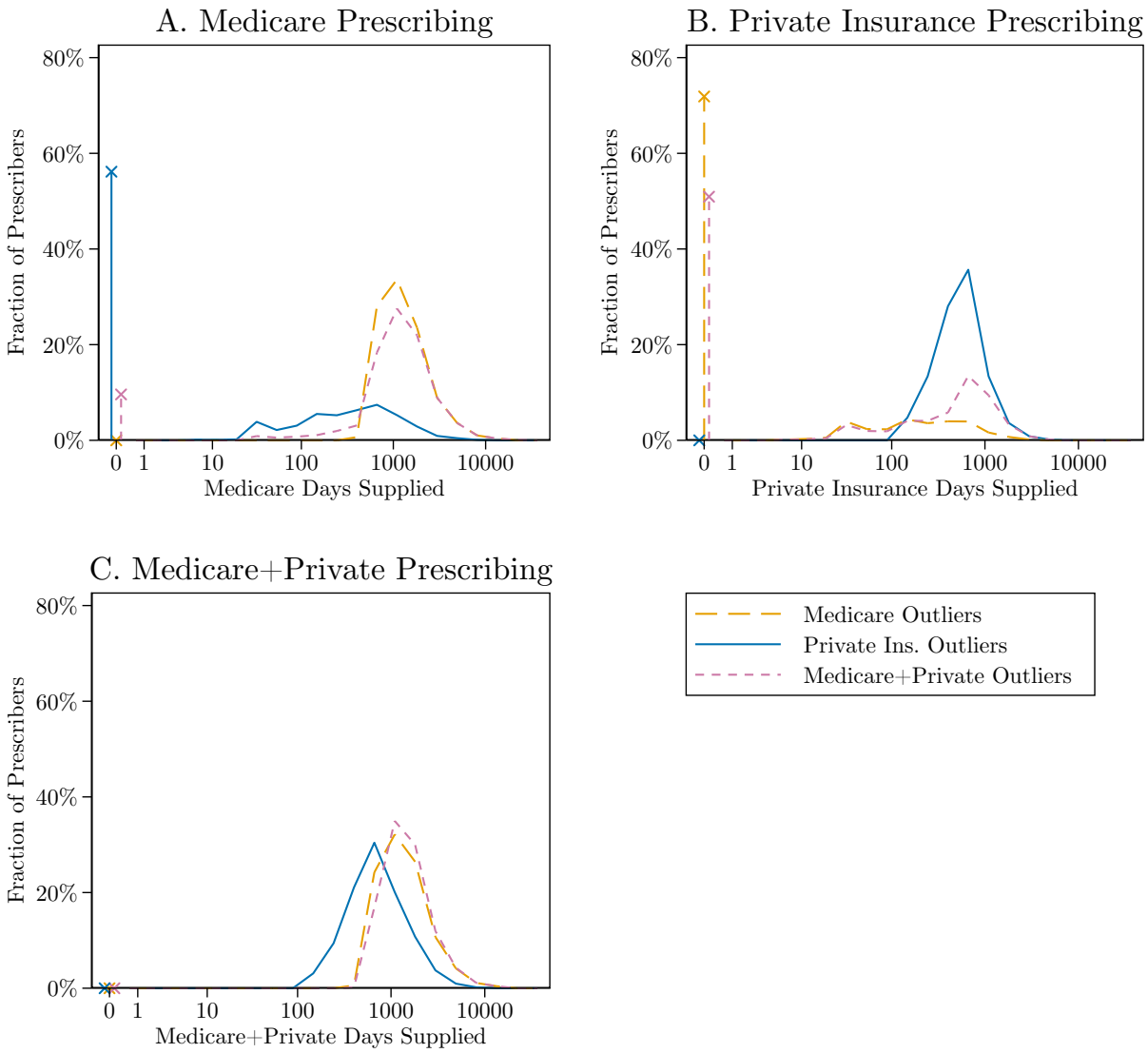
Figure 2 – Effects on Prescribing in Private Insurance and Medicare



Notes: Figure plots estimates of the effect of the intervention on prescribing in private insurance and Medicare. Estimates include quetiapine prescribing to all patients (study primary outcome, top panel), to patients in specified age bins (second panel), to patients in specified appropriateness groups (third panel), and to guideline-concordant patients with and without insomnia (bottom panel). To facilitate comparisons of the effects across outcomes with different baseline levels of prescribing, we present percent effects (i.e. treatment effect divided by the control mean). Error bars show 95% confidence intervals. See Table 2 and Appendix Table A5 for more details.

† Outcome not pre-specified.

Figure 3 – Quetiapine Prescribing of Outlier PCPs in Targeting Simulations



Notes: Figure plots the distribution of quetiapine prescribing volume for PCPs selected in targeting simulations. It depicts three groups of outlier PCPs: Medicare (dashed yellow line), private insurance (solid blue), and Medicare+private insurance (short dashed red). Each panel shows histograms of prescribing volume covered by the given insurer. The x-axis scale is produced by taking log(1+days supply). The spikes above 0 indicate the share of PCPs in the group with no prescribing in that insurer. Panel A plots prescribing in Medicare. Panel B plots prescribing in private insurance. Panel C plots prescribing in Medicare and private insurance combined. See Appendix Table A7 and text for more details.

Tables

Table 1 - Summary Statistics of Study Prescribers

Characteristic	(1) Control	(2) Treatment	(3) P-Value
Female	17.8%	17.8%	0.936
Primary Specialty			
Family Medicine	47%	49%	0.125
General Practice	4%	5%	0.156
Internal Medicine	49%	46%	0.027
Any Psychiatric Specialty	<1%	<1%	0.999
No Quetiapine Prescribing During Baseline Period			
To Privately Insured Patients	74.2%	74.4%	0.853
To Medicare Patients	40.8%	43.1%	0.096
Days Supply of Quetiapine During Baseline Period			
To Privately Insured Patients	65.0 (184.7)	64.7 (204.6)	0.963
To Medicare Patients	338.7 (723.1)	309.4 (543.5)	0.104
Unique Patients Prescribed Quetiapine During Baseline Period			
Privately Insured Patients	0.5 (1.4)	0.5 (1.7)	0.720
Medicare Patients	1.9 (3.6)	1.8 (2.9)	0.089
Unique Patients Seen During Baseline Period*			
Privately Insured Patients	164.6 (221.1)	170.5 (273.8)	0.401
Medicare Patients	81.7 (105.9)	84.9 (118.2)	0.316
P-value, omnibus test of equality			0.157
N	2,528	2,527	

Notes: This table reports summary statistics of the study prescribers. Binary variables displayed as percentages and continuous variables displayed as means (standard deviations). Data on prescriber sex and specialization come from pre-intervention NPPES files. A small number (<1%) of prescribers had a primary specialization outside the three categories in the table. Quetiapine prescribing measures only consider the baseline period (the year prior to the intervention).
* Counts patients with an encounter with the physician, whether or not they were prescribed quetiapine.

Table 2 - Effects on Key Prescribing Outcomes

	(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
Days Supply*	209.5	-24.5	-11.7%	1,094.5	-183.6	-16.8%	[0.344]
		(10.5)	(5.0%)		(30.1)	(2.7%)	
Days Supply	387.7	-28.2	-7.3%	2,002.1	-195.3	-9.8%	[0.563]
(All Antipsychotics)		(14.8)	(3.8%)		(49.7)	(2.5%)	
Patients per	0.28	-0.04	-12.7%	1.24	-0.23	-18.3%	[0.311]
Quarter†‡		(0.01)	(5.1%)		(0.03)	(2.7%)	
Days Supply of Quetiapine Stratified by Prior Prescribing of Quetiapine in Private Insurance							
No Prior Rx†	61.9	-16.0	-25.8%	912.4	-175.7	-19.3%	[0.459]
(N=3,757)		(5.3)	(8.5%)		(32.2)	(3.5%)	
Prior Rx†	634.1	-49.4	-7.8%	1,618.3	-200.8	-12.4%	[0.488]
(N=1,298)		(38.0)	(6.0%)		(71.3)	(4.4%)	

N=5,055. Notes: Table reports estimates for prescriber-level outcomes for private insurance (columns 1-3) and Medicare (columns 4-6). All measures count quetiapine prescribing during the outcome period (April 21, 2015 through December 31, 2017) except the second measure which includes all antipsychotics. 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.

* Pre-specified primary outcome.

† Outcome not pre-specified.

‡ Average no. of patients prescribed quetiapine in each post-intervention quarter.

Table 3 - Effects on Baseline Patients

Patient Cohort	(1)	(2)	(3)		(4)	(5)	(6)		(7)
	Private Insurance				Medicare				P-Val, %
	Control	Treatment	Percent		Control	Treatment	Percent		Effects
Outcome	Mean	Effect	Effect	N	Mean	Effect	Effect	N	Equal
Quetiapine Days	260.7	-23.2	-8.9%	1,980	441.0	-22.0	-5.0%	7,384	[0.481]
Received		(13.3)	(5.1%)			(10.0)	(2.3%)		
By Specified Patient Appropriateness Subgroup									
Guideline-	317.3	-39.0	-12.3%	1,001	484.9	-22.7	-4.7%	4,255	[0.284]
Concordant		(20.9)	(6.6%)			(13.0)	(2.7%)		
Intermediate	213.2	-2.5	-1.2%	235	433.3	-15.9	-3.7%	552	[0.883]
Evidence		(32.8)	(15.4%)			(31.5)	(7.3%)		
Low Value /	228.5	-15.1	-6.6%	327	361.6	-38.4	-10.6%	1,536	[0.766]
Inappropriate		(28.4)	(12.4%)			(19.2)	(5.3%)		
Unknown	174.1	1.6	0.9%	417	383.1	0.2	0.1%	1,041	[0.949]
		(22.0)	(12.6%)			(23.6)	(6.2%)		
Antipsychotics	293.3	-27.3	-9.3%	1,980	496.8	-23.9	-4.8%	7,384	[0.408]
Days Received		(14.7)	(5.0%)			(10.7)	(2.1%)		
Inpatient Stays	0.39	-0.02	-4.4%	1,980	0.87	0.04	4.0%	7,384	[0.522]
		(0.05)	(12.3%)			(0.04)	(4.6%)		
ED Visits	0.99	-0.04	-4.4%	1,980	1.75	0.07	3.9%	7,384	[0.487]
		(0.10)	(9.8%)			(0.12)	(6.6%)		
Psychiatrist	1.16	-0.26	-22.2%	1,980	1.14	0.07	6.4%	7,384	[0.072]
Visits		(0.16)	(13.7%)			(0.09)	(7.7%)		
Psychologist	0.33	0.24	71.2%	1,980	0.84	-0.07	-8.5%	7,384	[0.115]
Visits		(0.13)	(39.8%)			(0.26)	(30.9%)		
Spending ($) on Health Care Services by Service Category[‡]									
Total[†]	26,510	-304	-1.1%	1,980	25,317	2,258	8.9%	7,384	[0.342]
		(2,624)	(9.9%)			(994)	(3.9%)		
Inpatient[†]	8,139	-1,403	-17.2%	1,980	11,124	1,315	11.8%	7,384	[0.097]
		(1,359)	(16.7%)			(604)	(5.4%)		
Outpatient[†]	8,123	1,863	22.9%	1,980	5,247	414	7.9%	7,384	[0.382]
		(1,335)	(16.4%)			(274)	(5.2%)		
Physician	8,484	-613	-7.2%	1,980	7,488	519	6.9%	7,384	[0.139]
Services[†]		(754)	(8.9%)			(276)	(3.7%)		
Prescription	1,765	66	3.8%	1,980	1,459	74	5.1%	7,384	[0.906]
Drugs[†]		(181)	(10.3%)			(70)	(4.8%)		

Notes: 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 and the approach to assigning patients to groups. 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.

[†]Outcome not pre-specified.

[‡] Spending equal to sum of allowed charges (insurer+patient payments) within each service category.

Online Appendix:

Common Practice: Spillovers from Medicare on Private Health Care

Michael Barnett, Andrew Olenski, and Adam Sacarny

January 26, 2022

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

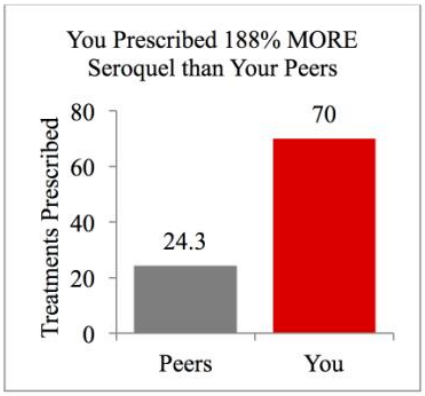
April 20, 2015

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.