Short Communication

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Off-label antipsychotic use patterns among Texas Medicaid adults 2013–2016

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Aim: To describe trends in off-label antipsychotic use among Texas Medicaid adults and examine whether demographic and clinical characteristics were associated with off-label use. **Methods:** Three diagnostic groups (i.e. no diagnosis, on label and off-label) were created based on mental health disorder diagnoses and related antipsychotic prescriptions. **Results:** During 2013–2016, the prevalence of off-label antipsychotic use decreased from 22.5% to 17.4% and the proportions of no mental health diagnosis remained stable (7.3–9.4%). Patients aged ≥25 years and second-generation antipsychotic users had significantly lower odds of receiving antipsychotics off-label or with no diagnosis. **Conclusion:** Compared with previous Medicaid database studies, the proportions of off-label antipsychotic use and antipsychotic use with no concurrent psychiatric diagnosis were notably lower.

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Keywords: antipsychotic agents • Medicaid • off-label use • prevalence • retrospective studies • treatment trends

Background

Antipsychotics have been US FDA-approved for a range of psychiatric conditions including schizophrenia, bipolar disorder, major depressive disorder (MDD), irritability in autism and Tourette syndrome. Off-label use refers to FDA-approved medications that are prescribed for unapproved clinical indications, age groups or dosage forms [1]. Off-label use is widely adopted in clinical practice, especially in psychiatry [2,3] and antipsychotic medications have been prescribed frequently for patients without FDA-approved indications [4–8]. Although off-label use is common, antipsychotics have been associated with adverse effects such as extrapyramidal symptoms [9], cardiovascular and metabolic abnormalities [10,11] and increased risk of death among older people [12]. Thus, it is important to continually monitor trends regarding off-label antipsychotic use.

In the early 2000s, approximately over one-half (49.0%–63.6%) of antipsychotics prescribed were for off-label use, which has shown a decline over time for Medicaid populations. Antipsychotic off-label use in Georgia Medicaid was 63.6% in 2001 [5], while a 42-state Medicaid study reported 49.0% of antipsychotic-treated adults received off-label prescriptions in 2003 [6]. Similar findings were reported in a study using 2001–2002 commercial claims where 58.6% of antipsychotics were prescribed off-label during office visits [13]. However, a remarkably lower rate of off-label use was observed in studies using data after 2009, which could be attributed to more FDA-approved indications for antipsychotics since 2006. A study using national commercial data from 2009 to 2010 reported that 13.7% of second-generation antipsychotics (SGAs) were prescribed off-label [14]. Similarly, a nationally representative survey (i.e. National Ambulatory Medical Care Survey [NAMCS]) using 2012–2013 data reported that 17.4% of office visits associated with antipsychotic prescriptions were off-label [3].

Some studies examined antipsychotic-treated patients with no documented mental health diagnosis and prevalence varied widely (5.9%–67.1%) [4,6,15–17]. Of those with lower prevalence, one was conducted using 2009–2010 national commercial data where 5.9% of adults who received SGAs had no diagnosis [14]. Another study was conducted using 42-state 2003 Medicaid data where 10.8% of antipsychotic-treated patients (including children and elderly) had no mental health diagnosis [6]. Several studies were conducted using nationally representative survey (i.e., NAMCS) data over three time periods with varying results regarding antipsychotic prescribing for adults with no documented mental health diagnosis: 2005–2009: 34.2% [16]; 2012–2013: ~48.0% [15]; 2014–2015:

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~31.0% [15]. The highest prevalence of no mental health diagnosis occurred in studies using 2009 IMS claims data, where over three-quarters (76.8%) of antipsychotic-treated adults had no mental health diagnoses [4] and similarly, most (67.1%) young adults (19–24 years) who received antipsychotic medications did not have any mental health diagnoses [17]. Some of the no mental health diagnosis prevalence estimates could be explained by provider efforts and/or patient requests to not document mental health conditions due to potential stigma and disparate treatment [16]. In addition, antipsychotic medications might be prescribed to patients who experience insomnia or behavioral symptoms but not meet the diagnostic criteria for mental health disorders [16,18]. Additionally, in some studies, occasions of no diagnosis may be caused by database documentation limitations where only a subset had clinical diagnoses recorded and/or where a maximum number of diagnoses (i.e., ≤3 diagnoses) could be listed per visit [4,15–17]. As mentioned previously, since 2006, more expanded FDA indications have been approved for antipsychotics. Specifically, risperidone was the first approved SGA for treating irritability in autism for patients aged ≥5 years (2006). Several SGAs (i.e., aripiprazole in 2007, olanzapine in 2009 and quetiapine in 2009) have added indications such as augmentation combined with antidepressants for MDD.

A comparative effectiveness report by the Agency for Healthcare Research and Quality was updated in 2011 and new evidence regarding off-label antipsychotic use was added [19]. However, while most antipsychotic utilization pattern studies focused on elderly or young populations as the Agency for Healthcare Research and Quality guideline mentioned [19], studies in adult populations were limited. Early Medicaid database research (i.e., before 2003) does not provide up-to-date information for policymakers, payers and providers regarding antipsychotic off-label use [5,6]. Additionally, because most studies examined only 1 year of data, the literature examining off-label antipsychotic use trends is limited [5,6,14], and little is known regarding these issues in Texas Medicaid. Therefore, this study was conducted to describe the proportion of antipsychotic off-label use over time and to examine factors associated with off-label use among adults enrolled in Texas Medicaid who were prescribed antipsychotics.

Methods

Data/population source

A retrospective database analysis of Texas Medicaid data from 1 January 2013 to 31 August 2016 was conducted. Adults aged 18–63 years with ≥1 antipsychotic prescription and continuously enrolled for at least 1 year duration anytime during the study period were included. Prescription claims data were used to identify antipsychotic prescriptions and included gender, age, dispense dates, days of supply, drug name, generic code number, American Hospital Formulary Service Pharmacologic-Therapeutic Classification code and National Drug Code. Medical claims were used to identify mental health diagnoses using ICD-9-CM and ICD-10-CM codes (Supplementary Table 1). Prescription data and medical data were merged using a de-identified patient identification. The earliest date of receiving an antipsychotic prescription was considered as the index date. Patients who were on ≥2 index antipsychotic medications and those on antipsychotic combination therapy (defined as receiving two or more antipsychotics simultaneously for at least 42 days [20]) were excluded. Patients who received two or more antipsychotic prescriptions simultaneously for a period less than 42 days were considered as switching antipsychotics and the index drug was utilized in determining off-label use.

Study measurements

Outcomes

The primary study outcome was diagnostic status (on-label, off-label and no diagnosis) for antipsychotic drug use. To determine on-label and off-label use, a conservative approach (individual vs class level indications) as in prior research [5,13] was employed. Individual level refers to FDA-approved indications for a specific antipsychotic, while class level refers to all antipsychotics within the class (e.g., SGA vs first-generation antipsychotic [FGA]). FDA-approved indications for individual antipsychotic agents during the same calendar year were used as the reference. Three mutually exclusive categories were created. First, included patients with no mental health disorder diagnoses (ICD-9 codes: 290–319 or ICD-10 codes: F00–F99) were identified and considered as antipsychotic users with "no diagnosis." After "no diagnosis" patients were removed, patients were grouped as "on-label" if there was a documented mental health diagnosis that was FDA approved (during that same year) for the index antipsychotic. Lastly, the remaining patients were assigned "off-label," which means that there was a mental health diagnosis, but not one that was FDA approved for the index drug. After assigning patients into the three groups, mental health diagnoses were assigned for on-label and off-label groups. For on-label users who had more than one psychiatric diagnosis, the diagnosis closest to the index antipsychotic date was used. If multiple diagnoses existed

Table 1. FDA-approved antipsychotic indications for adults.

Antipsychotics	FDA-approved indications
First-generation antipsychotics[†]	
Chlorpromazine	Behavioral problems[¶]; hyperactivity[¶]; bipolar disorder; schizophrenia/psychotic disorders
Fluphenazine	Psychotic disorders; chronic schizophrenia
Haloperidol	Behavioral disorders[¶]; hyperactivity[¶]; psychotic disorders; schizophrenia; Tourette disorder
Loxapine	Schizophrenia; agitation associated with schizophrenia or bipolar I disorder
Perphenazine	Schizophrenia
Pimozide	Tourette disorder
Prochlorperazine	Generalized nonpsychotic anxiety; psychotic disorders; schizophrenia
Thiothixene	Schizophrenia
Second-generation antipsychotics[‡]	
Aripiprazole	Bipolar I disorder; irritability associated with autistic disorder; MDD; schizophrenia; Tourette disorder
Asenapine	Bipolar disorder; schizophrenia
Brexpiprazole[#]	Schizophrenia; MDD
Cariprazine[#]	Bipolar disorder; schizophrenia
Clozapine	Suicidal behavior in schizophrenia or schizoaffective disorder; schizophrenia, treatment resistant
Iloperidone	Schizophrenia
Lurasidone	Bipolar depression; schizophrenia
Olanzapine	Schizophrenia; bipolar I disorder; MDD (with fluoxetine)
Paliperidone	Schizophrenia
Quetiapine	Schizophrenia; bipolar disorder; MDD (adjunctive treatment)
Risperidone	Schizophrenia; alone, or in combination with lithium or valproate, for the short-term treatment of acute manic or mixed episodes associated with bipolar I disorder; autistic disorder
Ziprasidone	Bipolar disorder; schizophrenia

[†]Class level FDA-approved indications for FGAs: schizophrenia, psychotic disorders, bipolar disorder, Tourette disorder.
[‡]Class level FDA-approved indications for SGAs: schizophrenia, bipolar disorder, Tourette disorder, MDD, autistic disorder.
[¶]Approved indications based on Lexicomp. Behavior problems and hyperactivity were not considered as FDA-approved indications in our analysis due to their ambiguous definition.
[#]Brexpiprazole and cariprazine were approved in 2015 and available in Texas Medicaid in 2016.
FGA: First-generation antipsychotic; MDD: Major depressive disorder; SGA: Second-generation antipsychotic.

on the same day, a hierarchical classification approach (i.e., schizophrenia, followed by autistic disorder, bipolar disorder, psychotic disorders and anxiety disorder) was employed [21]. For off-label users, all mental health diagnoses on record in the same year were documented. As such, patients in the off-label group could be assigned to more than one psychiatric diagnosis. A sensitivity analysis regarding diagnostic status (i.e. on-label, off-label and no diagnosis) based on drug class level (FGA and SGA) versus individual class level was conducted (Table 1). For example, for drug class level, any SGA prescribed that was associated with a diagnosis of MDD was treated as 'on-label' use, because several SGAs, such as olanzapine, were approved for adjunctive therapy for major depression disorder. The sensitivity analysis was conducted to compare with other studies with a similar approach [6,7,14].

Independent variables

Demographic (age and gender) and clinical (antipsychotic type) characteristics comprised the independent variables. Age was measured continuously and categorically (18–24, 25–34, 35–44, 45–54, 55–63 years) and antipsychotic type was dichotomized as FGA versus SGA.

Statistical procedures

All analyses were performed at the patient level. First, demographics and clinical characteristics were described, as well as the yearly proportions of diagnostic status (i.e., on-label, off-label and no diagnosis) during the study period. Second, chi-square analyses were performed to examine the relationship between diagnostic status and demographic and clinical characteristics. Last, multivariable logistic regression analysis was conducted to examine the association between independent variables and diagnostic status (on-label vs off-label and no diagnosis). Note that off-label and no diagnoses were combined for the multivariate analysis. All data analyses were conducted using SAS Version 9.4 (SAS Institute, Inc., NC, USA) and 2015 data was used for chi-square analysis and logistic regression since it

Table 2. 2013–2016 demographic and clinical information for antipsychotic recipients in Texas Medicaid.

	2013 (n = 51,257)		2014 (n = 54,523)		2015 (n = 49,843)		2016† (n = 39,151)	
	n	%	n	%	n	%	n	%
Age group								
– 18–24	7994	15.6%	8609	15.8%	7877	15.8%	6228	15.9%
– 25–34	9978	19.5%	10,819	19.8%	9868	19.8%	7663	19.6%
– 35–44	9799	19.1%	10,353	19.0%	9374	18.8%	7140	18.2%
– 45–54	13,658	26.6%	13,959	25.6%	12,439	25.0%	9600	24.5%
– 55–63	9828	19.2%	10,783	19.8%	10,285	20.6%	8520	21.8%
Gender								
– Female	29,487	57.5%	31,152	57.2%	27,941	56.1%	21,149	54.0%
– Male	21,770	42.5%	23,371	42.8%	21,902	43.9%	18,002	46.0%
Antipsychotic type								
– FGA	5599	10.9%	5422	9.9%	4477	9.0%	3075	7.8%
– SGA	45,658	89.1%	49,101	90.1%	45,366	91.0%	36,076	92.2%
Diagnostic status								
– On-label	35,875	70.0%	37,747	69.2%	36,283	72.8%	28,669	73.2%
– Off-label	11,543	22.5%	12,353	22.7%	9932	19.9%	6802	17.4%
– No Diagnosis	3839	7.5%	4423	8.1%	3628	7.3%	3680	9.4%

†2016 data available from 1 January to 31 August.
FGA: First-generation antipsychotic; SGA: Second-generation antipsychotic.

was the latest date with a full year of data available. This study was approved by the Institutional Review Board of the University of Texas at Austin.

Results

From 2013 to 2016, 51,257, 54,523, 49,843 and 39,151 (January–August data only available in 2016) patients with prevalent antipsychotic use were identified from Texas Medicaid data, respectively (Table 2). The proportion of antipsychotics prescribed among each age group was stable during the study period. Regarding age groups, the proportion of Medicaid patients who received antipsychotics were ~16% (18–24 years), ~20% (25–34 years), ~19% (35–44 years), ~25% (45–55 years) and ~20% (55–63 years). More than half (54.0%–57.5%) of those prescribed antipsychotics were female and approximately 90% were on SGAs. In 2015, the mean age for the study sample was 41.1 ± 13.5 years.

The proportions of off-label antipsychotic users decreased from 22.5% in 2013 to 17.4% in 2016. When employing the sensitivity analysis (i.e., diagnostic groups based on drug class level vs individual drug), the proportion of off-label use was lower (~6–7 percentage points) and ranged from 16.1% in 2013 to 10.3% in 2016 (data not shown in Table 2). Less than 10% (7.5%, 8.1%, 7.3% and 9.4%, from 2013 to 2016, respectively) of patients receiving antipsychotic prescriptions had no diagnosis (Table 2).

As shown in Table 3, during 2015, among those with off-label antipsychotic use, prevalence was highest in young adults aged 18–24 years (25.5%), followed by the 55–63 age group (20.6%). Of note is that the middle-aged patients (35–44 years and 45–54 years) had the lowest proportion of off-label use (17.6%). Among young adults (18–24 years) with an off-label diagnosis, pervasive developmental disorder (29.1%) and attention-deficit/hyperactivity disorder (ADHD; 22.6%) were most common. Among adults aged 25–34 years, pervasive developmental disorder (25.8%) and depression (20.3%) were most prevalent. Among age groups ≥35 years old, depression was the most common off-label diagnosis (range: 29.5%–33.5%) followed by anxiety (range: 21.3%–23.0%).

As shown in Table 4, the proportion of off-label use/no diagnosis (combined) across each age group was significantly ($p < 0.0001$) different. Chi-square analysis also showed males had a significantly ($p < 0.0001$) higher proportion of off-label use/no diagnosis compared with females (28.3% vs 26.3%, respectively). Last of all, FGA-treated patients had a significantly ($p < 0.0001$) higher proportion of off-label use/no diagnosis than SGA-treated patients (49.8% vs 25.0%, respectively).

When controlling for covariates, age group and antipsychotic class were statistically significantly associated with off-label use/no diagnosis (Table 5). Young adults aged 18–24 years and those prescribed FGAs were more likely

Table 3. On-label, off-label and no diagnosis for adults with antipsychotic prescriptions by age group, 2015.

Age group	18–24 (n = 7877)		25–34 (n = 9868)		35–44 (n = 9374)		45–54 (n = 12,439)		55–63 (n = 10,285)		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
On-label diagnoses†	**5114 (64.9%)**		**7143 (72.4%)**		**7110 (75.8%)**		**9500 (76.4%)**		**7416 (72.1%)**		**36,283**	
Bipolar disorder	2451	47.9	3096	43.3	3307	46.5	3574	37.6	2351	31.7	14,779	40.7
Schizophrenia	1413	27.6	2891	40.5	2679	37.7	4225	44.5	3462	46.7	14,670	40.4
MDD	561	11.0	834	11.7	1024	14.4	1647	17.3	1565	21.1	5631	15.5
Autistic disorder	661	12.9	283	4.0	64	0.9	13	0.1	3	0.0	1024	2.8
Psychotic disorders	25	0.5	34	0.5	34	0.5	40	0.4	35	0.5	168	0.5
Tourette disorder	3	0.1	5	0.1	2	0.0	1	0.0	0	0.0	11	0.0
Off-label diagnoses‡	**2006 (25.5%)**		**1981 (20.1%)**		**1646 (17.6%)**		**2185 (17.6%)**		**2114 (20.6%)**		**9932**	
Depression	255	12.7	403	20.3	485	29.5	732	33.5	683	32.3	2558	25.8
Anxiety	233	11.6	325	16.4	379	23.0	466	21.3	453	21.4	1856	18.7
Pervasive developmental disorder	584	29.1	512	25.8	233	14.2	125	5.4	64	3.0	1518	15.3
Alcohol/substance abuse	134	6.7	266	13.4	312	19.0	579	26.5	523	24.7	1291	13.0
ADHD	453	22.6	137	6.9	41	2.5	28	1.3	19	0.9	678	6.8
Unspecified mood disorder	276	13.8	145	7.3	82	5.0	87	4.0	59	2.8	635	6.4
Bipolar disorder	112	5.6	139	7.0	119	7.2	163	7.5	93	4.4	626	6.3
Disruptive behavior disorders	252	12.6	170	8.6	83	5.0	51	2.3	22	1.0	578	5.8
Dementia	2	0.1	5	0.3	7	0.4	29	1.3	96	4.5	139	1.4
No diagnosis	**757 (9.6%)**		**744 (7.5%)**		**618 (6.6%)**		**754 (6.1%)**		**755 (7.3%)**		**3628**	

No patient in the on-label group had anxiety disorder after the hierarchical classification approach was applied.
†Hierarchical classification approach was applied for on-label diagnoses with order as (1) schizophrenia, (2) autistic disorder, (3) bipolar disorder, (4) Tourette disorder and (5) psychotic disorders (6) anxiety disorder. On-label diagnostic groups are mutually exclusive.
‡Off-label diagnostic groups are not mutually exclusive; patients can have more than one off-label diagnosis.
ADHD: Attention-deficit/hyperactivity disorder; MDD: Major depressive disorder.

Table 4. Chi-square comparison of demographic and clinical characteristics and antipsychotic on-label versus off-label/no diagnosis use in 2015.

Characteristics	On-label		Off-label/no diagnosis		Chi-square test		
	n	Row %	n	Row %	χ^2	df	p-value
Age group					374.3	4	<0.0001
– 18–24	5114	64.9	2763	35.1			
– 25–34	7143	72.4	2725	27.6			
– 35–44	7110	75.8	2264	24.2			
– 45–54	9500	76.4	2939	23.6			
– 55–63	7416	72.1	2869	27.9			
Gender					24.8	1	<0.0001
– Male	15,698	71.7	6204	28.3			
– Female	20,585	73.7	7356	26.3			
Antipsychotic type					1266.6	1	<0.0001
– FGA	2248	50.2	2229	49.8			
– SGA	34,035	75.0	11,331	25.0			

n = 49,843.
df: Degree of freedom; FGA: First-generation antipsychotic; SGA: Second-generation antipsychotic.

to receive antipsychotics off-label/no diagnosis. Compared with young adults aged 18–24 years, patients in all older age groups were significantly ($p < 0.0001$) less likely to be prescribed antipsychotics off-label/no diagnosis. Compared with young adults aged 18–24 years, the odds of receiving antipsychotics off-label/no diagnosis were

Table 5. Logistic regression analysis of factors associated with off-label/no diagnosis antipsychotic use in 2015.

Factor (reference group)	Odds ratio	95% CI	p-value
Age group (18-24)			
– 25–34	0.68	0.64–0.72	<0.0001
– 35–44	0.55	0.52–0.59	<0.0001
– 45–54	0.53	0.49–0.56	<0.0001
– 55–63	0.65	0.61–0.70	<0.0001
Antipsychotic type (FGAs)			
– SGAs	0.32	0.30–0.34	<0.0001
Gender (female)			
– Male	1.03	0.99–1.07	0.1452

n = 49,843.
FGA: First-generation antipsychotic; SGA: Second-generation antipsychotic.

32% lower for adults aged 25–34 years ($p < 0.0001$; OR: 0.68; 95% CI: 0.64–0.72), 45% lower for adults aged 35–44 years ($p < 0.0001$; OR: 0.55; 95% CI: 0.52–0.59), 47% lower for adults aged 45–54 years ($p < 0.0001$; OR: 0.53; 95% CI: 0.49–0.56) and 35% lower for adults aged 55–63 years ($p < 0.0001$; OR: 0.65; 95% CI: 0.61–0.70). SGA recipients had a 68% lower likelihood of off-label use/no diagnosis antipsychotic use compared with FGA recipients ($p < 0.0001$; OR: 0.32; 95% CI: 0.30–0.34).

Discussion

From 2013–2016, the proportion of off-label use/no diagnosis decreased from 30.0% to 26.8%, which represented a 10.7% decline. This modest decrease was robust when using sensitivity analyses that defined diagnostic status (i.e., on-label, off-label and no diagnosis) based on drug class level (vs individual drug level). When using the less conservative sensitivity analysis of class versus individual level, our results ranged 10.3%–16.1% for off-label, and 7.3%–9.4% for no diagnosis, which was comparable to a study using 2009–2010 national commercial data, which reported 13.7% for off-label use and 5.9% for no diagnosis [14]. In our study, 19.9% of antipsychotics were prescribed off-label and 7.3% had no mental health diagnosis in 2015. However, these results were notably lower when compared with previous Medicaid database studies (49.0%–63.6%), which were conducted using data from 2001–2003 [5,22]. It might be reasonable that early Medicaid studies had a higher proportion of off-label use due to several factors including: limited FDA-approved indications, different definitions for off-label use, and different inclusion criteria. Regarding limited FDA-approved indications, since 2006, antipsychotics have been approved for several additional indications including irritability in autistic disorders and MDD. The difference between Georgia Medicaid study and our study was likely due to more approved indications after 2006, since both our study and the Georgia Medicaid determined diagnostic status at the individual drug level [5]. Despite the approved indication additions, the difference between the 42-state Medicaid study and our results can be explained by different definitions for off-label use. In the 42-state Medicaid study by Leslie and Rosenheck, off-label use was determined based on drug class level and any diagnosis with the exception of schizophrenia or bipolar disorder were off-label [6]. Additionally, inclusion of the elderly population in the Georgia Medicaid study may account for a higher prevalence of off-label use when compared with our study, which only included nonelderly adults aged 18–63 years. The Georgia Medicaid study revealed that patients ≥65 years were 5 times more likely to receive antipsychotics off-label than patients younger than 65 years [5]. Olfson *et al.* also indicated that the prevalence of dementia, the most common off-label diagnosis among elderly, increased as advancing age among antipsychotic-treated patients [4]. This exclusion of patients ≥64 in our study may contribute to a lower prevalence of no mental health diagnosis when compared with the Leslie and Rosenheck [6]. This is also supported by a recent NAMCS study (2019) that found the odds of no mental health diagnosis were two-fold higher for elderly aged ≥65 years when compared with 18–44 years [15].

As expected, bipolar disorder and schizophrenia were the most prevalent on-label indications. Our study results were similar to another study's findings, regarding depression and anxiety as the most prevalent off-label indications in adults [16], which is congruent with guidelines [23–25]. Practice guidelines suggested SGAs improve the response or remission rate of depressive symptoms even in patients without any psychotic symptoms [23,24]. Although the guidelines acknowledge that limited evidence exists to support this claim and that adverse effects exist, quetiapine

was recommended as second-line therapy for anxiety [25]. Antipsychotic use in pervasive developmental disorder, which was the third most commonly diagnosed off-label indication among adults, was also supported by guideline. Guideline supported the efficacy of aripiprazole and risperidone in 'reducing repetitive movements, self-injury and severe disruptive behavior' for patients with pervasive developmental disorder [26].

From the logistic regression, patients in age groups ≥25 years and receiving SGAs were associated with a lower likelihood of off-label antipsychotic use. The age pattern of off-label antipsychotics use can be linked to prevalent diagnosis of ADHD and developmental disorder diagnosis among young adults (18–24 years) [27]. The higher likelihood for FGA users receiving off-label prescribing compared with SGA users was also observed in the Georgia Medicaid study [5]. Most FGA medications have limited approved indications such as schizophrenia and psychotic disorders. Only chlorpromazine and loxapine have been approved for bipolar disorder, which was the most common on-label indication in our study. Although several studies indicated that males were associated with a lower likelihood of off-label use [5,6], our study did not indicate gender as a strong predictor of off-label use.

There were some limitations in this study. First, a psychiatric diagnosis associated with the index antipsychotic might have been misclassified. In addition, accurate diagnoses of mental health conditions may take years and involve trial and error. Patients might have received other diagnoses during the year and/or the previous year that were associated with the index prescription. It is difficult to accurately assess underlying reasons for off-label prescribing when claims data are used. However, our study utilized similar methods as other studies examining this issue [21,28]. Second, data such as race/ethnicity, community, metropolitan status area, and healthcare provider type were not available, which limited our capability to employ a conceptual framework (i.e., Anderson Behavioral Model) to identify other predictors and to assess their association with off-label antipsychotic use. There was no consensus regarding the association between provider type and likelihood of off-label prescribing. Some studies have shown that psychiatrists were less likely to prescribe antipsychotics for patients without an approved diagnosis (i.e. off-label prescribing/prescribing with no diagnosis) [15,16], while other studies found opposite results [3,5]. Third, this decrease in off-label use might not merely reflect the change in prescribing behaviors, but can also be explained by an increase in documentation of mental health disorders in Medicaid. Finally, our findings regarding off-label use patterns of antipsychotics were specific to the Texas Medicaid adult population, which might not be applicable to other populations.

Conclusion

In our analysis, off-label use of antipsychotics and antipsychotic use with no concurrent psychiatric diagnosis in Texas Medicaid declined from 2013 to 2016. Overall, depression and anxiety were the most common off-label diagnoses among adults, but ADHD was the most common diagnosis among young adults. Young adults and FGA recipients were more likely to have an off-label antipsychotic prescription. As adolescent patients transition to young adults, use of antipsychotics for ADHD may need to be closely monitored.

Future perspective

Future research should continue to examine off-label antipsychotic prescribing practices, especially for depression and anxiety diagnoses. In addition, additional research should examine if off-label use with these mental health conditions result in optimal patient outcomes.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/cer-2021-0048

Author contributions

All authors had substantial contributions to the conception or design of the work, involved in data interpretation, provided final approval of the version to be publish and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. S Chen analyzed and interpreted the data and drafted the manuscript; JC Barner and E Cho revised the manuscript critically.

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

This study was approved by the Institutional Review Board of the University of Texas at Austin.

Executive summary

- A retrospective analysis of 2013–2016 Texas Medicaid claims data for continuously enrolled adults (18–63 years) who received ≥1 antipsychotic prescription was conducted to examine patterns of and factors associated with off-label antipsychotic use.
- In Texas Medicaid, off-label use of antipsychotics and antipsychotic use with no mental health diagnosis declined from 30.0% in 2013 to 26.8% in 2016.
- Compared with previous Medicaid database studies, prevalence of off-label/no diagnosis antipsychotic use was lower.
- Compared with young adults aged 18–24 years, the older age groups (25–34, 35–44, 45–54, 55–63 years) had significantly ($p < 0.0001$) lower odds of receiving antipsychotics off-label or with no mental health diagnosis (ORs range: 0.53–0.68).
- Second-generation antipsychotics users, compared with first-generation antipsychotic users, had significantly ($p < 0.0001$) lower odds of receiving antipsychotics off-label/no diagnosis (OR: 0.32; 95% CI: 0.30–0.34).
- This study did not show gender as a strong predictor of off-label use.
- Depression and anxiety were the most prevalent off-label indications.
- Providers may want to consider risks and benefits when prescribing antipsychotics off-label to young adults and to those with depression and anxiety.

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