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Supplementary Material

Article Title: High-Deductible Health Plans Paired With Health-Savings Accounts Increased Medication Cost Burden Among Individuals With Bipolar Disorder

Author(s): Christine Y. Lu, PhD, MSc[a,*]; Fang Zhang, PhD[a]; Jamie Wallace, MPH[a]; Robert F. LeCates, MA[a]; Alisa B. Busch, MD, MS[b,c]; Jeanne Madden, PhD[a,d]; Matthew Callahan, MS[a]; Phyllis Foxworth, BS[e]; Stephen B. Soumerai, ScD[a]; Dennis Ross-Degnan, ScD[a]; and J. Frank Wharam, MB, BCh, BAO, MPH[a,f,g]

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List of Supplementary Material for the article

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Appendix 1

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[27,28].

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,[34,44,45] we classified members according to the income and education levels of their neighborhood. Income categories were based on living in neighborhoods with below poverty-levels of <5%, 5%-9.9%, 10%-19.9%, and >=20%. We categorized neighborhoods having proportions of households below the Federal Poverty Level of <9.9% as higher income and >=10% as lower income. We used a similar approach to categorize education levels (neighborhood residence with below-high-school education levels of <15%, 15%- 24.9%, 25%-39.9%, and >=40%). We classified neighborhoods having proportions of adults without a high school diploma of <25.0% as higher education and >=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 full names and geographic locations of individuals.[46,47] This validated approach of combining name analysis and Census data has positive and negative predictive values of approximately 80% and 90%, respectively.[47] To estimate morbidity, we applied the ACG algorithm to members' baseline year. The algorithm uses age, sex, and diagnoses to calculate a morbidity score and the average of the reference population is 1.0. Researchers have validated this morbidity score against premature mortality.[48,49] 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 used coarsened exact matching on the propensity (tertiles) of the employer to mandate high-deductible insurance (component variables described below), the propensity (tertiles) of individuals to work for such employers (component variables described below), year of index date, quartile for employer baseline out-of-pocket spending to standardized cost ratio, four categories of baseline total out-of-pocket spending, and quartile for a member's baseline total standardized cost. The logistic model for calculating employer propensity to join a HDHP predicted this likelihood based on employer size; proportion of women; proportions of members in each of 4 US regions and in race/ethnicity, age, education, and income categories; baseline monthly total standardized cost; the employer's mean ACG score; median copay; index month/year; and type of insurance plan (HMO, PPO, POS). We constructed the corresponding member-level propensity model to ensure contemporaneous study groups as well as to balance key characteristics, thus this model included age category, US region, employer size category, year of first qualifying diagnosis, baseline count of prescription medication categories, and baseline quarterly pharmacy out-of-pocket spending.

Standardized Medication Dose Measure Construction

We conducted several steps to create a repeated measure to examine medication use over time. First, we identified the median number of units dispensed per day (e.g., one tablet) for a specific product (e.g., lithium 600mg tablets) using data on units dispensed and days' supply in pharmacy claims among users from the entire population represented in our national database for each year during the study period. We then converted each dispensing during the year to the number of standardized medication doses (SMDs) dispensed per day. In our example, if the median number of daily units dispensed for all individuals in the population who took lithium 600mg was one tablet per day, a dispensing of two tablets per day would represent an SMD of 2.0. The value 2.0 would be assigned to each day following that particular dispensing for the number of days' supply dispensed. Finally, we estimated the average monthly and yearly numbers of SMD per person as the sum of SMD dispensed for medications of interest in 30-day time periods and in the baseline or follow-up year divided by the number of people in a given study group. Months were characterized as 30-day time periods relative to the index date.

Supplementary Table 1. Hierarchical ingredient code list (HICL) and generic names for medications included in analyses

Drug 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

Supplementary Table 2: Adjusted difference-in-differences estimates in average wholesale price for medications among members with bipolar disorder (BD) before and after a mandated switch to HSA-HDHPs, compared with contemporaneous matched members with bipolar disorder in low-deductible plans, by study group (all members, higher-income, and lower-income)

	HSA-HDHP		Control		Absolute Change HSA-HDHP vs. Control (95% CI)		Relative Change HSA-HDHP vs. Control (95% CI)	
	Baseline	Follow-Up	Baseline	Follow-Up				
Average wholesale price (AWP), by 30-day fill equivalent								
All members								
Bipolar disorder Medications[1]	214.2	213.5	216.2	230.9	-15.3	(-32.3, 1.7)	-6.7%	(-13.8%, 0.5%)
Antipsychotics	331.2	325.6	320.7	343.9	-29.5	(-70.5, 11.4)	-8.3%	(-19.4%, 2.8%)
Anticonvulsants	184.0	185.5	192.9	201.4	-6.6	(-21.8, 8.5)	-3.4%	(-11.2%, 4.3%)
Lithium	28.5	26.4	29.2	29.4	-2.4	(-6.1, 1.3)	-8.4%	(-20.7%, 3.8%)
Non-bipolar psychotropics	108.8	102.8	112.3	114.6	-8.3	(-18.8, 2.3)	-7.4%	(-16.4%, 1.5%)
All Other Medications	147.8	156.1	150.6	166.5	-7.4	(-39.8, 25.0)	-4.5%	(-24.1%, 15.0%)
Higher-Income								
Bipolar disorder Medications[1]	211.9	206.1	218.9	230.8	-17.2	(-39.6, 5.1)	-7.7%	(-17.3%, 1.9%)
Antipsychotics	318.8	316.7	321.3	347.2	-27.7	(-83.7, 28.3)	-8.0%	(-23.8%, 7.7%)
Anticonvulsants	178.6	186.8	195.7	201.0	3.4	(-16.7, 23.5)	1.9%	(-9.2%, 12.9%)
Lithium	28.8	25.7	30.8	29.9	-2.3	(-7.6, 3.1)	-8.1%	(-26.4%, 10.1%)
Non-bipolar psychotropics	115.6	106.6	113.3	115.5	-11.2	(-27.0, 4.6)	-9.5%	(-22.0%, 3.0%)
All other medications	160.7	165.6	150.0	175.0	-22.0	(-72.8, 28.8)	-11.7%	(-37.7%, 14.3%)
Lower-Income								
Bipolar disorder Medications[1]	212.8	222.4	212.7	231.2	-8.8	(-34.1, 16.4)	-3.8%	(-14.5%, 6.9%)
Antipsychotics	347.1	336.7	320.3	339.4	-31.1	(-87.1, 25.0)	-8.4%	(-22.9%, 6.9%)
Anticonvulsants	187.1	179.4	189.0	201.7	-20.3	(-40.7, 0.0)	**-10.2%**	**(-19.7%, -0.7%)**
Lithium	27.5	26.8	26.9	28.8	-2.7	(-5.4, -0.1)	**-9.2%**	**(-17.1%, -1.3%)**
Non-bipolar psychotropics	99.0	98.4	111.0	113.3	-2.6	(-12.9, 7.6)	-2.6%	(-12.5%, 7.3%)
All other medications	134.3	143.1	149.9	151.8	7.1	(-25.1, 39.4)	5.2%	(-18.8%, 29.3%)

Abbreviations: HSA-HDHP, high-deductible health plan eligible to have associated health savings account; AWP, average wholesale price

[1]Bipolar medications include the following medication classes: anticonvulsants, antipsychotics and lithium