Medication Adherence, Health Care Utilization, and Costs in Patients With Major Depressive Disorder Initiating Adjunctive Atypical Antipsychotic Treatment☆

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ABSTRACT

Purpose: The purpose of this study was to compare medication adherence, health care utilization, and cost among patients receiving adjunctive treatment for major depressive disorder (MDD) with brexpiprazole, quetiapine, or lurasidone.

Methods: Using Truven Health MarketScan® Commercial, Medicaid, and Medicare Supplemental Databases, we identified adults with MDD initiating adjunctive treatment with brexpiprazole, quetiapine, or lurasidone (index atypical antipsychotic [AAP]). We compared medication adherence and persistence measured by proportion of days covered (PDC) and treatment duration of index AAP, all-cause and psychiatric hospital care (hospitalization or emergency department visit), and medical costs during 6-month follow-up. Models performed included logistic regression for hospital care, linear regression for PDC and cost, and Cox proportional hazards regression for time to discontinuation, adjusting for demographic, clinical, and utilization differences during the 6 months before index AAP.

Findings: The total sample included 778 brexpiprazole, 626 lurasidone, and 3458 quetiapine therapy initiators. Adjusting for baseline differences, the risk of discontinuation of index AAP was statistically significantly higher for quetiapine than for brexpiprazole (hazard ratio [HR] = 1.13; 95% CI, 1.02−1.25; $P = 0.023$) and did not differ between lurasidone and brexpiprazole (HR = 1.14; 95% CI, 1.00−1.29; $P = 0.054$). The adjusted rate of all-cause hospitalization or emergency department visit in the postindex period was lowest for brexpiprazole at 27.4% (95% CI, 24.0%−31.0%), compared with 31.1% (95% CI, 27.3%−35.2%) for lurasidone and 35.3% (95% CI, 33.5%−37.1%) for quetiapine ($P< 0.001$ for all comparisons). Quetiapine users had increased all-cause costs compared with brexpiprazole users (estimate = $2309; 95% CI, $31−$4587; $P = 0.047$); all-cause medical costs did not differ between lurasidone and brexpiprazole (estimate = $913; 95% CI, $–2033 −$3859; $P = 0.543$). Adjusted psychiatric hospital care, psychiatric costs, and PDC did not differ significantly among the groups.

Implications: In patients with MDD and a variety of insurance types, brexpiprazole use was associated with statistically significantly lower risks of discontinuation, risk of hospital care (hospitalization and ED visits), and all-cause medical costs compared with adjunctive quetiapine. Differences between brexpiprazole and lurasidone were not statistically significant. These findings suggest that drug choice is associated with subsequent health care utilization and costs. (*Clin Ther*. xxxx;xxx:xxx) © 2018 Published by Elsevier Inc.

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INTRODUCTION

Major depressive disorder (MDD), or unipolar major depression, is characterized by a history of ≥1 major depressive episodes without evidence of mania or hypomania. In 2015, an estimated 16.1 million people in the United States had at least 1 major depressive episode in the past year (approximately 1 in 15 of all US adults).[1] MDD is associated with alarmingly high costs (as much as $200 billion per year in direct and indirect costs according to 1 recent study[2]) and may be responsible for more human pain than any other mental or behavioral disorder.[1] Furthermore, despite available therapies, costs appear to have increased steadily in recent decades.[3]

The recommended initial therapy guidelines for MDD from both the American Psychiatric Association (APA) and the Texas Medication Algorithm Project consist of a combination of treatment with pharmacologic therapy and psychotherapy, based on trials that found the combination was more effective than either treatment alone.[4–6] A wide variety of antidepressants can be used as initial pharmacotherapy. Selective serotonin reuptake inhibitors are the most widely prescribed class, with no clear advantage to any other particular therapy at preventing relapse or recurrence.[7,8] Patients with inadequate relief of symptoms after initial treatment often fare much worse over the long run.[9]

Two common strategies for managing depression that has not resolved with initial treatment are switching treatment and augmenting initial antidepressant with an agent from another pharmacologic class.[5,10] Augmentation strategies frequently involve the use of atypical antipsychotic (AAP) medication, but there is little clinical trial evidence to help clinicians choose a particular augmentation strategy.[11] Both branded and generic options for treatment exist, and selection on the basis of price is common. Brexpiprazole, quetiapine, and lurasidone are branded AAPs commonly used in this setting. Among these 3 AAPs, brexpiprazole is the latest AAP approved by the US Food and Drug Administration (FDA) as an augmentation treatment to an antidepressant medication to treat adults with MDD. Although lurasidone is not indicated for MDD, it was selected because it was the newest AAP, with strong evidence from a randomized clinical trial supporting use in patients with MDD.[12] On the basis of our PubMed search, there are no head-to-head retrospective studies comparing these commonly used AAPs in MDD in the real-world setting. In the absence of comparative trials, retrospective studies can support clinical decision making. Although such evidence is always subject to more biases than randomized trials, retrospective studies may be larger, be more generalizable, and produce results sooner. Within the large population of patients with inadequately treated MDD, randomized trials of necessity focus on a small subset of patients. To supplement the clinical data on the optimal augmentation strategy for inadequately treated MDD, we conducted a retrospective, exploratory study using the most recent data from Medicare, Medicaid, and commercial insurance to compare health care utilization and costs among patients with MDD receiving the latest approved brexpiprazole with commonly used branded AAPs including quetiapine or lurasidone.

METHODS

This was a retrospective cohort study using the Truven Health Analytics MarketScan® Commercial, Medicaid, and Medicare Supplemental Databases. All databases comply with the Health Insurance Portability and Accountability Act.

The MarketScan Commercial Database includes medical and pharmacy claims for approximately 65 million individuals and their dependents, who are covered through employer-sponsored private health insurance plans. The MarketScan Medicare Supplemental Database contains records on approximately 5.3 million retired employees and spouses >65 years old who are enrolled in Medicare with supplemental Medigap insurance paid by their former employers. The MarketScan Medicaid Database contains the pooled health care experience of approximately 40 million Medicaid enrollees from multiple states. It includes inpatient and outpatient services, outpatient prescription drug claims, as well as information on enrollment, long-term care, and other medical care. In addition to standard demographic variables, such as age and sex, the database includes variables of particular value to researchers investigating Medicaid populations (such

as ethnicity, maintenance assistance status, and Medicare eligibility).

Patients with MDD were identified by the presence of at least 1 inpatient or 2 outpatient claims for MDD (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 296.2x, 296.3x; *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] codes F32.0-F32.5, F32.9, F33.0x-F33.4x, F33.9x) in any diagnosis field of a claim during the study period, which was January 1, 2015 to December 31, 2016, for Medicaid data and January 1, 2015 to September 30, 2016, for Commercial and Medicare Supplemental data.

Adult patients with MDD who had at least 1 fill of brexpiprazole, quetiapine, or lurasidone during the identification period (July 1, 2015 to June 30, 2016, for Medicaid data and July 1, 2015 to March 31, 2016, for Commercial and Medicare Supplemental data) were included in the analysis with a mutually exclusive cohort for each medication (Figure 1). The start date of the first prescription fill of the adjunctive antipsychotic was the index date. We excluded patients who had used the index antipsychotic in the 6 months before the index date (baseline period) to ensure at least a 6-month clean period. In addition, patients were required to have at least 1 antidepressant pharmacy claim in both the 90 days before and the 90 days after the index date. In addition, we required at least 15 days' antidepressant supply overlapping with the first prescription of the index therapy. Patients who used multiple AAPs on the index date were excluded. All patients were required to have continuous enrollment for the 6 months before and after the index date.

For the resulting cohorts, we compared baseline demographic characteristics, insurance type, measures of chronic and acute illness, and utilization and cost. In the follow-up period, we compared medication persistence and adherence using proportion of days covered (PDC) (defined as days with index therapy available divided by 180), discontinuation (defined as a medication gap $\geq$30 days, starting the day after the last days' supply), and duration of use (without a gap $\geq$30 days). All-cause and psychiatric hospital care (hospitalization and emergency department [ED] visits) and all-cause and psychiatric medical cost were also compared. Descriptive statistics, including means, standard deviations (SD), and relative frequencies and percentages for continuous and categorical data, respectively, were reported. *t* tests or χ^2 were performed as appropriate. For time to treatment discontinuation, Kaplan–Meier plots with log-rank tests were performed. To examine the

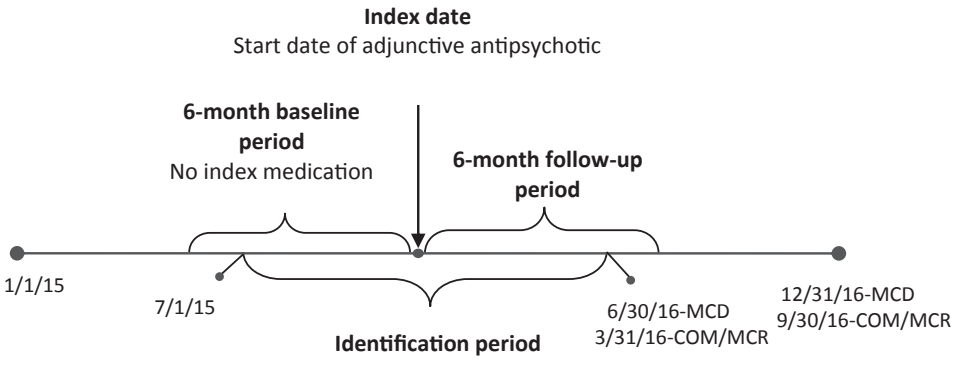

Figure 1. Study timeline. The study included adult patients with major depressive disorder who had at least 1 fill of brexpiprazole, quetiapine, or lurasidone during the identification period (July 1, 2015 to June 30, 2016, for Medicaid [MCD], July 1, 2015 to March 31, 2016 for Commercial [COM] and Medicare Supplemental [MCR]). The start date of the first prescription fill of the adjunctive antipsychotic was the index date. We required a 6-month clean period (no use of the index antipsychotic in the 6 months before the index date). The baseline and follow-up periods were defined as the 6 months before and after the index date, respectively.

association among the 3 antipsychotic cohorts and health outcomes, logistic regression was performed for hospital care, linear regression for PDC and cost, and Cox proportional hazards regression for time to discontinuation. The models were adjusted for baseline age group, sex, insurance type, Charlson Comorbidity Index[13,14] (excluding diabetes mellitus type 2, which was included separately), number of Healthcare Cost and Utilization Project chronic conditions,[15] psychiatric comorbidities, inpatient hospitalization, ED visit, nonpsychiatric medication use, and use of nonindex antipsychotic medication. In the absence of a single measure of MDD severity available in administrative claims data, ED and hospital utilization as well as medication use were considered proxies for severity of MDD. All data transformations and statistical analyses were performed using SAS© software, version 9.4 (SAS Institute, Cary, North Carolina).

RESULTS

Patient Selection and Baseline Characteristics

Across the Medicaid, Commercial, and Medicare databases, 879,540 patients had 1 inpatient or 2 outpatient claims for MDD. After excluding patients with schizophrenia or bipolar I disorder (for which an AAP can also be prescribed) during the study period, 779,733 individuals remained, of whom 17,818 filled a new prescription for brexpiprazole, quetiapine, or lurasidone in the identification period. In this group, 6907 had a prior diagnosis of MDD and had added the index therapy to prior antidepressant treatment. After excluding patients with <6 months of continuous enrollment before and after the index date and those <18 years old, 4862 were included in the final study sample: 778 brexpiprazole, 626 lurasidone, and 3458 quetiapine therapy initiators (Figure 2).

The mean (SD) age of the population was 47.4 (16.2) years, although the groups differed significantly, with lurasidone users a mean (SD) of 44.2 (14.0) years old at initiation compared with 47.8 (13.2) years old for brexpiprazole and 48.0 (17.1) years old for quetiapine ($P < 0.001$). Women predominated in all groups (69.7% overall) but made up 77.8% of lurasidone users compared with 74.0% of brexpiprazole and 67.2% of quetiapine users ($P < 0.001$). Commercially insured patients made up most of all groups (65.9%), but there were statistically significant differences in the proportion of commercial, Medicaid, and Medicare patients by index drug use ($P < 0.001$) (Table I).

Before adjunctive AAP therapy was initiated, there were statistically significant group differences in comorbid illness. The Charlson Comorbidity Index was higher in quetiapine users than in the other groups ($P < 0.001$), as was the Healthcare Cost and Utilization Project chronic condition indicator ($P = 0.025$). A higher percentage of quetiapine users had previous hospitalization and ED visits ($P < 0.001$) (Table II).

Medication Adherence, Health Care Utilization, and Costs

After adjustment for baseline differences, the risk of discontinuation of index AAP was statistically significantly higher for quetiapine than for brexpiprazole (hazard ratio [HR] = 1.13; 95% CI, 1.02−1.25; $P = 0.023$) and did not differ between lurasidone and brexpiprazole (HR = 1.14; 95% CI, 1.00−1.29; $P = 0.054$). The adjusted rate of all-cause hospitalization or ED visit in the 6-month postindex period was lowest for brexpiprazole at 27.4% (95% CI, 24.0%−31.0%) compared with 31.1% (95% CI, 27.3%−35.2%) for lurasidone and 35.3% (95% CI, 33.5%−37.1%) for quetiapine ($P < 0.001$ for all comparisons). The risk of all-cause hospital care was higher in quetiapine compared with brexpiprazole users (odds ratio [OR] = 1.45; 95% CI, 1.19−1.76; $P < 0.001$) but did not differ between lurasidone and brexpiprazole users (OR = 1.20; 95% CI, 0.03−1.54; $P = 0.153$). Quetiapine users had increased all-cause costs compared with brexpiprazole users (estimate = $2309; 95% CI, $31−$4587; $P = 0.047$); all-cause medical costs did not differ between lurasidone and brexpiprazole (estimate = $913; 95% CI, −$2033−$3859; $P = 0.543$). Adjusted psychiatric hospital care, psychiatric costs, and adjusted PDC did not differ significantly among the groups (Tables III and IV).

DISCUSSION

In this study of patients from 3 different types of insurance coverage (commercial, Medicare, and Medicaid) with MDD who began adjunctive antipsychotic treatment with 1 of 3 medications, the specific antipsychotic administered was a statistically significant indicator of therapy discontinuation and of the need for all-cause hospital care during the next 6

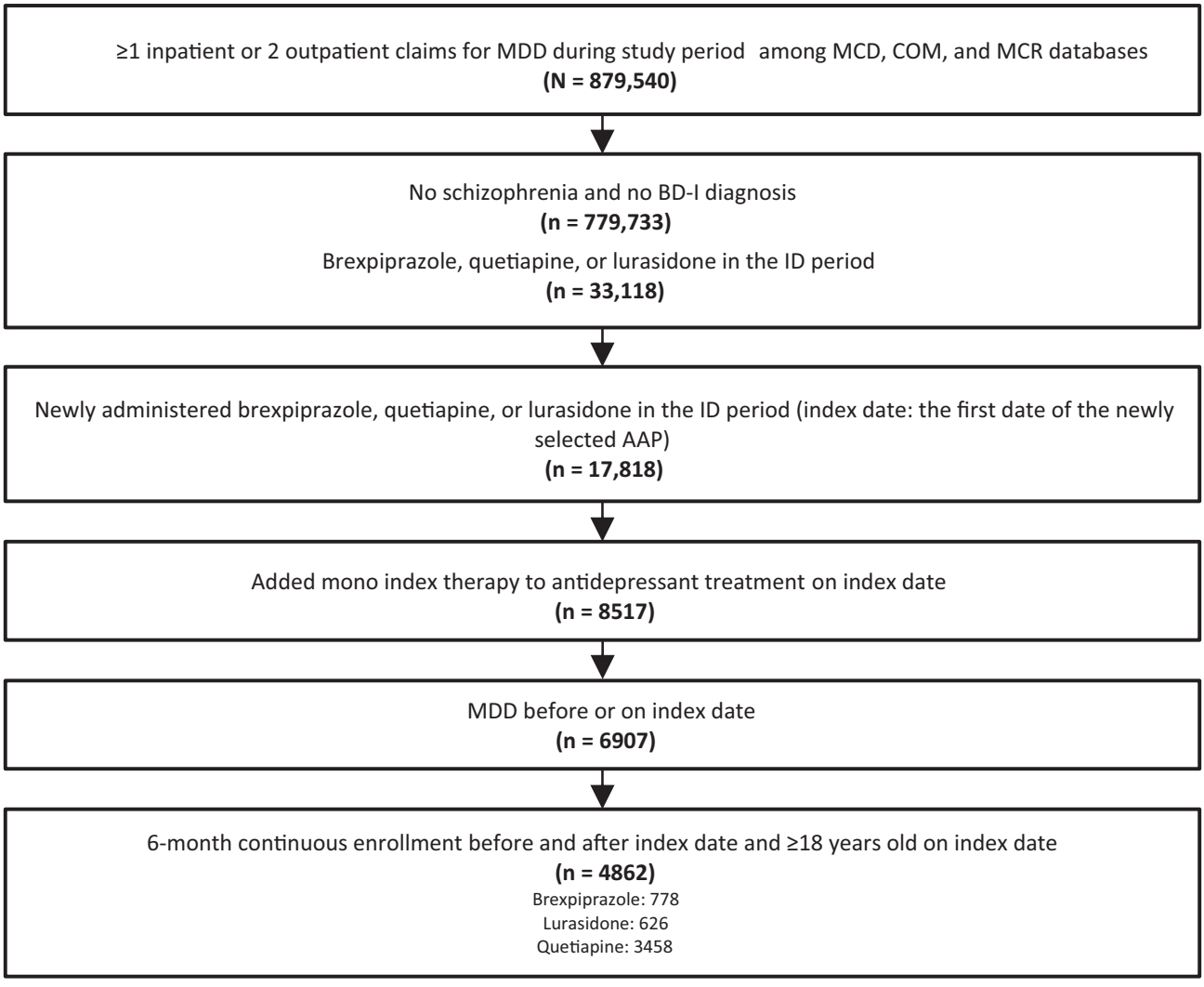

Figure 2. Patient attrition. Across the databases, there were 879,540 patients with major depressive disorder (MDD) during the study period (January 1, 2015 to December 31, 2016 for Medicaid [MCD] or January 1, 2015 to September 30, 2016 for Commercial [COM] and Medicare Supplemental [MCR]). After excluding patients with schizophrenia or bipolar I disorder (BD-I) during the ID period (July 1, 2015 to June 30, 2016, for Medicaid [MCD], July 1, 2015 to March 31, 2016 for Commercial with capital C [COM] and Medicare Supplemental [MCR]), 779,733 individuals remained, of whom 17,818 filled a new prescription for brexpiprazole, quetiapine, or lurasidone in the identification (ID) period. In this group, 6907 had a prior diagnosis of MDD and had added the index therapy before antidepressant treatment. After excluding patients with <6 months of continuous enrollment before and after the index date and those <18 years old, the final study sample included 4862 patients: 778 brexpiprazole, 626 lurasidone, and 3458 quetiapine therapy initiators. Mono index therapy indicates at least 1 antidepressant pharmacy claim each in 90 days before and 90 days after the index date (the first claim of index antipsychotic) and at least 15 days' supply overlapping with the first prescription of the index therapy days' supply. AAP = atypical antipsychotic.

Table I. Demographic characteristics of 4862 patients with major depressive disorder who initiated adjunctive atypical antipsychotic treatment.

Characteristic	Brexpiprazole (n = 778)	Lurasidone (n = 626)	Quetiapine (n = 3458)	All (N = 4862)	*P*
Age, mean (SD) [median], y	47.8 (13.2) [50]	44.2 (14.0) [45]	48.0 (17.1) [49]	47.4 (16.2) [49]	<0.001
Age group, No. (%)					<0.001
18–34	126 (16.2)	162 (25.9)	809 (23.4)	1097 (22.6)	
35–44	157 (20.2)	139 (22.2)	580 (16.8)	876 (18.0)	
45–54	218 (28.0)	162 (25.9)	848 (24.5)	1228 (25.3)	
55–64	231 (29.7)	134 (21.4)	792 (22.9)	1157 (23.8)	
≥65	46 (5.9)	29 (4.6)	429 (12.4)	504 (10.4)	
Female, No. (%)	576 (74.0)	487 (77.8)	2325 (67.2)	3388 (69.7)	<0.001
Insurance type, No. (%)					<0.001
Medicaid	159 (20.4)	193 (30.8)	770 (22.3)	1122 (23.1)	
Commercial	566 (72.8)	400 (63.9)	2237 (64.7)	3203 (65.9)	
Medicare Supplemental	53 (6.8)	33 (5.3)	451 (13.0)	537 (11.0)	

months compared with brexpiprazole and quetiapine. After adjustment for potential confounders, including demographic characteristics, insurance type, and various proxies for disease severity, only the differences with respect to quetiapine on risk of discontinuation and all-cause medical costs, as well as hospital care rates, remained significant. There were significant differences in the baseline characteristics, including age, ED visits, and hospitalizations, among the 3 cohorts, suggesting that the brexpiprazole-treated patients may be healthier, which may explain the inconsistency between the unadjusted and adjusted results.

Table II. Selected conditions, medications, and health care use before beginning adjunctive atypical antipsychotic treatment.

Variable	Brexpiprazole (n = 778)	Lurasidone (n = 626)	Quetiapine (n = 3458)	All (N = 4862)	*P*
Charlson Comorbidity Index, mean (SD)	0.7 (1.3)	0.7 (1.4)	1.0 (1.7)	0.9 (1.6)	<0.001
No. of chronic conditions (HCUP), mean (SD)	3.5 (2.0)	3.5 (2.0)	3.7 (2.1)	3.6 (2.1)	0.025
Anxiety, No. (%)	453 (58.2)	406 (64.9)	2227 (64.4)	3086 (63.5)	0.004
Personality disorder, No. (%)	19 (2.4)	27 (4.3)	119 (3.4)	165 (3.4)	0.151
Substance abuse disorders, No. (%)	61 (7.8)	85 (13.6)	707 (20.4)	853 (17.5)	<0.001
Obesity, No. (%)	114 (14.7)	105 (16.8)	421 (12.2)	640 (13.2)	0.003
Type 2 diabetes mellitus, No. (%)	110 (14.1)	82 (13.1)	451 (13.0)	643 (13.2)	0.713
Nonpsychiatric medication use, No. (%)	442 (56.8)	332 (53.0)	1914 (55.3)	2688 (55.3)	0.364
Nonindex antipsychotic use, No. (%)	358 (46.0)	288 (46.0)	644 (18.6)	1290 (26.5)	<0.001
Any baseline inpatient hospitalization, No. (%)	81 (10.4)	100 (16.0)	1062 (30.7)	1243 (25.6)	<0.001
Any baseline ED visits, No. (%)	197 (25.3)	196 (31.3)	1227 (35.5)	1620 (33.3)	<0.001

ED = emergency department; HCUP = Healthcare Cost and Utilization Project.

In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, after treatment with an initial antidepressant, 37% of patients experienced remission of symptoms and 49% had at least some response.[16] Efficacy in real-world clinical practice is unlikely to be as high as in a clinical trial setting with free care, careful follow-up, and a committed research staff. Considering these differences in care and the >16 million adults with depressive episodes every year in the United States, the relatively low response rate still leaves a large population requiring additional treatment. Although a switching strategy like the one in STAR*D, where use of the initial antidepressant medication is discontinued and use of a different antidepressant medication is initiated, incrementally increases the response rate, it still leaves a substantial proportion (30%–40% when including dropouts) severely symptomatic.

Increasing initial antidepressant dose, switching within class, switching to a different class, adding psychotherapy, or adding other nonpharmacologic treatments have all been studied as treatment options.[7,17–20] Despite (or maybe as a result of) the wide variety of choices, a 2013 systematic review of the literature concluded that "empirical data concerning the choice of the appropriate strategy are limited."[7] Some of the problems with studies that have been published include lack of randomization, lack of adequate observation time, nonrepresentative population, and lack of adequate power to detect a meaningful difference, among others.[7] Data comparing the effect of selecting one AAP instead of another are sparse.

The current retrospective study design has important advantages compared with clinical trials or medical record reviews. First, the number of patients we were able to examine was an order of magnitude higher than commonly enrolled in randomized trials of augmentation strategies for the treatment of MDD.[21] Second, the population was broadly representative of the US population with MDD, with a similar ratio of females to males, a similarly broad distribution of ages,[22] and similar insurance coverage to the general population[23] (although our study notably lacked data on the uninsured). Third, we used a 6-month observation period, a period several practice guidelines suggest should be adequate and is longer than most clinical trials.[7,21,24]

Limitations

This study was limited by its design and data source. First, although health insurance claims data are a valuable resource for real-world studies because of their coverage of large validated populations, there are inherent limitations. Claims are designed for reimbursement, rather than research purposes, and can contain errors (eg, misclassification, coding errors). In addition, information, such as disease severity or reason for treatment discontinuation, are not directly captured or clinically confirmed in claims data. Second, the choice of adjunctive therapy must, at least in part, have been driven by differences we could not measure. For example, some authorities have suggested an augmentation strategy is better suited for individuals who have inadequate, but partial, response to treatment compared with a switching strategy for patients with no response.[17,18] We could not determine which category our patients were in because this information is not available through insurance claims data. Similarly, we could not determine the number of antidepressants an individual had tried before initiating adjunctive treatment to classify them as resistant or highly resistant. There were measurable differences between groups—with quetiapine users having higher baseline levels of comorbid illness, health care utilization, and health care cost. Adjusting for these differences attenuated our findings but did not eliminate them completely. However, there may have been additional differences we could not measure or adjust for in models. Third, the study was conducted in a population that, although drawn from 3 disparate sources, may not represent the general population of all patients with inadequately treated depression. Specifically, although we included Medicare patients, this group had supplemental coverage, which suggests they have more comprehensive coverage than the broader Medicare population and may also imply they differ in other unmeasurable ways. Fourth, the outcome of greatest interest to a depressed person—the relief of symptoms—could not be measured in this claims-based study. Fifth, in this exploratory analysis, we included brexpiprazole, quetiapine, and lurasidone, 3 commonly used branded AAPs, based on FDA-approved indication for MDD and/or strong evidence supporting its efficacy in reducing depressive symptoms.[12] We are

Table III. Adjusted medication adherence, all-cause health care use, and costs during the 6 months after adjunctive antipsychotic treatment initiation.

Variable	Risk of Discontinuation of Index Antipsychotic Use		PDC of Index Antipsychotic After 6 mo		Any Inpatient Hospitalization or ED Visit After 6 mo		Total All-Cause Medical Costs After 6 mo	
	HR (95% CI)	*P*	Estimate, % (95% CI)	*P*	OR (95% CI)	*P*	Estimate, $ (95% CI)	*P*
Age group, y								
18–34 vs ≥ 55	1.21 (1.08–1.35)	0.001	−6.6 (−9.6 to −3.6)	<0.001	1.91 (1.54–2.36)	<0.001	1417 (−1172 to 4007)	0.283
35–44 vs ≥ 55	1.17 (1.0–1.31)	0.007	−4.5 (−7.5 to −1.5)	0.004	1.46 (1.18–1.80)	<0.001	−348 (−2903 to 2207)	0.790
45–54 vs ≥ 55	1.05 (0.95–1.16)	0.371	−1.6 (−4.3 to 1.0)	0.230	1.10 (0.91–1.33)	0.334	−399 (−2674 to 1876)	0.731
Female vs male	1.01 (0.94–1.09)	0.791	−0.3 (−2.3 to 1.7)	0.766	1.25 (1.09–1.45)	0.002	−423 (−2155 to 1309)	0.632
Insurance type								
MCD vs COM	1.02 (0.94–1.11)	0.642	1.1 (−1.2 to 3.5)	0.343	2.13 (1.82–2.48)	<0.001	−7251 (−9258 to −5244)	<0.001
MCR vs COM	0.87 (0.76–1.00)	0.054	4.7 (1.2–8.2)	0.008	1.36 (1.07–1.74)	0.012	−4159 (−7157 to −1161)	0.007
Modified CCI without diabetes	0.99 (0.96–1.02)	0.579	0.6 (−0.2 to 1.4)	0.155	1.06 (1.01–1.12)	0.028	3351 (2645–4056)	<0.001
No. of chronic conditions (HCUP)	0.99 (0.96–1.01)	0.234	0.5 (−0.1 to 1.2)	0.109	1.07 (1.02–1.12)	0.002	1021 (476–1567)	<0.001
Anxiety (yes vs no)	0.94 (0.87–1.01)	0.112	1.2 (−0.8 to 3.1)	0.248	1.02 (0.89–1.17)	0.810	−181 (−1865 to 1503)	0.833
Personality disorder (yes vs no)	1.01 (0.83–1.22)	0.952	0.9 (−4.2 to 6.1)	0.719	1.20 (0.85–1.70)	0.302	809 (−3577 to 5195)	0.718
Substance abuse disorder (yes vs no)	1.08 (0.98–1.19)	0.112	−1.7 (−4.4 to 0.9)	0.198	1.50 (1.26–1.78)	<0.001	5491 (3247–7735)	<0.001
Obesity (yes vs no)	1.02 (0.92–1.14)	0.675	−2.3 (−5.2 to 0.6)	0.125	1.17 (0.96–1.43)	0.111	1646 (−859 to 4151)	0.198
Type 2 diabetes mellitus (yes vs no)	0.98 (0.87–1.10)	0.715	−0.2 (−3.1 to 2.8)	0.898	1.25 (1.02–1.52)	0.029	1248 (−1273 to 3769)	0.332

Table III. (*Continued*)

Any baseline inpatient hospitalization (yes vs no)	1.06 (0.97–1.16)	0.202	1.5 (–3.9 to 0.9)	0.216	1.34 (1.14–1.57)	<0.001	4643 (2595–6691)	<0.001
Any baseline ED visit (yes vs no)	1.09 (1.01–1.18)	0.034	–2.8 (–4.9% to –0.7)	0.009	2.53 (2.20–2.90)	<0.001	4453 (2646–6260)	<0.001
Nonpsychiatric medication use (yes vs no)	1.00 (0.93–1.09)	0.914	1.1 (–1.0 to 3.3)	0.304	1.08 (0.93–1.26)	0.308	1210 (–654 to 3074)	0.203
Nonindex antipsychotic use (yes vs no)	1.18 (1.09–1.28)	<0.001	4.7 (2.6–6.9)	<0.001	1.14 (0.98–1.33)	0.084	545 (–1313 to 2402)	0.565
Index antipsychotic								
Lurasidone vs brexpiprazole	1.14 (1.00–1.29)	0.054	–3.4 (–6.9 to 0.0)	0.051	1.20 (0.93–1.54)	0.153	913 (–2033 to 3859)	0.543
Quetiapine vs brexpiprazole	1.13 (1.02–1.25)	0.023	–1.4 (–4.0 to 1.3)	0.313	1.45 (1.19–1.76)	<0.001	2309 (31–4587)	0.047

	Adjusted Rate* (95% CI)	*P*	Adjusted Rate* (95% CI)	*P*	Adjusted Mean* (95% CI)	*P*
Index antipsychotic		0.148		<0.001		0.111
Lurasidone	55.5 (52.9–58.1)		31.1 (27.3–35.2)		11,024 (8793–13,255)	
Quetiapine	57.5 (56.4–58.7)		35.3 (33.5–37.1)		12,420 (11,473 to 13,367)	
Brexpiprazole	58.9 (56.5–61.3)		27.4 (24.0–31.0)		10,111 (8087–12,135)	

CCI = Charlson Comorbidity Index; COM = Commercial; ED = emergency department; HCUP = Healthcare Cost and Utilization Project; HR = hazard ratio; MCD = Medicaid; MCR = Medicare; OR = odds ratio; PDC = proportion of days covered.

* Adjusted by age group, sex, insurance type, CCI (modified), numbers of of HCUP chronic conditions, baseline psychiatric comorbidities (including anxiety, personality disorder, substance abuse disorder), baseline obesity, baseline type 2 diabetes mellitus, baseline inpatient hospitalization, baseline ED visit, baseline nonpsychiatric medication use, and any use of nonindex antipsychotic in baseline.

Table IV. Adjusted psychiatric health care use and costs during the 6 months following adjunctive antipsychotic treatment initiation.

Variable	Any Psychiatric-Specific Inpatient Hospitalization or ED Visit After 6 mo OR (95% CI)	*P*	Total Psychiatric-Specific Medical Costs After 6 mo, $ Estimate (95% CI)	*P*
Age group, y				
18–34 vs ≥ 55	1.47 (1.07–2.04)	0.019	2324 (1053–3594)	<0.001
35–44 vs ≥ 55	1.00 (0.71–1.41)	0.984	–481 (–1735 to 772)	0.451
45–54 vs ≥ 55	1.10 (0.81–1.49)	0.540	–84 (–1200 to 1032)	0.883
Female vs male	0.85 (0.69–1.05)	0.123	–217 (–1067 to 632)	0.616
Insurance type				
MCD vs COM	0.62 (0.47–0.80)	<0.001	–2733 (–3718 to –1748)	<0.001
MCR vs COM	1.10 (0.75–1.61)	0.639	–1020 (–2490 to 451)	0.174
Modified CCI without diabetes	0.98 (0.90–1.06)	0.579	–167 (–513 to 179)	0.345
No. of chronic conditions (HCUP)	1.00 (0.93–1.07)	0.938	–338 (–605 to –70)	0.013
Anxiety (yes vs no)	1.07 (0.85–1.33)	0.575	600 (–226 to 1426)	0.155
Personality disorder (yes vs no)	1.54 (1.01–2.36)	0.045	209 (–1943 to 2361)	0.849
Substance abuse disorder (yes vs no)	1.97 (1.56–2.48)	<–0.001	5872 (4772–6973)	<0.001
Obesity (yes vs no)	1.17 (0.86–1.58)	0.323	351 (–878 to 1580)	0.576
Type 2 diabetes mellitus (yes vs no)	0.98 (0.71–1.35)	0.911	–160 (–1397 to 1077)	0.800
Any baseline inpatient hospitalization (yes vs no)	2.45 (1.96–3.07)	<–0.001	3747 (2742–4751)	<0.001
Any baseline ED visit (yes vs no)	2.16 (1.75–2.67)	<–0.001	910 (23–1796)	0.044
Nonpsychiatric medication use (yes vs no)	0.94 (0.74–1.18)	0.586	1021 (106–1935)	0.029
Nonindex antipsychotic use (yes vs no)	1.30 (1.03–1.63)	0.026	–42 (–953 to 869)	0.928
Index antipsychotic				
Lurasidone vs brexpiprazole	1.12 (0.73–1.73)	0.594	1065 (–380 to 2511)	0.148
Quetiapine vs brexpiprazole	1.36 (0.97–1.92)	0.073	619 (–498 to 1737)	0.277
	Adjusted Rate, %* (95% CI)	*P*	Adjusted Mean, $* (95% CI)	*P*
Index antipsychotic		0.143		0.336
Lurasidone	7.0 (5.2–9.3)		4376 (3282–5471)	
Quetiapine	8.4 (7.4–9.4)		3930 (3466–4395)	
Brexpiprazole	6.3 (4.7–8.4)		3311 (2318–4304)	

CCI = Charlson Comorbidity Index; COM = Commercial; ED = emergency department; HCUP = Healthcare Cost and Utilization Project; HR = hazard ratio; MCD = Medicaid; MCR = Medicare; OR = odds ratio.

*Adjusted by age group, sex, insurance type, CCI (modified), number of HCUP chronic conditions, baseline psychiatric comorbidities (including anxiety, personality disorder, substance abuse disorder), baseline obesity, baseline type 2 diabetes mellitus, baseline inpatient hospitalization, baseline ED visit, baseline nonpsychiatric medication use, and any use of nonindex antipsychotic during the baseline.

planning to include a broad list of generic antipsychotics in a future study using the most recently available data, and it is likely that some of the generics would have similar or greater reductions in health care use and costs compared with the branded AAPs included in the present study. Finally, because of the availability of data, we were only able to follow up patients for 6 months. However, given that for most patients MDD is a recurrent and chronic condition and affects individuals throughout their lifetimes,[25] future studies are warranted to examine the long-term effects of the antipsychotic treatments on health outcomes.

CONCLUSION

In patients with MDD and a variety of insurance types, use of brexpiprazole was associated with lower risk of discontinuation, risk of hospital care (hospitalization and ED visits), and all-cause medical costs compared with adjunctive quetiapine. Brexpiprazole also had the lowest hospital care rates compared with quetiapine and lurasidone. Even though this is a retrospective, observational study and no causal relationship should be drawn, our study findings suggest drug choice may affect subsequent health care utilization and costs.

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CONFLICTS OF INTEREST

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