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I. Methods

Annual Deductible Imputation

To estimate employer annual deductibles, we used a benefits variable available for most smaller employers (approximately ≤ 100 employees) and for larger employers, we imputed deductible levels using out-of-pocket costs among employees who utilized health services, an algorithm that had 96.2% sensitivity and 97.0% specificity.

Bipolar Cohort and Bipolar Type Identification Algorithm

We included individuals with diagnosis codes for bipolar I (International Classification of Diseases, 9th revision [ICD-9-CM] codes: 296.0x-296.1x, 296.4x-296.7), bipolar II (296.89), or other unspecified bipolar disorder (296.80-296.82, 301.11, 301.13), and assigned them to one of those three categories based on their earliest qualifying diagnoses of either 1 inpatient claim (with a first position diagnosis), or 2 outpatient claims (with a first or second position diagnosis) on separate days within 24 months of each other. If individuals had more than one qualifying bipolar category, bipolar I was given priority, then bipolar II. Individuals also qualified if their only diagnoses were from outpatient claims within the 2-year timeframe and on different days, but from different bipolar categories. These members were categorized as other unspecified bipolar disorder. Then we excluded members with schizophrenia or schizoaffective disorder diagnoses (ICD-9-CM: 295.0-295.95).

Medications for Treatment of Bipolar Disorder

We included the following: lithium, four guideline-recommended anticonvulsants (carbamazepine, divalproex sodium, lamotrigine, and valproic acid), and select first generation antipsychotic medications (chlorpromazine, droperidol, fluphenazine, haloperidol, loxapine, perphenazine, pimozide, prochlorperazine, thioridazine, thiothixene, trifluoperazine), and second-generation antipsychotics (aripiprazole, asenapine, clozapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone).

Covariates

Using 2008-2012 American Community Survey 5-year estimates at the census tract level (1–3), we classified members according to the income and education levels of their neighborhood. We categorized neighborhoods having proportions of households below the Federal Poverty Level of $< 9.9\%$ as higher income and $\geq 10\%$ as lower income. We consolidated neighborhoods having proportions of adults without a high school diploma of $< 25.0\%$ as higher education and $\geq 25.0\%$ as lower education. We used geocoding to classify participants as living in predominantly ($> 75\%$) white, black, Hispanic, or mixed neighborhoods, and we further overwrote the classification of select participants as Hispanic or Asian using the E-Tech system (Ethnic Technologies), which analyzes surnames and geographic locations of individuals (4,5). This validated approach of combining surname analysis and Census data has positive and negative predictive values of approximately 80%

and 90%, respectively (5). To estimate morbidity, we applied the ACG® algorithm based on age, sex, and diagnoses during the baseline year (6,7). Age categories were 12-18, 19-29, 30-39, 40-49, and 50-64 years. US regions of residence were West, Midwest, South, and Northeast. We created employer size categories of 0-99, 100-999, and 1000+ enrollees.

Matching Strategy

Coarsened exact matching tries to mimic the process of stratification by population characteristics and then randomization within the defined strata (i.e., fully blocked randomization). Coarsened exact matching is similar to exact matching but it classifies matching variables into discrete categories (e.g., 5-year age groups instead of continuous age in years). The final sample includes all members in both study groups that have common classification criteria. Coarsened exact matching software creates weights for all members in the matched strata to equalize the percentage of members in a given strata between the study groups.

We matched on employer- and member-level baseline covariates. These included quartile for employer baseline out-of-pocket costs to standardized costs ratio, four categories of baseline total out-of-pocket costs, and quartile for member's baseline total standardized cost. Matching variables also included employer and member-level propensity to join HDHPs. The employer-level propensity score included employer size; proportion of women; proportions of members in each of 4 US regions and in race/ethnicity, age, education, and income categories; baseline total standardized cost; mean employer Adjusted Clinical Groups (ACG) score; median copay; index month/year; and type of insurance plan (HMO, PPO, POS). The member-level propensity score included age category, US region, employer size, year of first qualifying diagnosis, baseline count of prescription medication categories, and baseline quarterly pharmacy out-of-pocket spending.

Standardized Medication Dose Measure Construction

Using data on units dispensed and days' supply in pharmacy claims for the entire population represented in our national database, we first identified the median number of units dispensed per day (e.g., one tablet) for a specific product (e.g., lithium 600mg tablets). Each dispensing can then be converted to the number of SMDs dispensed. In our example, if the median number of units dispensed for all individuals who took lithium 600mg was one tablet, a dispensing of two tablets per day would represent an SMD of 2.0, which would be assigned to each day following the dispensing for the days' supply indicated. We summed the SMD dispensed across medications within categories of interest each month, creating a repeated measure to examine medication use over time. Months were characterized as 30-day time periods relative to the index date.

Appropriate Laboratory Monitoring Measure Definition

The following definitions were used to measure rates of appropriate laboratory monitoring for specific medications: 1) annual proportion of individuals taking lithium (1970 members: 1639 controls and 331 HDHP members) who received testing for lithium level, thyroid stimulating hormone, calcium, and/or a combination of electrolytes, urea, and creatinine levels (EUC); 2) annual proportion of individuals taking carbamazepine (331 members: 272 controls and 59 HDHP members) who received testing for carbamazepine level, complete blood count, liver function, and/or EUC; 3) annual proportion of individuals on valproic acid (1088 members: 922 controls and 166 HDHP members) who received testing for valproate levels, and separately for complete blood count, and/or liver function; and, 4)

annual proportion of individuals on 2nd generation antipsychotics (4084 members: 3406 controls and 678 HDHP members) who received testing for lipid and/or serum glucose levels.

Appendix Table 1. HICL and Generic Names for Medications Included in Analyses

Medication Class	HICL Sequence Numbers	Generic Names
Guideline Anti-Convulsant	11735, 1893, 1884, 7378, 1883, 1882	Oxcarbazepine, Carbamazepine, Divalproex Sodium, Lamotrigine, Valproic Acid, Valproate Sodium
Typical Antipsychotics	1621, 1624, 1625, 1626, 1662, 1660, 1661, 1663, 1664, 1635, 1666, 1627, 13819, 1637, 1622, 1631, 1668, 1667, 1630, 1623	Chlorpromazine HCl, Fluphenazine Decanoate, Fluphenazine Enanthate, Fluphenazine HCl, Haloperidol, Haloperidol Decanoate, Haloperidol Lactate, Loxapine HCl, Loxapine Succinate, Mesoridazine Besylate, Molindone HCl, Perphenazine, Perphenazine/Amitriptyline HCl, Pimozide, Promazine HCl, Thioridazine HCl, Thiothixene, Thiothixene HCl, Trifluoperazine HCl, Triflupromazine HCl
Atypical Antipsychotics	24551, 42595, 36576, 42283, 4834, 36778, 37321, 11814, 36716, 25800, 34343, 36479, 14015, 8721, 25509, 21974, 23379	Aripiprazole, Aripiprazole Lauroxil, Asenapine Maleate, Brexpiprazole, Clozapine, Iloperidone, Lurasidone HCl, Olanzapine, Olanzapine Pamoate, Olanzapine/Fluoxetine HCl, Paliperidone, Paliperidone Palmitate, Quetiapine Fumarate, Risperidone, Risperidone Microspheres, Ziprasidone HCl, Ziprasidone Mesylate
Lithium	35133, 1669, 1670, 37605	Lithium Aspartate, Lithium Carbonate, Lithium Citrate, Lithium Citrate Tetrahydrate

II. Results

Appendix Table 2: Adjusted difference-in-differences estimates in annual utilization of non-bipolar psychotropic medications and all other medications among members with bipolar disorder before and after a mandated switch to HDHPs, compared with contemporaneous members with bipolar disorder in low-deductible plans (monthly number of standardized medication dose/member).

	HDHP		Control		Absolute Change, HDHP vs. Control (95% CI)		Relative Change, HDHP vs. Control (95% CI)	
	Baseline	Follow-Up	Baseline	Follow-Up				
Non-bipolar psychotropics medication classes								
ADHD Medications	3.8	3.9	4.3	4.6	-0.1	(-0.1, 0.0)	-2.5%	(-9.5%, 4.5%)
Antidepressants	18.0	17.6	18.4	17.9	0.2	(-0.4, 0.8)	1.2%	(-2.4%, 4.8%)
Benzodiazepines	7.0	7.4	6.8	7.3	0.0	(-0.4, 0.5)	0.0%	(-5.9%, 6.1%)
Anxiolytic, Sedatives and Hypnotics	2.3	2.5	2.3	2.5	0.1	(-0.2, 0.3)	2.8%	(7.2%, 12.8%)
Substance Abuse Disorder Medications	0.4	0.4	0.3	0.4	0.0	(-0.2, 0.1)	-10.4%	(-37.5%, 16.7%)
All other medications medication classes								
Antiarrhythmics	0.5	0.4	0.4	0.4	0.0	(-0.1, 0.1)	-6.4%	(-27.0%, 14.2%)
Anti-asthmatics	1.9	1.9	1.9	2.0	-0.1	(-0.3, 0.1)	-5.1%	(-13.3%, 3.0%)
Antibiotics	1.2	1.2	1.2	1.2	0.1	(-0.1, 0.1)	0.1%	(-7.1%, 8.6%)
Antiulcer Medications	2.2	2.2	2.2	2.3	-0.1	(-0.4, 0.1)	-6.2%	(-16.3%, 4.0%)
Cold and Allergy Medications	1.2	1.3	1.3	1.4	0.0	(-0.7, 0.7)	-2.1%	(-53.5%, 49.1%)
Gabapentin	1.1	1.2	1.1	1.1	0.0	(-0.1, 0.2)	3.4%	(-10.7%, 17.4%)
Antihypertensives	6.6	6.9	5.9	6.4	-0.3	(-0.9, 0.2)	-4.2%	(-11.6%, 3.2%)
Insulin	0.3	0.4	0.4	0.5	0.0	(-0.6, 0.8)	2.3%	(-16.8%, 21.4%)
Lipid Lowering Medications	2.8	3.2	2.8	3.2	-0.1	(-0.5, 0.2)	4.4%	(-13.2%, 4.3%)
Opiates	2.7	3.3	2.8	3.4	0.0	(-0.3, 0.3)	0.5%	(-8.6%, 9.7%)
Oral Anti-diabetes Medications	1.0	1.2	1.4	1.5	0.0	(-0.1, 0.2)	3.8%	(-12.5%, 20.0%)
Other Analgesics	2.3	4.3	2.2	2.5	1.8	(-1.9, 5.5)	69.8%	(-77.3%, 217.1%)
Antihistamines	0.2	0.1	0.2	0.2	-0.1	(-0.1, 0.0)	-36.0%	(-57.8%, -14.3%)
All Other Medications	13.5	14.6	12.5	13.5	0.0	(-0.6, 0.6)	0.0%	(-4.4%, 4.3%)

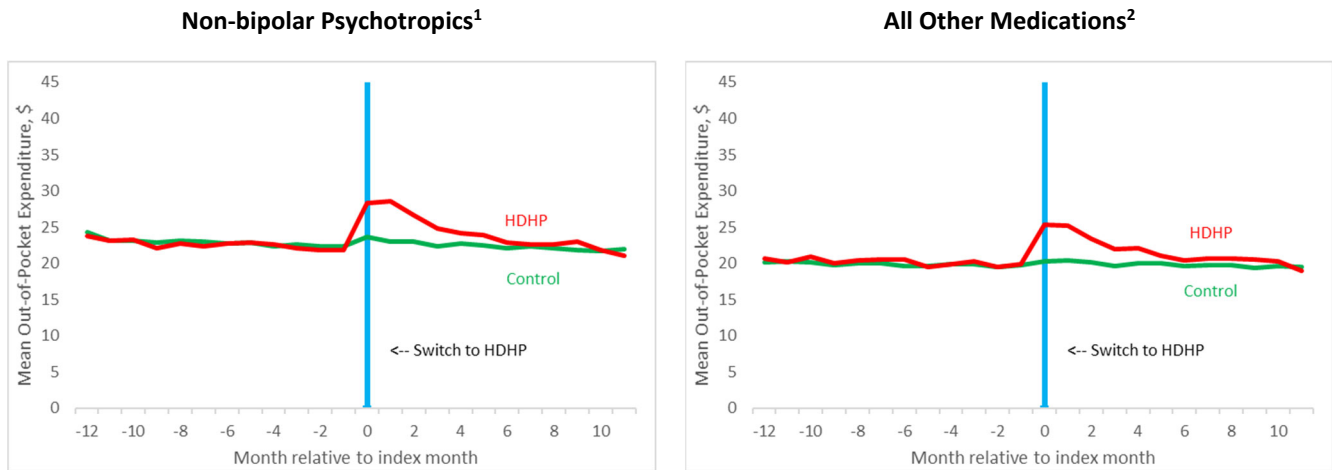
Abbreviation: HDHP, high-deductible health plan; ADHD = attention deficit hyperactivity disorder

Appendix Table 3: Annual percent of medication users receiving appropriate lab monitoring for Lithium, Antipsychotic, Carbamazepine and Valproic Acid

	HDHP		Control		Absolute Change, HDHP vs. Control (95% CI)		Relative Change, HDHP vs. Control (95% CI)	
	Baseline	Follow-Up	Baseline	Follow-Up				
Among Lithium Users								
Calcium	42%	37%	43%	39%	0.0	(-0.1, 0.1)	-3.1%	(-21.3%, 15.0%)
Electrolyte, Urea and Creatinine Test	60%	56%	62%	54%	0.0	(0.0, 0.1)	7.0%	(-6.2%, 20.1%)
Lithium	62%	58%	69%	57%	0.1	(0.0, 0.1)	10.7%	(-2.1%, 23.4%)
Thyroid Stimulating Hormone Test (TSH)	60%	60%	64%	58%	0.0	(0.0, 0.1)	9.1%	(-3.8%, 21.9%)
Among Antipsychotics Users								
Glucose	49%	48%	49%	44%	0.0	(0.0, 0.1)	10.0%	(-2.7%, 22.8%)
Lipid	39%	36%	36%	35%	0.0	(-0.1, 0.0)	-3.3%	(-16.7%, 10.1%)
Among Carbamazepine Users								
Complete Blood Count Test (CBC)	60%	53%	56%	58%	-0.1	(-0.3, 0.1)	-16.0%	(-44.2%, 12.1%)
Carbamazepine	43%	41%	51%	44%	0.0	(-0.1, 0.2)	11.9%	(-36.7%, 60.5%)
Electrolyte, Urea and Creatinine Test	44%	55%	54%	51%	0.14	(-0.1, 0.3)	33.1%	(-21.4, 87.5%)
Liver Function Test (LFT)	50%	60%	59%	58%	0.1	(-0.1, 0.3)	22.9%	(-18.9%, 64.6%)
Among Valproic Acid Users								
Complete Blood Count Test (CBC)	52%	45%	47%	46%	-0.1	(-0.2, 0.1)	-12.1%	(-32.4%, 8.2%)
Liver Function Test (LFT)	58%	50%	50%	48%	-0.1	(-0.2, 0.1)	-10.2%	(-28.8%, 8.4%)
Valproate Levels	4.5%	4.6%	6.4%	6.1%	0.0	(0.0, 0.0)	7.4%	(-9.6%, 111.1%)

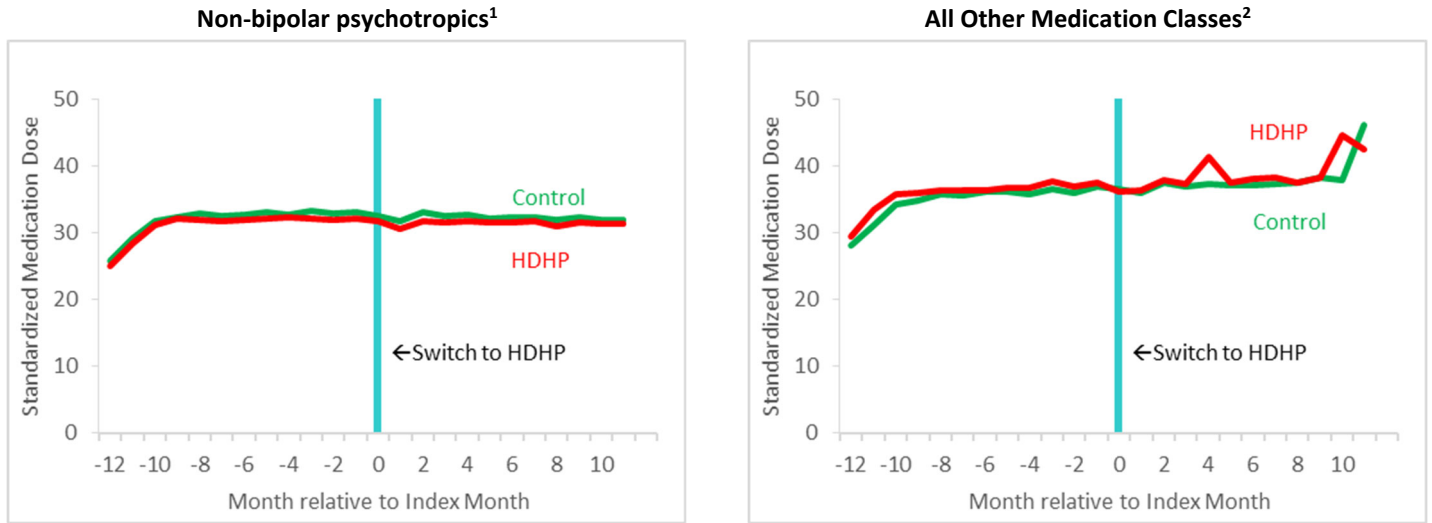
Abbreviation: HDHP, high-deductible health plan

Appendix Figure 1: Monthly out-of-pocket expenditures for all medications among members with bipolar disorder before and after a mandated switch to HDHPs, compared with matched controls who were in low-deductible plans in both years



Abbreviation: HDHP, high-deductible health plan ¹Non-bipolar psychotropic medications include the following medication classes: attention deficit hyperactivity disorder medications, antidepressants, benzodiazepines, substance abuse disorder medications, anxiolytics, sedatives and hypnotics; ²All other medications include all prescribed medications from classes not included in the bipolar and non-bipolar psychotropic categories

Appendix Figure 2: Monthly average number of standardized medication dose by medication class for bipolar, non-bipolar psychotropics and other medications among members with bipolar disorder before and after a mandated switch to HDHPs, compared with matched controls who were in low-deductible plans in both years



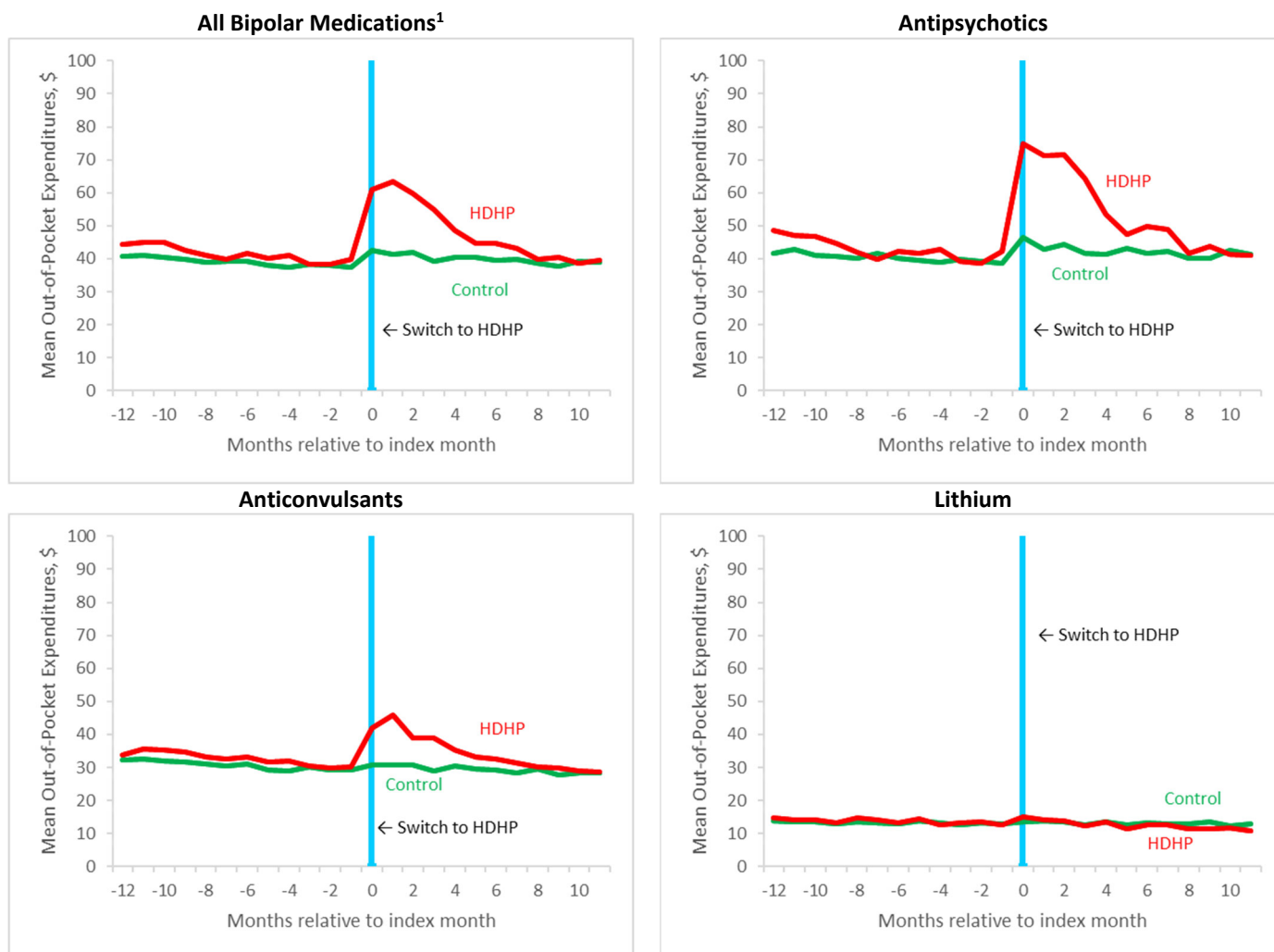
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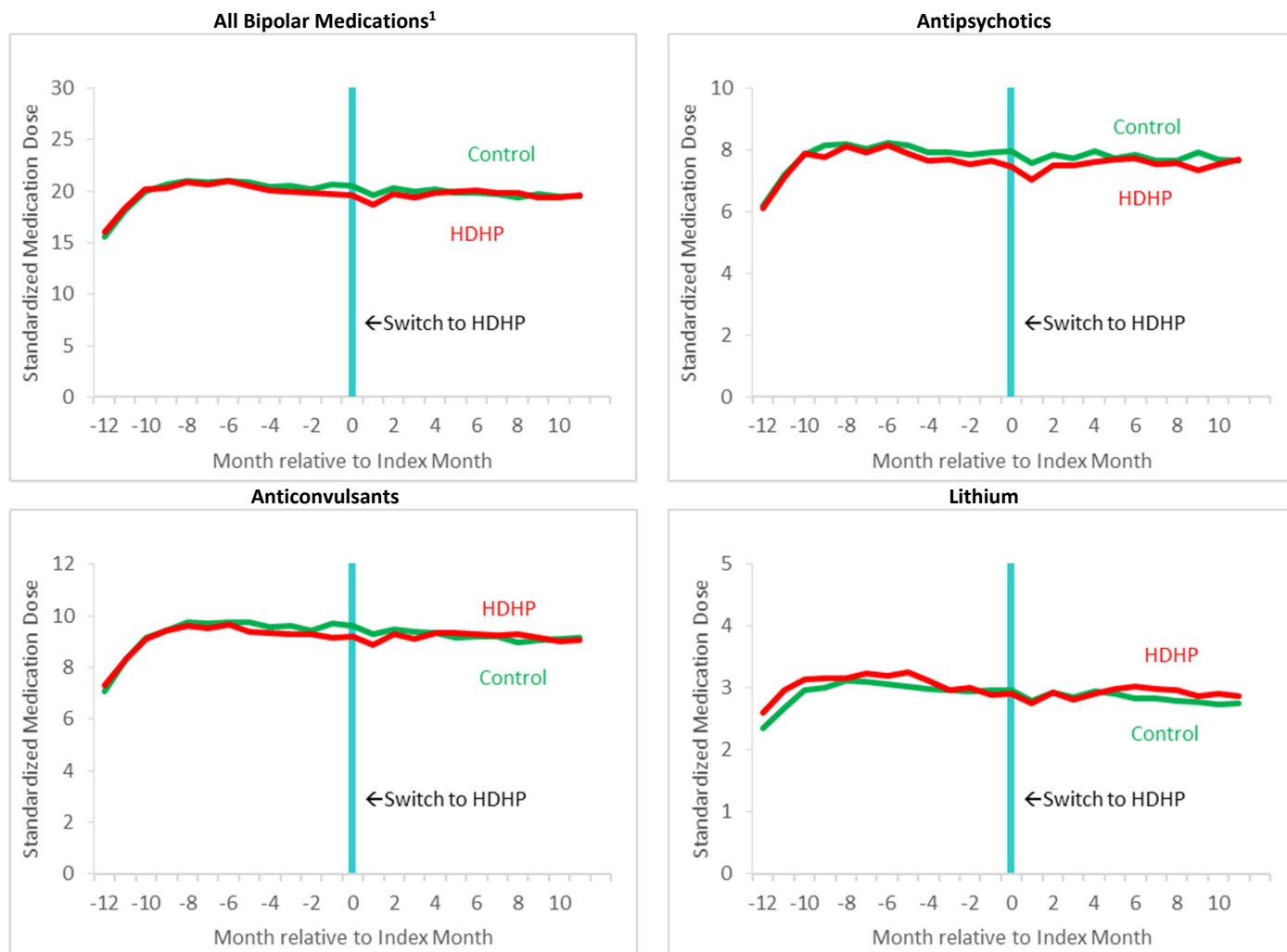
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Figure 1. Monthly out-of-pocket spending for all bipolar medications and by bipolar medication class among members with bipolar disorder before and after a mandated switch to HDHPs, compared with matched controls who were in low-deductible plans in both years.



Abbreviations: HDHP, high-deductible health plan. Vertical blue lines are centered at the index month when HDHP group members were switched into HDHPs. ¹Bipolar drugs include the following medication classes: anticonvulsants, antipsychotics and lithium

Figure 2. Average monthly number of standardized medication dose for bipolar medications (1st and 2nd generation antipsychotics, guideline-recommended anticonvulsants, or lithium) among members with bipolar disorder before and after a mandated switch to HDHPs, compared with matched controls in low-deductible plans in both years.



Abbreviations: HDHP, high-deductible health plan. Vertical blue lines are centered at the index month when HDHP group members were switched into HDHPs. ¹Bipolar drugs include the following medication classes: anticonvulsants, antipsychotics and lithium