Review of Outcomes Associated With Restricted Access to Atypical Antipsychotics

Krithika Rajagopalan, PhD; Mariam Hassan, PhD; Kimberly Boswell, MD; Evelyn Sarnes, PharmD, MPH; Kellie Meyer, PharmD, MPH; and Fred Grossman, MD, PhD

ABSTRACT

Objectives: Cost containment policies, such as prior authorization (PA), have increasingly been used by formulary decision makers to manage drug spending of the atypical antipsychotic (AAP) drug class. However, these drug cost containment policies may result in cost shifting rather than cost savings. Given the interest in coordination of care, the objective of this study was to evaluate the impact of restricted access to AAPs on healthcare costs and health outcomes in individuals with schizophrenia or bipolar disorder.

Study Design: Narrative literature review.

Methods: A literature search was conducted using MEDLINE (via PubMed) for studies published between January 1993 and December 2013.

Results: A total of 15 published studies were identified that evaluated restricted access to AAPs in regard to healthcare costs or health outcomes: 11 studies assessed PAs, 2 studies assessed carve-outs, 1 study assessed a payment limit (cap), and 1 study assessed Medicare Part D cost sharing. Among 8 studies evaluating changes in pharmacy costs and clinical outcomes, 5 studies reported that formulary restrictions were associated with pharmacy cost savings and increases in healthcare utilization or treatment discontinuation. Of the 4 studies that measured overall cost changes, 3 studies reported increases in overall cost burden and 1 study showed modest cost savings associated with formulary restrictions.

Conclusions: Study findings revealed there exists a gap in the literature as to whether restricted access to AAPs results in overall cost savings or, rather, shifts the cost burden from pharmacy spending to other parts of the healthcare system, such as service utilization.

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Approximately 1 in 4 (26.2%) adults in the United States suffers from a diagnosable mental disorder in a given year,[1] and owing to the high prevalence, mental disorders are associated with substantial financial burden on the healthcare system. The Substance Abuse and Mental Health Services Administration (SAMHSA) estimated that total direct costs for mental healthcare were $100 billion in 2003, representing 6.2% of all medical expenditures in the United States.[2] In 2003, public payers provided more than half (58%) of the funding for mental health, with Medicaid representing the largest source of public funding (45%).[2] Due to rising spend on pharmaceutical treatments in the last 2 decades, state Medicaid programs have increasingly been implementing pharmaceutical cost-containment strategies, such as prior authorizations (PAs), preferred drug lists, dispensing limits, mandatory use of generics, supplemental rebates, cost sharing, and step therapy.[3] Although the goal is to encourage appropriate use of medications and to contain costs, these strategies may have unintended consequences; for example, PA requirements have been shown to increase the probability of drug access problems by 20%.[4]

Treatment decisions for patients with mental illness are driven by a complex interplay that includes efficacy, tolerability, prior drug history, patient preference, access, and drug interactions; successful pharmacological treatment is often only achieved after multiple therapeutic trials.[5,6] Atypical antipsychotics (AAPs), which were introduced in the early 1990s, are considered standard pharmacotherapy for schizophrenia and bipolar disorder. Although AAPs are considered to belong to the same class, these drugs are quite heterogeneous as they exhibit different pharmacological profiles and may not be interchangeable. Patient responses to these agents can be variable—a lack of response to one agent does not necessarily predict a lack of response to another, even within the same drug class or vice versa.[5] Compounding the variable nature of the clinical response, treatment

resistance is a challenge to successful long-term management of the mentally ill. Given the absence of genetic biomarkers that can predict response with one agent compared with another, treatment optimization requires adequate trials of multiple antipsychotics.[5] As such, the potential disruption of stable pharmacological management due to medication access challenges or restrictions may have serious clinical consequences, including treatment discontinuation, relapse, and deterioration of symptoms and/or function.[5]

Take-Away Points

- Formulary restrictions aiming to curb pharmacy costs for atypical antipsychotics may result in higher medical care utilization and shift the overall cost burden to other parts of the healthcare system. A thorough review and synthesis of the literature was conducted to evaluate the impact of restricted access to atypical antipsychotics in individuals with either schizophrenia or bipolar disorder.
- Evidence from 5 of 8 studies evaluating changes in pharmacy costs and clinical outcomes demonstrated pharmacy cost savings and increases in healthcare utilization or treatment discontinuation associated with formulary restrictions.
- Of the studies that measured overall cost changes, 3 reported increases in overall cost burden and 1 study showed modest cost savings associated with formulary restrictions.

Our objective was to conduct a thorough review and synthesis of the literature to evaluate the impact of restricted access to AAPs on healthcare costs and health outcomes in individuals with either schizophrenia or bipolar disorder.

METHODS

A narrative review of all English-language studies published in peer-reviewed journals between January 1993 and December 2013 was conducted using MEDLINE (via PubMed). Inclusion criteria were as follows: studies conducted in the United States involving an evaluation of healthcare costs or health outcomes with regard to restrictions on access to antipsychotic medications in health plan populations, and encompassing schizophrenia or bipolar disorder. The search was limited to original research articles; therefore, commentaries, editorials, and reviews were excluded.

Search terms included the following: (*schizophrenia* OR *bipolar* OR *serious mental illness* OR *psychiatric illness*) AND (*atypical antipsychotic* OR *antipsychotic* OR *aripiprazole* OR *asenapine* OR *clozapine* OR *olanzapine* OR *lurasidone* OR *paliperidone* OR *quetiapine* OR *risperidone* OR *ziprasidone* OR *iloperidone* OR *haloperidol* OR *psychotherapeutic*) AND (*step edit* OR *step therapy* OR *formulary restriction* [*tier, control, cost*] OR *drug coverage restriction* OR *prior authorization* OR *drug utilization* OR *managed care* OR *Medicare* OR *Medicaid* OR *Veterans Affairs* OR *tiered therapy* OR *prescription limit* OR *open access*). The following filters were applied: publication date (from 01/01/1993), humans, and English.

The search resulted in 230 hits, of which 208 were excluded based on review of title and/or abstract (**Figure**). The remaining 22 were further assessed for eligibility by review of full-text article. Studies were excluded based on the following: non-schizophrenia or bipolar patient population, no abstract available, non-US study, nonprimary research article, or no evaluation of restricted access on antipsychotics with regard to healthcare costs or health outcomes.

RESULTS

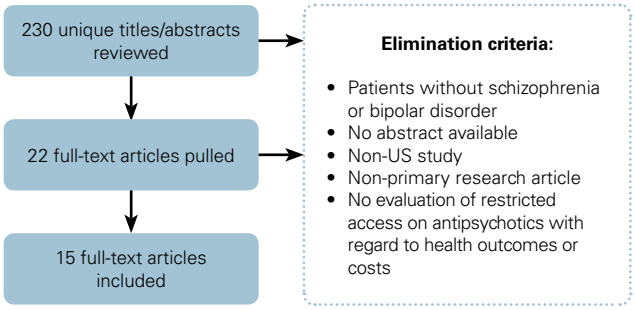
A total of 15 studies met the strict inclusion and exclusion criteria and were thus included in the review (**eAppendix**, available at **www.ajmc.com**). Among the 15 included studies, 11 assessed PAs, 2 assessed mental health benefit carve-outs, 1 assessed a payment limit (cap), and 1 assessed Medicare Part D cost sharing; of these, 1 study evaluated costs only. The remaining studies considered both costs and other outcomes, such as healthcare and drug utilization, treatment discontinuation, and quality of care. Studies were assessed based on their impact on pharmacy costs, nonpharmacy costs, overall costs, and clinical event rates (**Table**).

Impact on Expenditures

Findings from studies reporting the impact of cost-containment policies on healthcare expenditures are summarized below. Soumerai et al (1994) evaluated the effects of a New Hampshire Medicaid-imposed 3-prescription limit (cap) on the use of psychotropic drugs for schizophrenia during a study period from 1980 to 1983.[7] The cap was associated with an immediate drop in the utilization of these drugs. However, it was also associated with a corresponding increase in visits to community mental health centers (CMHCs) of 1 to 2 visits per member per month (PMPM) and an increase in utilization of emergency mental health services and partial hospitalization from 1.2 to 1.4 episodes PMPM. It was estimated that during the 11-month period the cap was in effect, the increase in the statewide cost of mental health services was $390,000. The estimated increase in mental health services exceeded the savings in drug costs by a factor of 17.

Farley et al conducted a retrospective assessment of a step-therapy PA for AAPs implemented in the Geor-

Figure. Literature Review Flowchart



gia Medicaid program (1996-1997),[8] where patients were required to fail 2 typical antipsychotics before receiving an AAP. In the subset of patients with schizophrenia, the PA policy demonstrated a $19.62 PMPM decrease in AAP expenditures; however, the savings were outweighed by a $31.59 PMPM increase in expenditures for outpatient services. The authors further explored the effect of the PA policy on the frequency of outpatient visits and found that the number of outpatient visits declined, albeit outpatient payments increased. This finding suggested the unintended consequence of greater payments per outpatient visit following the PA policy implementation.

McCombs et al evaluated the impact of a change in policy to allow open access (ie, remove formulary restrictions) to AAPs in the California Medicaid program during the period of 1994 to 2000.[9] In the year following the initiation of open access, there was an increase in drug utilization and expenditures—this was especially noted in institutionalized patients; however, the increases in drug expenditures may have been offset by decreases in nursing home utilization. Additionally, total monthly costs increased in both the restricted and open-access periods, although the increase was greater in the restricted period compared with the open-access period (19.5% vs 15.2%, respectively).

Abouzaid et al developed a decision-analytic model to compare the economic impact of a PA for AAPs in the treatment of schizophrenia versus no PA over a 1-year time horizon.[10] Researchers concluded that only modest potential cost savings would be recognized, without considering the potential increase in hospitalizations (ie, best-case scenario). Cost savings equated to $29 per patient per year when including increased costs of outpatient care and administrative costs associated with the PA program (2008 US dollars). The model was sensitive to the rate of hospitalizations; an increase in the subsequent hospitalization rate of only 0.5% would make the PA arm the more costly option.

Although most studies demonstrated that cost-containment policies reduce pharmacy expenditures, some demonstrated minimal savings in drug cost. Law et al conducted an evaluation of PA policies for AAPs in West Virginia and Texas Medicaid programs from 1991 to 2005. The West Virginia PA required a 14-day trial of a preferred agent, with the following drugs subject to PA: aripiprazole, brand name clozapine, olanzapine/fluoxetine, and olanzapine. The Texas policy required treatment failure, contraindication, or allergic reaction to a preferred agent, with the following drugs subject to PA: brand name clozapine, olanzapine/fluoxetine, and olanzapine. Results demonstrated a reduction in market share for nonpreferred AAPs, but no appreciable decrease in pharmacy expenditures.[11] Notably, there were extensive grandfathering provisions for patients already receiving AAPs. However, researchers hypothesized that the lack of change in pharmacy expenditures could be a result of alternative medications also being costly. Furthermore, providers may respond to PA policies by increasing the dose of less-optimal medications or combining medications (polypharmacy); both of these scenarios would reduce any savings.

In another study, from 2005 to 2007 in the Vermont Medicaid program, Simeone et al evaluated the effects of a rescission of a PA exemption on cost and utilization of behavioral health medications.[12] In this phase-out of the PA exemption for patients with severe and persistent mental illness, beneficiaries were exempt from PA requirements for medications not on the Medicaid preferred drug list. The phase-out demonstrated modest increases in formerly exempt behavioral health medications (2.1% PMPM) and was associated with a reduction in the rate of mental health–related inpatient hospitalizations (from 0.6% to 0.4%).

Impact on Medication Adherence and Clinical Outcomes

Disruption of treatment is an unintended and potentially serious consequence of restricted access to AAPs among patients with schizophrenia or bipolar disorder, especially considering that nonadherence and poor persistence to therapy is an ongoing challenge for patients with mental illness[5]—with or without formulary restrictions. Zhang et al evaluated the association of PAs for psychiatric drugs with medication discontinuation among patients with bipolar disorder in the Maine Medicaid program from 2001 to 2004.[13] The PA policy was associated with an 8% reduction in utilization of nonpreferred AAPs and anticonvulsants without a corresponding increase in utilization of preferred agents, indicating that patients were discontinuing treatment rather than switching to the program-preferred agents. Rates of medication discontinuation were over

Table. Summary of Cost and Clinical Event Changes Associated With Policy Change

Study	Type of Policy Change	Pharmacy Cost Change	Nonpharmacy Cost Change	Overall Cost Change	Change in Clinical Events
Fung V et al (2013)[20]	Medicare Part D coverage gap	Part D spending: ↓ Out-of-pocket Part D spending: ↑	Not measured	Not measured	ED visits: ↑ Hospitalizations: ↑
Robst J (2012)[19]	Implementation of managed behavioral health carve-out	↓	Not measured	Not measured	Not measured
Lu CY et al (2011)[15]	Implementation of PA policy	Not measured	Not measured	Not measured	Treatment discontinuation: ↑ Psychiatric visits: ↓ ED visits: ↑ Hospitalizations: no change
Vogt WB et al (2011)[16]	Implementation of PA policy	↑[a]	Not measured	Not measured	Not measured
Walthour A et al (2010)[21]	Implementation of PA policy	↓	Not measured	Not measured	ED visits: ↓ Hospitalizations: ↓
Simeone JC et al (2010)[12]	Rescission of PA exemption	↑	Not measured	Not measured	Hospitalizations: ↓
Abouzaid S et al (2010)[10]	Decision analytic model ± PA policy	Not measured	Not measured	↓	Not measured[b]
Lu CY et al (2010)[17]	Implementation of PA policy	Not measured	Not measured	Not measured	Treatment initiation: ↓ Treatment switching: no change
Zhang Y et al (2009)[13]	Implementation of PA policy	↓	Not measured	Not measured	Treatment discontinuation: ↑
Soumerai SB et al (2008)[14]	Implementation of PA policy	↓	Not measured	Not measured	Treatment discontinuation: ↑
Farley JF et al (2008)[8]	Implementation of step-therapy PA policy	↓	↑	↑	Outpatient visits: ↓
Law MR et al (2008)[11]	Implementation of PA policy	No change	Not measured	Not measured	Not measured
McCombs JS et al (2004)[9]	Closed formulary access to open access	↑	↓	↓	Hospitalizations: ↓ Nursing home care: ↓
Busch AB et al (2004)[18]	Implementation of managed behavioral health carve-out	Not measured	Not measured	Not measured	Medication quality: no change Individual and/or group therapy and psychosocial rehabilitation: ↓
Soumerai SB et al (1994)[7]	3-prescription monthly payment limit (cap)	↓	↑	↑	Hospital admissions: no change Emergency mental health services/ partial hospitalization: ↑ CMHC visits: ↑

↑ indicates increased; ↓, decreased; CMHC, community mental health center; ED, emergency department; PA, prior authorization.
[a]Programs instituting a PA policy experienced lower growth in spending.
[b]A second analysis considered the incremental impact of a PA policy on hospitalizations. Small increases in hospitalizations made the PA policy a more costly option than no PA policy.

twice as high with implementation of the PA policy (hazard ratio, 2.28). Researchers concluded that a modest reduction in pharmacy spending ($27 per patient during the 8-month policy period) may have largely been driven by higher rates of medication discontinuation. Using the same data for patients with schizophrenia, Soumerai et al (2008) found that initiation of AAPs during the implementation of the Maine Medicaid PA policy resulted in a 29% greater risk of treatment discontinuation versus before the policy, while providing only minimal pharmacy savings.[14]

Similarly, Lu et al evaluated the association of PAs (affecting new prescriptions for nonpreferred AAPs [including olanzapine, olanzapine/fluoxetine, and aripiprazole] and anticonvulsants) with medication discontinuation among patients with bipolar disorder in the Maine Medicaid program (2001-2004).[15] Compared with pre-policy, implementation of the PA policy was associated with increased medication discontinuation for patients who visited CMHCs and patients who did not: CMHC attenders (ie, ≥2 visits) (38% vs 31%, respectively) and non-attenders (ie, <2 visits) (41% vs

33%, respectively). The frequency of psychiatric visits was reduced among CMHC attenders (−64 per 100 patients per month); however, emergency visits were increased among non-attenders (+16 per 100 patients per month). Researchers suggested that the administrative barriers associated with PA policies could affect continuity of care, leading to relapse while off treatment. Also, for CMHC non-attenders, attempts were being made to manage medication access issues in outpatient emergency departments (EDs).

The impact of formulary restrictions on AAP drug utilization was evaluated among 30 state Medicaid programs.[16] Among 11 states that instituted PAs between 1999 and 2008, AAP utilization per enrollee increased by 14%—a smaller increase than that observed in the 19 states without PA requirements (19%). However, overall antipsychotic utilization decreased by 3.1% in states with PA policies, which suggests that the reduction in targeted AAPs was not offset by the substitution of other antipsychotics. A similar finding was reported in a 2001 to 2004 study by Lu et al of patients with bipolar disorder in the Maine Medicaid program.[17] The PA policy was associated with an immediate decrease in the rate of initiation of bipolar treatments (1.8%). By 4 months after policy implementation, the relative rate of bipolar treatment initiation decreased by 32.3% without a corresponding increase in the initiation of preferred agents, indicating a potential failure to treat.

Busch et al conducted a study to evaluate the effect of a managed behavioral health carve-out on the quality of outpatient care for Medicaid patients with schizophrenia from 1994 to 2000.[18] Quality of care was measured by treatment recommendations established by the schizophrenia Patient Outcomes Research Team. Results showed that the carve-out was negatively associated with achieving quality care, with reduced odds of receiving any individual therapy (odds ratio [OR], 0.27; 95% CI, 0.22-0.33), group therapy (OR, 0.19; 95% CI, 0.14-0.25), and psychosocial rehabilitation (OR, 0.31; 95% CI, 0.26-0.38). However, the likelihood of receiving AAPs was the same whether or not a patient was in the carve-out program, and prescribing these medications had no direct economic consequence for the carve-out vendor. In another study from 2005 to 2007, a mental health carve-out in the Florida Medicaid program was assessed to determine if the implementation was associated with changes in drug utilization.[19] The introduction of the carve-out plan was associated with both positive (increased penetration and reduced polypharmacy) and negative changes (reduced adherence). Since overall Medicaid expenditures for antipsychotics declined, researchers cautioned whether the cost savings may have contributed to reduced quality of care.

Fung et al evaluated Medicare Advantage Part D cost sharing on antipsychotic drug spending, adherence, and clinical outcomes from 2006 to 2007 for beneficiaries with schizophrenia, bipolar disorder, or no mental health diagnosis.[20] Among beneficiaries with a coverage gap, greater patient cost sharing during the gap decreased Medicare antipsychotic drug expenditures while increasing patient out-of-pocket costs. However, hospitalizations and ED visits increased during the gap, and adherence rates (as measured by proportion of days covered) decreased during the gap (schizophrenia: −20.6%; bipolar disorder: −18.1%).

Walthour et al demonstrated an improvement in patient outcomes after implementation of the PA policy for AAPs among patients with schizophrenia in the Georgia Medicaid program from 2003 to 2006.[21] Olanzapine, aripiprazole, and olanzapine/fluoxetine were nonpreferred AAPs under the PA policy. New prescriptions were required to obtain a PA; patients already taking any of these medications at the time of implementation were eligible for grandfathering. Criteria for PA approval included trial of a generic typical antipsychotic agent; however, new and continuing prescriptions for other AAPs (ziprasidone, risperidone, clozapine, and olanzapine injection) did not require a PA. During the PA policy period, decreases in the mean number of all-cause ED visits (absolute difference = −0.042 PMPM; relative difference = −20.92%) and all-cause hospital admissions (absolute difference = −0.010 PMPM; relative difference = −22.27%) were observed. The analysis of utilization was not restricted to schizophrenia-related ED visits and hospitalizations. Of note, this Georgia Medicaid PA policy was far less restrictive than many other PA policies, providing both grandfathering of existing medications and multiple AAPs not requiring a PA.

Our review of the literature revealed that, when evaluated, formulary restrictions more often than not were associated with pharmacy cost savings. Eight of the 15 studies included an assessment of the impact of AAP formulary restrictions on both changes in pharmacy costs and clinical outcomes. Among these, 5 studies suggested that pharmacy cost savings were accompanied by increases in healthcare utilization (eg, hospitalizations, ED visits, and nursing home visits) or treatment discontinuation.[7,9,13,14,20] Two studies suggested that pharmacy cost savings were accompanied by decreases in healthcare utilization (eg, hospitalizations, ED visits, and outpatient visits).[8,21] An additional study, which evaluated a rescission of a PA exemption in a mental health subgroup, suggested that pharmacy cost increases were associated with a reduction in hospitalizations.[12] Assessment of overall cost burden of formulary restrictions was limited in the litera-

ture: 2 studies reported increases in overall costs after the implementation of formulary restrictions,[7,8] another study reported reduced overall costs after a shift from closed formulary access to open access,[9] and a decision analytical model estimated potential modest cost savings associated with the PA policy in another study.[10]

DISCUSSION

The intent of a PA is to encourage appropriate use of medications and to contain costs without negatively affecting clinical outcomes. Overall, although PA programs are common, there is a lack of adequately evaluated outcomes of these programs, including the long-term impact.[22] Based on an underlying concern that formulary restrictions may result in a similar or higher overall cost burden after implementation, states, such as California, have reversed their restriction policies. In these situations, pharmacy spending may be reduced following implementation of formulary restrictions, but the healthcare system's overall cost burden may have simply shifted to other parts of the system (eg, medical resource utilization).[7,8,20] In addition, increases in medication discontinuation rates have been reported after implementation of PA policies, suggesting that for some healthcare systems, a component of the pharmacy cost savings may be a result of patient nonadherence and a decline in medication utilization rather than a migration to lower-cost therapies.[13-15] The potential impact on adherence is critical when considering cost-containment approaches, as medication nonadherence is already a concern for patients with mental illness. It is estimated that half of patients with schizophrenia are nonadherent to therapy, with poor adherence linked to worse functional outcomes and increased risk of hospitalization.[23-26]

Restricted access may have an untoward effect on patients with mental illness by creating an administrative barrier to refilling medications.[13] Further, restrictions can be burdensome to administer and expensive to implement. A survey of Medicaid providers in Texas assessed the effects of a PA for psychiatric medications.[27] Administrative issues associated with PA policies included costs, time away from patients, uncompensated administrative time, and an extra step in providing care. In the Texas preferred drug list program evaluated in this review, the administrative costs were $4.4 million for all drug classes in 2005.[11] Moreover, restricting access for a drug class with a high treatment response variability could negatively affect patient care.[28,29] A patient who fails to respond to initial treatment with one drug may have a positive response to treatment with another drug; therefore, open access is essential for a drug class that requires such individualized patient care.

Limitations

This literature review is bound by the limitations of each respective study. Many of the studies are based on administrative and pharmacy claims data, which may be limited by potential inaccuracies and the inability to establish causality for treatment discontinuation. Also, estimates of drug expenditures likely did not account for manufacturer rebates offered to state Medicaid programs. Further, although we did seek to be more inclusionary given the limited evaluations in the literature, there was much heterogeneity among the studies reviewed (eg, study period, evaluation period, geographic area, inclusion of control, outcomes measured, and type of cost containment policy evaluated). Seven of the 15 studies evaluated did not include a control comparison from another state. In most studies, the follow-up period after policy implementation was relatively short (≤1 year). Although the studies represented multiple states and geographic regions, the policies may not be representative of all states and may not be generalizable. In addition to the policy restrictions imposed, outcomes can be affected by a number of other factors, including the underlying patient population (eg, disease state, gender, age, socioeconomic status), provider prescribing behavior, and patient response.

CONCLUSIONS

Formulary restrictions are often used as a cost-containment strategy in an environment of rising prescription drug costs. Although most studies that evaluated a pharmacy cost change demonstrated a reduction in costs, the overall cost change in most cases was not measured. A reduction in pharmacy costs after the implementation of formulary restriction policies is often accompanied by increases in healthcare utilization, such as hospitalizations and treatment discontinuation. There exists a gap in the literature as to whether restricted access to AAPs results in overall cost savings or, rather, shifts the cost burden from pharmacy spending to other parts of the healthcare system. Further investigation is warranted to fully understand the clinical and economic impacts of formulary restriction of AAPs for individuals with schizophrenia or bipolar disorder.

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Address correspondence to: Kimberly Boswell, MD, 4114 Woodlands Pkwy, Ste 500, Palm Harbor, FL 34685. E-mail: kim.boswell@xcenda.com.

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eAppendix. Overview of Studies

Study	Disease Area	Data Source		Study Period	Evaluation Period, Months	Outcomes Measured	Key Findings
		Study Cohort	Comparison Cohort (control)				
Fung V et al (2013)[1]	Schizophrenia or bipolar disorder[a]	Medicare (national)	N/A	2006-2007	Pre-gap: up to 5 Post gap: up to 5	• Drug spending, adherence, and healthcare utilization (hospitalizations and ED visits) before and after reaching the Part D coverage gap threshold	• For beneficiaries with a gap who reached it compared with those with no gap, total monthly expenditures on antipsychotic drugs ↓ (schizophrenia: −$123 [95% CI, −$138 to −$108]; bipolar: −$93 [95% CI, −$105 to −$82]) and out-of-pocket spending ↑ (schizophrenia: $104 [95% CI, $98-$110]; bipolar: $64 [95% CI, $59-$69]) • Adherence (PDC) similarly ↓ (schizophrenia: −20.6% [95% CI, −22.3 to −18.9]; bipolar: −18.1% [95% CI, −20.0 to −16.2]) • Hospitalizations and ED visits ↑ with cost sharing ↑ in the gap (schizophrenia: HR [99.5% CI]: 1.32 [1.06-1.65] and 1.14 [0.97-1.34], respectively; bipolar: HR [99.5% CI]: 1.45 [1.16-1.82] and 1.17 [1.00-1.37], respectively)
Robst J (2012)[2]	Schizophrenia or episodic mood disorder	Florida Medicaid	N/A	Feb. 2005-Mar. 2007	Pre-policy: 6 Post policy: 6	• Drug utilization before and after mental health carve-out	• Policy was associated with ↑ penetration (OR, 1.04; 95% CI, 1.01-1.07) and ↓ adherence (OR, 0.86; 95% CI, 0.83-0.89), polypharmacy (OR, 0.87; 95% CI, 0.82-0.92), and expenditures (coefficient, −0.454; P <.001)
Lu CY et al (2011)[3]	Bipolar disorder	Maine Medicaid	N/A	Jan. 2001-Feb. 2004	Pre-policy: 8 Post policy: 8	• Rates of AAP and anticonvulsant discontinuation before and after PA policy in	• PA policy was associated with ↑ rate of medication discontinuation (vs pre-policy) in both CMHC attenders and

						newly treated patients, stratified by severity of illness (CMHC attenders, [at least 2 visits] and non-attenders [<2 visits]) • Healthcare utilization	non-attenders • Hazard of discontinuation was ↑ for PA policy cohort for those initiated on AAPs (HR, 1.65; 95% CI, 1.16-2.35; *P* <.05) • PA policy associated with ↓ psychiatric visits after discontinuing medication among CMHC attenders (−64/100 patients per month; *P* <.05) and ↑ ED visits after discontinuing medication among non-attenders (16/100 patients per month; *P* <.05)
Vogt WB et al (2011)[4]	Mental health diagnosis	State Medicaid[b]	State Medicaid[b]	1999-2008	NR	• Drug utilization in programs with and without PA and other restrictions	• AAP utilization per enrollee ↑ by 14% with PA policy vs 19% without PA policy • Overall antipsychotic utilization ↓ by 3.1%
WalthourA et al (2010)[5]	Schizophrenia	Georgia Medicaid	N/A	Jul. 2003-Apr. 2006	Pre-policy: 14 Post policy: 20	• Healthcare utilization before and after PA policy for AAPs	• A ↓ was observed post policy in mean number of ED visits (absolute difference = −0.042 PMPM; relative difference = −20.92%) and mean number of hospital admissions PMPM (absolute difference = −0.010 PMPM; relative difference = −22.27%) • No significant differences were observed for outpatient office visits or hospital length of stay
Simeone JC et al (2010)[6]	Mental health diagnosis	Vermont Medicaid	N/A	Jul. 2005-Dec. 2007	Pre-policy: 12 Post policy: 12	• Drug utilization and costs of behavioral health medications (antipsychotics, antidepressants, and anxiolytics/ sedative hypnotics) before and after PA policy (following rescission of PA exemption)	• PMPM pharmacy costs ↑ by 2.1% (compared with 12.2% ↑ for all nonbehavioral health medications) • Little change observed in utilization of behavioral health medications pre- and post policy • For subgroup taking AAPs, high-dose

							prescriptions ↓ from 3.1% to 2.2% (ie, met threshold for PA) • Mental health inpatient hospitalizations ↓ from 0.6% to 0.4%
Abouzaid S et al (2010)[7]	Schizophrenia	State Medicaid perspective (decision analytic model)	N/A	N/A	1-year time horizon	• Total cost of care with or without PA policy for AAPs	• PA policy would save approximately $29 per patient per year (mean yearly total medical cost of $12,967 vs $12,996 for PA policy vs no PA policy, respectively) • Under assumption of equal rates of hospitalization, PA policy produced modest cost savings 56% of the time • Sensitivity analyses demonstrated that an ↑ in hospitalizations of 0.5% would make the PA policy the more costly option
Lu CY et al (2010)[8]	Bipolar disorder	Maine Medicaid	New Hampshire Medicaid	2001-2004	Pre-policy: 10 Phase-in: 3 Policy: 7	• Rates of treatment initiation and switching of AAPs and anticonvulsants before and after PA policy	• PA policy was associated with a ↓ in rates of initiation of bipolar treatments (driven primarily by non-preferred agents without offsetting ↑ in preferred agents); immediate ↓ of 1.8% (95% CI, −3.20 to −0.42; P <.05) in new starts and a ↓ in slope of 0.5% (95% CI, −0.76 to −0.28; P <.05) • No impact from PA policy on rates of switching therapy
Zhang Y et al (2009)[9]	Bipolar disorder	Maine Medicaid	New Hampshire Medicaid	2001-2004	Pre-policy: 8 Policy: 8 Post policy: 8	• Drug utilization of AAPs and anticonvulsants, discontinuations in therapy, and pharmacy costs before and after PA policy	• PA policy resulted in 8% ↓ in use of nonpreferred AAPs and anticonvulsants but did not ↑ use of preferred agents (ie, no PA) or rates of switching • PA policy ↓ pharmacy reimbursements by $3.40 PMPM during policy period • Compared to pre-

							policy period, the policy period was associated with 2.28 (95% CI, 1.15-4.52) ↑ adjusted hazard of treatment discontinuation (all bipolar drugs)
Soumerai SB et al (2008)[10]	Schizophrenia	Maine Medicaid	New Hampshire Medicaid	2001-2004	Pre-policy: 8 Policy: 8 Post policy: 8	• Utilization of AAPs, risk of treatment discontinuation, and reimbursement of AAPs for patients initiating treatment before and after PA policy for AAPs	• PA policy ↓ utilization of restricted AAPs • PA policy ↑ risk of treatment discontinuation by 29% compared to the pre-policy cohort (P = .036), while risk remained the same throughout the study for control state with no PA policy • Over 8-month PA policy period, there were minimal ↓ in reimbursements of AAPs in both states (−$2.33 PMPM in Maine vs −$3.58 PMPM in New Hampshire [control])
Farley JF et al (2008)[11]	Schizophrenia[c]	Georgia Medicaid	Mississippi Medicaid	Jan. 1996-Dec. 1997	Pre-policy:10 Policy: 11 Post policy: 3	• Prescription and other psychiatric health service expenditures before, during, and after step therapy PA policy for AAPs	• AAP expenditures ↓ by $19.62 PMPM (partially offset by a $2.20 PMPM ↑ in typical antipsychotic expenditures); P <.001, both • Expenditures for outpatient services ↑ by $31.59 PMPM; P <.001
Law MR et al (2008)[12]	Mental health diagnosis	West Virginia and Texas Medicaid	State Medicaid from 38 states	1991-2005	Pre-policy: 24 Post policy: 21-33	• Market shares and reimbursement of all antipsychotics before and after PA policy for AAPs	• PA policy ↓ the market share of nonpreferred drugs by 3.5% (P = .003) in West Virginia and 2.6% (P = .055) in Texas • PA policy had no significant effect on overall pharmacy reimbursements of antipsychotics in either state
McCombs JS et al (2004)[13]	Mental health diagnosis[d]	California Medicaid	N/A	Jan. 1994-Aug. 2000	Policy: 45 Transition: 6 Post policy:	• Prescription and other health service expenditures and	• Total expenditures per month after initiating treatment ↑ by 15.2% in the open access

					12	utilization before and after PA policy for AAPs	period, down from 19.5% in the PA policy period • Total expenditure ↓ in the open access period was attributed to ↓ nursing home utilization, despite ↑ drug costs
Busch AB et al (2004)[14]	Schizophrenia	State Medicaid	2 similarly urban regions	Jul. 1994-Jun. 2000	NR	• Quality of outpatient care before and after managed behavioral care carve-out, measured by treatment recommendations from the schizophrenia PORT	• No statistical difference pre- and post policy in likelihood of receiving any antipsychotic medication (OR, 1.02; 95% CI, 0.81-1.29) or AAPs (including clozapine, OR: 1.05; 95% CI, 0.86-1.28; not including clozapine, OR, 1.05; 95% CI, 0.85-1.29) • Policy was negatively associated with receiving any individual therapy (OR, 0.27; 95% CI, 0.22-0.33), group therapy (OR, 0.19; 95% CI, 0.14-0.25), and psychosocial rehabilitation (OR, 0.31; 95% CI, 0.26-0.38)
Soumerai SB et al (1994)[15]	Schizophrenia	New Hampshire Medicaid	New Jersey Medicaid	Jul. 1980-Dec. 1983	Pre-policy: 14 Policy: 11 Post policy: 17	• Utilization and reimbursement of antipsychotics and acute mental health services before, during, and after a 3-prescription monthly payment limit (cap)	• The cap ↓ antipsychotic expenditures by $5.14 PMPM, a ↓ of 23% from the pre-policy baseline of $21.97 PMPM; *P* <.001 • The cap was associated with a substantial ↑ in antipsychotics administered at CMHCs and the number of emergency services utilized at CMHCs • Based on ↑ service utilization, the cap was associated with ↑ costs at CMHCs of $139 PMPM • Mental health service

							costs exceeded drug reimbursement savings by a factor of 17

↑ indicates increased; ↓, decreased; AAP, atypical antipsychotic; CMHC, community mental health center; ED, emergency department; HR, hazard ratio; N/A, not applicable; NR, not reported; OR, odds ratio; PA, prior authorization; PDC, proportion of days covered; PMPM, per member per month; PORT, Patient Outcomes Research Team.

[a]Study cohort also included antipsychotic use by individuals with no mental health diagnosis.

[b]Total of 30 state Medicaid programs were evaluated with and without PA restrictions.

[c]Based on sub-analysis of this population.

[d]Schizophrenia was most common mental health diagnosis (46%).

eAPPENDIX REFERENCES

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