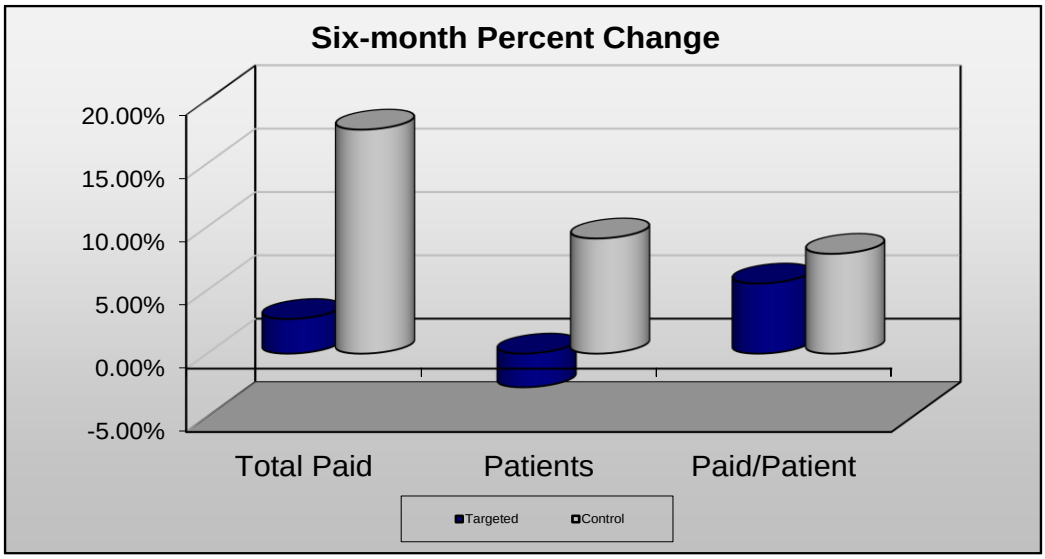
Bipolar Disorder Management

Prepared for Texas Medicaid in September 2022

EXECUTIVE SUMMARY

Purpose of Intervention	To promote safe and effective drug therapy in patients with Bipolar Disorder (BD). The National Institute for Health and Care Excellence (NICE) clinical guideline[1], the Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative guidelines[2], and the British Association for Psychopharmacology (BAP) guideline for the management of bipolar disorder[3] provide the foundation for this proposal. These guidelines, along with recently published major studies, provide performance indicators to evaluate the medication management of BD.

Intervention	Intervention Type	Population-based mailing
	Intervention Mailing Date	11/23/2021
	Pre-intervention Period (Baseline)	June 2021 – November 2021
	Post-intervention Period (Post)	January 2022 – June 2022
	Number of Letters Mailed	322
	Number of Targeted Physicians	322



SAVINGS CALCULATION

State Cost Savings Calculation:	
Targeted Group: Actual Bipolar Management Drugs Average Cost Per Patient Per Month (Pre)	$279.99
% Change in Control Group from Pre to Post	7.88%
Estimated Bipolar Management Drugs Paid Amount Per Targeted Patient Per Month if No Intervention	$302.05
Targeted Group: Bipolar Management Drugs Cost Per Patient Per Month (Post)	$295.48
Estimated Cost Savings Per Patient Per Month	$6.57
Total Monthly Number of Targeted Panel Patients Served in Post Period	105,430
6-Month Total Savings	$692,675.10
6-Month State General Revenue Funds Savings	$277,139.31
12-Month Total State Savings	$554,278.62

BACKGROUND

Bipolar Disorder (BD) is a complex, long-term illness characterized by a repeating course of relapse and remission. BD has an estimated lifetime prevalence of 4.4% for adults in the United States and is associated with significant psychosocial impairment and disability along with a reduced quality of life.[2,4,5] Pharmacotherapy is the mainstay of treatment for BD, and treatment guidelines recommend such regimens be built around adequate dosing of a mood stabilizer.[1-3] Additional medication classes commonly employed include atypical antipsychotic agents, antidepressants, and stimulants.[6,7] The principles to effectively employ and combine these different medication groups to obtain optimal outcomes with minimal risks are the focus of this intervention.

Indicator #1: Antidepressant use without a Mood Stabilizer/Atypical Antipsychotic

Depression is a common feature of BD and many patients have more frequent depressive episodes than manic episodes. Antidepressants have long been used in this patient population, despite ongoing controversy regarding their safety and efficacy.[8] No antidepressants are specifically FDA-approved for use in the treatment of depression associated with BD. Unfortunately, antidepressants may destabilize patients with BD and result in a switch into mania. The risk for destabilization appears to vary slightly among available antidepressants but has been estimated at 20% to 40%.[8-10] Treatment guidelines recommend use of antidepressants only in combination with a mood stabilizer.[1-3]

Candidates (denominator):	Patients who have therapy with an antidepressant in the past 45 days with a history of a BD diagnosis (submitted ICD-10 codes) in the past 2 years.
Exception Criteria (numerator):	Candidates who do not have therapy with a mood stabilizer/atypical antipsychotic (Table 1) in the last 45 days.

Indicator #2: Use of Multiple Antipsychotics as Mood Stabilizers

Psychosis is a common feature in patients with BD, and antipsychotic agents have been used as adjunctive therapy to manage it, although until recently there was limited published evidence to support such use.[11] In the past several years, many antipsychotics have received FDA-approved indications for the management of BD. These indications are primarily for acute use in the management of manic or mixed episodes. However, a few indications are approved for maintenance use, either as monotherapy or as an adjunct to another mood stabilizer. The use of multiple antipsychotics should not occur in patients with BD. If the response to an atypical antipsychotic is inadequate, a different type of mood stabilizer should be added.[1-3]

Candidates (denominator):	Patients who have therapy with an antipsychotic in the past 90 days with a diagnosis of BD (submitted ICD-10 codes) in the past 2 years and who do not have a diagnosis of schizophrenia (submitted ICD-10 codes) in the past 2 years.
Exception Criteria (numerator):	Candidates who received therapy with more than one antipsychotic for greater than 60 out of the last 90 days.

Indicator #3: Use of a Stimulant Medication

The problems associated with antidepressant use in patients with BD have led clinicians to attempt to manage bipolar depression with alternative agents. Stimulants, such as methylphenidate, have been reported to be one such alternative.[12] In addition, BD is being diagnosed with increasing frequency in the pediatric population, resulting in clinicians more frequently attempting to manage attention-deficit hyperactivity disorder (ADHD) and BD simultaneously.[7] Unfortunately, empiric evidence to support and guide the use of stimulants in the BD population is limited, and they do not appear to be any safer than antidepressants in terms of the risk of destabilization.[13] Available treatment guidelines for BD do not adequately address the appropriate use of stimulants, but available research indicates such use should be limited to those with co-morbid ADHD and BD, be in conjunction with a mood stabilizer, and combinations of a stimulant and an antidepressant should be avoided to minimize the risk of manic switch.[13]

Candidates (denominator): Patients who have therapy with a stimulant in the past 45 days with a history of BD diagnosis (submitted ICD-10 codes) in the past 2 years.

Exception Criteria (numerator):

1. Candidates who do not have a diagnosis of ADHD (submitted ICD-10 codes) in the past 2 years.
2. Candidates with a diagnosis of ADHD (submitted ICD-10 codes) in the past 2 years who:
    - do not have therapy with a mood stabilizer or atypical antipsychotic (Table 1) in the last 45 days.

Indicator #4: Monitoring of Lithium: Serum Lithium Level, Renal Function, Thyroid Function

Lithium is a very effective mood stabilizer, but it has a narrow therapeutic index and serum lithium levels must be monitored for patient safety. In addition, it is associated with potential adverse effects on renal and thyroid function that require periodic monitoring.[14,15]

Candidates (denominator): Patients who have therapy with lithium in the past 45 days with a history of BD diagnosis (submitted ICD-10 codes) in the past 2 years.

Exception Criteria (numerator): Candidates who do not have documentation of the following labs (submitted CPT codes) in the past year:

1. serum lithium level
2. renal function
3. thyroid-stimulating hormone level

Indicator #5: Monitoring of Atypical Antipsychotics: Blood Glucose/A1C and Lipid Panel

Atypical antipsychotics may be effective when used appropriately in the management of BD, but their long-term use may result in metabolic adverse effects. Given these risks, baseline and ongoing monitoring is recommended.[16]

Candidates (denominator):	Patients who have therapy with an atypical antipsychotic (Table 1) in the past 45 days with a history of BD diagnosis (submitted ICD-10 codes) in the past 2 years.
Exception Criteria (numerator):	Candidates who do not have documentation of the following labs (submitted CPT codes): 1. blood glucose or hemoglobin A1C in the past year 2. lipid panel in the past 2 years

Indicator #6: Monitoring of Anticonvulsants: Hepatic Function, Renal Function and Complete Blood Count

Carbamazepine and valproic acid analogs are effective mood stabilizers used in the management of BD. Their use, however, has been associated with potential serious adverse effects on the liver, kidney, and platelets which require periodic monitoring.[17,18]

Candidates (denominator):	Patients who have therapy with carbamazepine or a valproic acid analog in the past 45 days with a history of BD diagnosis (submitted ICD-10 codes) in the past 2 years.
Exception Criteria (numerator):	1. Candidates on carbamazepine who do not have documentation of hepatic and renal function tests (submitted CPT codes) in the past year. 2. Candidates on a valproic acid analog who do not have documentation of hepatic function tests and a complete blood count (submitted CPT codes) in the past year.

Indicator #7: Nonadherence with Maintenance Bipolar Medications

Long-term treatment for BD is effective in preventing disease relapse. Since, BD is a chronic, recurring medical condition, maintenance medication therapy, along with psychosocial intervention, is critical for long-term success. Unfortunately, poor treatment adherence is common in patients with BD, especially early in the course of the disease as well as in younger patients. Medication nonadherence, if unrecognized, can lead to unnecessary dose increases, the addition of adjunctive medications, or changes in treatment regimens. It can also increase the risk of relapse, hospitalization, worsening quality of life, and even suicide.[1-3]

Candidates (denominator):	Patients receiving a non-injectable atypical antipsychotic or mood stabilizer (Table 1) in the most recent 45 days and 90 to 135 days ago (identifies chronic therapy) with a history of BD diagnosis (submitted ICD-10 codes) in the past 2 years.
Exception Criteria (numerator):	Candidates who received less than a 60-day supply of the medication during the last 90-day period.

Exclusion: Patients who are currently pregnant. Patients with history of an injectable long-acting atypical antipsychotic in the last 120 days will also be excluded from assessment of nonadherence with an oral atypical antipsychotic.

METHODOLOGY

In November 2021, all physicians treating patients with any of the aforementioned drug-related problems were identified. Based on the distribution of patients/physician, the minimum patient/month threshold was set at greater than two patients (i.e. physicians with three or more patients having a drug-related problem received the mailing). Providers were mailed the intervention materials on November 23, 2021.

Operational definitions:

Targeted Group – physicians treating one or more patients with any of the aforementioned drug-related problem(s) and who received mailed intervention materials *(Section 1.e.1.A Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Control Group - physicians treating patients taking an intervention-related drug but did not receive mailed intervention materials *(Section 1.e.1.A Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Intervention Drugs – Mood Stabilizers, Antidepressants, Anticonvulsant Agents, Antipsychotic Agents, and Stimulants

Pre Intervention Time Period – June 2021 through November 2021

Post Intervention Time Period – January 2022 through June 2022

Total Paid 6-month pre and post – total drug costs can be defined as the total amount of paid intervention-related drug claims for the above time periods for the prescribers in the control and target groups. The target group consisted of those prescribers who had prescribed intervention-related drug therapy to more than two Medicaid patients. The control group consisted of all other prescribers who prescribed intervention-related drug therapy agents in the designated time periods *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Average Number of Panel Patients per Month - during the 6-month pre and post time periods, the number of unique Medicaid patients with a drug claim submitted using a respective provider number was captured each month. Medicaid patients that did not have a drug claim were not counted in the prescriber's panel. The monthly numbers were summed then divided by six to calculate the monthly average. For example, in Table 3, the physician (with provider number AB123456) had an average of 12 patients with at least one drug claim per month. If a patient had two different claims in June, they would be counted as one patient. By evaluating all patients seen by a specific physician, changes in prescribing patterns can be evaluated on existing and new patients *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Table 3: Average Number of Panel Patients per Month

Provider Number	Month #	Number of Unique Patients with a Drug Claim
AB123456	1	10
	2	10
	3	10
	4	12
	5	13
	6	17
Total		72
Average Number of Panel Patients per Month		12

Average Cost/Patient per Month – this was calculated by dividing the total dollars paid for drug claims during the analysis time period by the total number of Medicaid panel patients during the respective time period. For example, in the targeted group post analysis; there were 105,430 patients who had a drug claim during the six-month review period. The total amount of dollars paid for drug claims for these patients during the post analysis was $31,152,527. Dividing these two numbers ($31,152,527/105,430) yields an average cost per patient of $295.48 *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

$$\text{Average Cost/Patient/per Month} = \frac{\text{Total Amount Paid for Bipolar Therapy Drugs}}{\text{Average number of Panel Patients per Month}} / \text{(\# Months)}$$

Total State Savings *(Sections 1.e.3 and 1.e.4 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal)***:**

- Intervention Average Cost Savings per Month - the percent change seen in the control group was applied to the intervention group baseline Average Cost per Patient per Month. This amount represents the estimated Amount Paid per Targeted Physician per Patient in the absence of the intervention (i.e., Estimated Paid Amount). The Estimated Paid Amount per Patient per Month was then subtracted from the actual Intervention Target Group Average Cost per Patient per Month to estimate the Average Cost Savings per Patient per Month.
- 6-Month Total Savings - the Intervention Average Cost Savings per Patient per Month was multiplied by the total number of targeted patients served over the 6-month time frame.
- 6-Month State General Revenue Funds Savings= 6-Month Total State Savings X 0.4001.
- Total State Savings = 6-Month State General Revenue Funds Savings X 2.

RESULTS

Population-based intervention

A total of 322 physicians were targeted and received intervention materials. Table 4 compares the 6-month total amount paid for bipolar therapy drugs, the total number of patients in each physician's panel per month, and the average cost per patient for the targeted and control groups during the six-month pre and post periods. When comparing the pre-Average Cost per Patient per Month between the targeted and control groups, the cost was approximately $82 higher for the targeted group. This difference may be due to such factors as the targeted group having more patients prescribed intervention-related drugs per physician or that associated average intervention-related drug costs are inherently higher in the targeted group.

The target group saw a 2.73% increase in the amount paid for intervention-related drugs while the control group saw a 17.68% increase. Additionally, the average number of monthly patients for the physician's panel decreased 2.66% for the targeted group and increased 9.09% for the control group. To control for changes in case load variance (i.e., the change in the number of panel patients) between the two groups, the average cost per patient was also calculated. Total amount paid and number of panel patient trends led to a 5.53% increase in average cost per patient per month in the targeted group and a 7.88% increase for the control group.

Table 4: Six-Month Trends for Overall Targeted vs Control Group

Group	Bipolar Management Drugs -- Six Months Total Paid Pre/Post			Average Number of Panel Patients per Month			Bipolar Management Drugs Average Cost per Patient per Month		
	Pre	Post	Change	Pre	Post	Change	Pre	Post	Change
Targeted	$30,324,948	$31,152,527	2.73%	18,051	17,572	-2.66%	$279.99	$295.48	5.53%
Control	$134,084,367	$157,792,997	17.68%	112,604	122,840	9.09%	$198.46	$214.09	7.88%

Table 5 shows the Intervention Average Cost Savings per Patient per Month and the savings calculations. Had the intervention not been mailed, the targeted pre average cost per patient per month would have increased 7.88% from $279.99 to $302.05. The net difference between the actual and estimated average cost/patient for the targeted group was $6.57. Based on 105,430 targeted patients served per month during the six-month post period, the six-month Total Savings and Total State Savings are $692,675.10 and $277,139.31 respectively. Over a twelve-month period, the Total State Savings is $554,278.62.

Table 5: Overall Intervention Average Cost Savings

State Cost Savings Calculation:	
Targeted Group: Actual Bipolar Management Drugs Average Cost Per Patient Per Month (Pre)	$279.99
% Change in Control Group from Pre to Post	7.88%
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Table 6 shows the changes in the clinical indicators based on the intervention. The overall change in indicators is a decrease of 31.9%.

Clinical Indicators	Target		
	Baseline	Jun-22	% Change
Use of an antidepressant in the absence of a mood stabilizer/atypical antipsychotic	135	92	-31.9%
Use of multiple antipsychotics simultaneously as mood stabilizers	3	2	-33.3%
Use of a stimulant medication	26	17	-34.6%
Lithium monitoring: serum levels, renal function, and thyroid function	35	28	-20.0%
Atypical antipsychotic monitoring: blood glucose/hemoglobin A1C and lipid levels	237	151	-36.3%
Anticonvulsant monitoring: complete blood count, hepatic function, and renal function	44	32	-27.3%
Medication nonadherence with an atypical antipsychotic or mood stabilizer	65	49	-24.6%
Total	545	371	-31.9%

CONCLUSIONS

This population-based intervention was successful in encouraging appropriate use of bipolar management therapy drugs and providing prescribers with educational tools to better communicate with their patients' issues regarding appropriate treatment. This resulted in an economic impact on Texas Medicaid's pharmacy program expenditures, with a calculated twelve-month overall savings of $1,385,350.20 and savings to the state of $554,278.62 and a 31.9% decrease in clinical indicators

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Table 1. Agents Used in the Management of Bipolar Disorder[1-3]

Mood Stabilizers	• Carbamazepine • Lamotrigine • Lithium • Oxcarbazepine • Valproic acid analogs
Atypical Antipsychotics	• Aripiprazole • Asenapine • Cariprazine • Clozapine • Lurasidone • Olanzapine • Olanzapine/fluoxetine • Paliperidone • Quetiapine • Risperidone • Ziprasidone