See commentary by Thase

Antipsychotic Medication Treatment Patterns in Adult Depression

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ABSTRACT

Objective: To characterize the role of antipsychotic medications in the community treatment of adult depression.

Methods: We identified adults (aged 18–64 years) with new episodes of depression treatment (*ICD-9-CM* 296.2, 296.3, 300.4, or 311) in US national Medicaid data (2001–2010). Patients with alternative *ICD-9-CM* antipsychotic indications, such as schizophrenia or bipolar disorder, were excluded. Each patient was followed for at least 1 year to characterize antipsychotic and antidepressant treatment and emerging alternative antipsychotic indications. For patients without alternative indications through day 45 following start of antipsychotic treatment, antipsychotics were considered to be intended for treatment of depression. Among this group, we determined whether antipsychotic initiation was preceded by minimally adequate treatment with antidepressants, defined as active antidepressant treatment for ≥ 31 days prior to and including the day of antipsychotic initiation.

Results: Within 1 year following onset, 14.0% of patients started an antipsychotic medication. A total of 41.3% of antipsychotic initiators developed an antipsychotic indication other than depression through day 45 following antipsychotic initiation, most often bipolar disorder or depression with psychotic features. The remaining 58.7% of antipsychotic initiators presumably started antipsychotics for nonpsychotic depression. Of these, 71.3% did not have minimally adequate antidepressant treatment prior to starting the antipsychotic medication.

Conclusion: Antipsychotic medications are used in approximately 1 in 7 patients with a new episode of depression. For 1 in 12 patients, the antipsychotic was considered to be intended for nonpsychotic depression. Almost three-quarters of these patients did not receive minimally adequate treatment with antidepressants prior to antipsychotic initiation. This pattern suggests potentially inappropriate and premature initiation of a drug class with substantial adverse effects and medical risks.

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Depressive disorders affect more than 15 million US adults and cause substantial emotional, physical, and economic burden on the affected individuals, their families, and their communities.[1–3] Approximately two-thirds of depressed patients fail to achieve remission from a first antidepressant trial.[4] For those who do not achieve remission, switching to another antidepressant is recommended, followed by a variety of augmentation strategies.[5] Augmentation with second-generation antipsychotics (SGAs) is arguably the best-supported and the only US Food and Drug Administration (FDA)–approved pharmacologic alternative for patients with major depressive disorder who have failed 2 or more trials of antidepressant monotherapy.[6,7] Since 2007, the FDA has approved olanzapine-plus-fluoxetine, aripiprazole, quetiapine, and brexpiprazole as adjunctive treatments to antidepressants for adults with major depressive disorder. Each year in the United States, roughly 2 million outpatient visits for adult depression include an SGA.[8]

The role of antipsychotics in the community treatment of depression remains poorly understood. SGAs are associated with increased risks for extrapyramidal side effects, tardive dyskinesia, weight gain, diabetes, dyslipidemia, and increased mortality.[9–14] A study of the US Veterans Affairs (VA) system[15] reported that 43% of patients treated with SGAs for major depressive disorder received antipsychotics at doses at or above those recommended for schizophrenia rather than at the lower doses recommended for depression. Because antipsychotics have significant adverse effects, their inappropriate use—including as monotherapy rather than as augmenting agents, their initiation before failure of response to antidepressant medications could be reasonably established, or their use above the dosing range indicated for treatment of depression—could pose quality of care concerns. However, none of these issues has been examined in community practice. The present study is the first detailed characterization of antipsychotic use patterns in relationship to antidepressant treatment in the community management of adult depression.

METHODS

We conducted a retrospective cohort study using US Medicaid Analytic Extract (MAX) data from 44 states from January 1, 2001, through December 31, 2010. All

Clinical Points

- Approximately 1 in 12 depressed patients receives antipsychotics for nonpsychotic depression. Only a minority of these patients first receive a full antidepressant trial.
- To reduce unnecessary use of antipsychotics in depression, it is important for patients to first receive a full trial of antidepressant medication treatment.

Table 1. Characteristics of Adult Medicaid Beneficiaries With New Depressive Episodes by Treatment With Oral Antipsychotic Medications

Variable	Total Patients With Episodes, N = 1,594,180 (100%)	Antipsychotic Medication Initiators, n = 223,430 (14.0%)		Antipsychotic Medication Non-Initiators, n = 1,370,750 (86.0%)		$P(\chi^2)$
		n	%	n	%	
Demographic[a]						
Sex						<.0001
Male	351,141	70,172	31.4	280,969	20.5	
Female	1,243,018	153,257	68.6	1,089,761	79.5	
Age, y						<.0001
18–24	366,984	43,452	19.5	323,532	23.6	
25–34	436,432	56,920	25.5	379,512	27.7	
35–44	363,539	58,826	26.3	304,713	22.2	
45–54	271,765	45,373	20.3	226,392	16.5	
55–64	155,460	18,859	8.4	136,601	10.0	
Race/ethnicity						<.0001
White, non-Hispanic	847,429	109,183	48.9	738,246	53.9	
African American, non-Hispanic	364,213	62,815	28.1	301,398	22.0	
Hispanic	229,011	29,452	13.2	199,559	14.6	
Other	153,527	21,980	9.8	131,547	9.6	
Medicaid eligibility						<.0001
Disability	602,389	114,774	51.4	487,615	35.6	
Low income	644,988	67,520	30.2	577,468	42.1	
Other	346,803	41,136	18.4	305,667	22.3	
Managed care (not FFS)	608,939	73,106	32.7	535,833	39.1	<.0001
Clinical and Utilization[b]						
Primary depression diagnosis[c]	1,151,853	182,702	81.8	969,151	70.7	<.0001
Major depressive disorder[c]	515,680	116,569	52.2	399,111	29.1	<.0001
Anxiety	129,006	20,845	9.3	108,161	7.9	<.0001
Substance use disorder	179,800	36,817	16.5	142,983	10.4	<.0001
Personality disorders	5,827	1,552	0.7	4,275	0.3	<.0001
Self-harm	2,282	496	0.2	1,786	0.1	<.0001
Diabetes	130,165	17,016	7.6	113,149	8.3	<.0001
Cardiovascular disease	276,154	38,711	17.3	237,443	17.3	.9662
Cerebrovascular disease	26,636	3,981	1.8	22,655	1.7	.0001
Psychotherapy	42,795	6,942	3.1	35,853	2.2	<.0001
Mental health emergency department visit[d]						<.0001
No visit	1,544,285	210,808	94.4	1,333,477	97.3	
1 to 2 visits	46,140	11,657	5.2	34,483	2.5	
3 or more visits	3,755	965	0.4	2,790	0.2	
Mental health hospital admissions[d]	15,888	5,087	2.3	10,801	0.8	<.0001
Mental health outpatient visits[d]						<.0001
No visit	1,312,994	167,919	75.2	1,145,075	83.5	
1 or 2 visits	164,266	30,543	13.7	133723	9.8	
3 or more visits	116,920	24,968	11.2	91952	6.7	

[a]At index date. Mean (SD) age was 35.9 (12.5) years for the total sample, 36.8 (12.0) years for antipsychotic medication initiators, and 35.8 (12.5) years for antipsychotic medication non-initiators.
[b]During 180-day baseline period including index date.
[c]Within the range of index date and index date + 30 days.
[d]Primary diagnosis.
Abbreviation: FFS = fee-for-service.

adults (aged 18–64 years) with a new episode of depression were included. A new episode of depression was defined by a diagnosis claim for depression (single inpatient or outpatient claim of *ICD-9-CM* 296.2, 296.3, 300.4, or 311 in any position) following at least 180 days of uninterrupted Medicaid eligibility without (1) any diagnostic claims for depression, (2) any claims for antidepressant medications (eAppendix 1 at PSYCHIATRIST.COM), and (3) any claims for exclusion diagnoses including schizophrenia (*ICD-9-CM* 295), bipolar disorder (296.00–296.16, 296.4–296.81, or 296.89), major depressive disorder with psychotic features (296.24 or 296.34), pervasive development disorder (299), dementia (290, 294.1, 331.0–2, 331.82, or 331.9), delusional disorders (297), depressive-type psychosis (298.0), or cyclothymic disorder (301.13).

To allow for antidepressant medication initiations just prior to documentation of a depression diagnosis, we allowed for antidepressant claims up to 30 days prior to a new depression diagnosis if the 180-day period prior to the first antidepressant claim met criteria 1 through 3. Patients were excluded if they met any of the exclusion conditions during the 180-day pre-index period, including any prescription claims for antipsychotics, any of the exclusion diagnoses, or eligibility for Medicare.

The start of follow-up (index date) was the initial diagnosis date or antidepressant claim, whichever came first. Only episodes with at least 1 year of continuous eligibility after the index date were included. For patients with more than 1 new depressive episode, only the first episode was considered for analysis. Baseline characteristics were ascertained over the 180-day pre-index period.

Each patient was followed for at least 1 year to characterize initiation and patterns of antidepressant and antipsychotic medication treatment. For initiators of antipsychotics (eAppendix 1), we examined whether antipsychotic indications other than depression developed between the index date through day 45 following antipsychotic initiation. Those without alternative indications were considered to have initiated the antipsychotic for the treatment of depression. Characteristics of the depressive episode (presence of major depressive disorder and whether or not depression was recorded as a primary diagnosis) were ascertained from all diagnostic claims starting at the index date and including the following 30 days.

We determined the total duration of antipsychotic treatment by calculating the sum of days' supply for antipsychotic medications during the year following antipsychotic initiation. We also determined the single prescription fill with the highest daily dose. Prescription claims with missing information for the days' supply variable (missing in 0.15% of patients who initiated antipsychotic treatment) were excluded from analysis.

To prevent undue influence of administrative errors, we further excluded patients with prescription claims with daily doses outside of a clinically reasonable range from the dose analyses (approximately 1.8% of antipsychotic treatment initiators; eAppendix 2). Among those considered to have initiated antipsychotic medication treatment for depression, we determined whether treatment initiation was preceded by minimally adequate treatment with antidepressants. Minimally adequate antidepressant treatment was defined conservatively as at least 31 days of antidepressant supply prior to antipsychotic medication initiation (to examine potentially premature antipsychotic initiation) and active antidepressant treatment on the day of antipsychotic initiation (to examine potential antipsychotic monotherapy). Among those who initiated an antipsychotic for depression, we used multivariate logistic regression to identify risk factors for antipsychotic initiation without minimally adequate prior antidepressant treatment. Further, we implemented sensitivity analyses limited to depressive episodes occurring after January 1, 2008, to examine whether FDA approval and labeling of aripiprazole for adjunctive treatment of depression in late 2007 impacted antipsychotic use patterns in patients with depression.

The study used deidentified data and was approved by the Rutgers Institutional Review Board. Analyses were conducted using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

Between 2001 and 2009, 1,594,180 patients met the criteria for a new episode of depression. Mean age at onset was 36 years. Women accounted for more than three-quarters of patients with new depressive episodes (Table 1). Within 1 year of onset, antipsychotic medication was initiated in 14.0% of these patients. Antipsychotic initiators were more likely to be male, African American, and eligible for Medicaid through disability and less likely to be in managed care. Initiators were also more likely to be diagnosed with major depressive disorder. In addition, they were more likely to have a primary diagnosis of depression, any diagnosis of substance use disorder, and greater recent use of emergency department visits, number of hospitalizations, and number of outpatient mental health visits. Altogether, 96.8% of antipsychotic initiations were for a second-generation antipsychotic. Mean (SD) time from the start of the depressive episode to antipsychotic initiation was 98.8 (106.0) days. From the start of the depressive episode through day 45 of antipsychotic medication initiation, 41.3% of patients who initiated an antipsychotic had 1 or more new alternative indications for an antipsychotic recorded (Table 2). The most common alternative indications were major depressive disorder with psychotic features, bipolar disorder, and schizophrenia. The remaining patients who initiated antipsychotic treatment but did not develop an alternative antipsychotic indication, representing 58.7% of antipsychotic initiators or 8.2% of all patients with new depressive episodes, were presumed to have initiated antipsychotic treatment for nonpsychotic depression. No time trend was apparent across the study period years, with initiation rates ranging from a low of 8.0% in 2001 to a high of 9.3% in 2004 (data not shown).

Table 2. Antipsychotic Use in the Year Following a New Depressive Episode by Antipsychotic Indications Diagnosed in the Period From the New Depressive Episode to 45 Days Following the Antipsychotic Medication Initiation

	Antipsychotic Medication Initiators (n = 223,430)	
Variable	n	%
No alternative antipsychotic medication indication[a]	131,176	58.7
At least 1 alternative antipsychotic medication indication[a]	92,254	41.3
Schizophrenia	23,829	10.7
Bipolar disorder	40,214	18.0
Depressed[b]	10,995	4.9
Manic[c]	6,289	2.8
Mixed[d]	6,337	2.8
Other[e]	26,994	12.1
Major depressive disorder with psychotic features	41,333	18.5
Dementia	2,348	1.1
Other[f]	3,613	1.6

[a]From the index date to 45 days following antipsychotic initiation.
[b]*ICD-9-CM* 296.5, 296.50–296.56.
[c]*ICD-9-CM* 296.01–296.06, 296.4, 296.40–46.
[d]*ICD-9-CM* 296.6, 296.61–296.66.
[e]*ICD-9-CM* 296.7, 296.80, 296.89.
[f]Pervasive development disorder, delusional disorder, depressive type psychosis, cyclothymic disorder.

Patients who initiated an antipsychotic for depression had a mean age of 37 years, were predominantly female, and were most commonly eligible for Medicaid due to disability. Within the first 30 days after onset, 80% had a primary depression diagnosis and slightly fewer than half were diagnosed with major depressive disorder. Patients who initiated an antipsychotic for depression generally resembled patients who initiated an antipsychotic for alternative indications (Table 3). Those who initiated antipsychotics for depression included a smaller proportion of African Americans, a lower rate of Medicaid eligibility through disability, and a lower rate of major depressive disorder.

Mean duration of antipsychotic medication treatment ranged from 96.8 days (ziprasidone) to 121.6 days (quetiapine) (Table 4). The proportion of antipsychotic-treated patients who received >30 days of treatment ranged from 60.5% (ziprasidone) to 70.6% (quetiapine) (eAppendix 3). The mean values of the highest observed doses for each of the individual antipsychotics are shown in Table 4. Doses were consistently lower in patients

Table 3. Characteristics of Initiators of Antipsychotic Medications by Presence of Antipsychotic Indication During the Period From a New Depressive Episode to 45 Days Following an Antipsychotic Medication Initiation

	No Alternative Antipsychotic Medication Indication During Follow-Up (n = 131,176)		At Least 1 Alternative Antipsychotic Medication Indication During Follow-Up (n = 92,254)		
Variable	n	%	n	%	P (χ^2)
Demographic[a]					
Sex					< .0001
Male	40,172	30.6	30,000	32.5	
Female	91,004	69.4	62,253	67.5	
Age, y					< .0001
18–24	24,984	19.1	18,468	20.0	
25–34	33,554	25.6	23,366	25.3	
35–44	34,644	26.4	24,182	26.2	
45–54	26,620	20.3	18,753	20.3	
55–64	11,374	8.7	7,485	8.1	
Race/ethnicity					< .0001
White, non-Hispanic	68,150	52.0	41,033	44.5	
African American, non-Hispanic	32,433	24.7	30,382	32.9	
Hispanic	17,024	13.0	12,428	13.5	
Other	13,569	10.3	8,411	9.1	
Medicaid eligibility					< .0001
Disability	63,308	48.3	51,466	55.8	
Low income	42,209	32.2	25,311	27.4	
Other	25,659	19.6	15,477	16.8	
Managed care (not FFS)	44,239	33.7	28,867	31.3	< .0001
Clinical and Utilization[b]					
Primary depression disorder[c]	105,462	80.4	77,240	83.7	< .0001
Major depressive disorder[c]	60,073	45.8	56,496	61.2	< .0001
Anxiety	13,063	10.0	7,782	8.4	< .0001
Substance use disorder	22,044	16.8	14,773	16.0	< .0001
Personality disorders	882	0.7	670	0.7	.1311
Self-harm	245	0.2	251	0.3	< .0001
Diabetes	9,913	7.6	7,103	7.7	.2116
Cardiovascular disease	23,021	17.6	15,690	17.0	.0009
Cerebrovascular disease	2,399	1.8	1,582	1.7	.0449
Psychotherapy	4,279	3.3	2,663	2.9	< .0001
Mental health emergency department visit[d]					< .0001
No visit	124,453	94.9	86,355	93.6	
1 to 2 visits	6,198	4.7	5,459	5.9	
3 or more visits	525	0.4	440	0.5	
Mental health hospital admissions[d]					.0003
No admission	128,255	97.8	90,088	97.7	
1 or more admissions	2,921	2.2	2,166	2.4	
Mental health outpatient visits[d]					< .0001
No visit	98,169	74.8	69,750	75.6	
1 or 2 visits	17,498	13.3	13,045	14.1	
3 or more visits	15,509	11.8	9,459	10.3	

[a]At index date. Mean (SD) age was 37.0 (12.0) years for those with no alternative antipsychotic medication indication and 36.7 (12.0) years for those with at least 1 alternative antipsychotic medication indication.
[b]During 180-day baseline period including index date.
[c]Within the range of index date and index date + 30 days.
[d]Primary diagnosis.
Abbreviation: FFS = fee-for-service.

without alternative indications for antipsychotics than in patients with alternative indications. eAppendix 3 depicts respective doses at the 95th percentile of the dose distribution. The highest approved antipsychotic dose for depression (eAppendix 4) was exceeded by 14.7% (quetiapine, 300 mg), 26.6% (olanzapine, 12 mg), and 17.3% (aripiprazole, 15 mg) of patients without alternative antipsychotic indications, respectively (data not shown).

Altogether, 71.3% of patients initiating antipsychotics for depression did not have minimally adequate antidepressant treatment prior to antipsychotic initiation. Of those, 53.1% did not have at least 31 days of prior antidepressant use, 7.2% did not have active antidepressant supply on the day of the antipsychotic initiation, and 39.7% did not have either. The risk for not having received minimally adequate antidepressant treatment prior to initiating an antipsychotic was particularly high for African Americans, younger individuals, men, and those eligible for Medicaid due to disability (Table 5). Results from sensitivity analyses limited to new depressive episodes on or after January 1, 2008, were close to identical to the results obtained from the full cohort (eAppendices 5–10).

DISCUSSION

Antipsychotics are used in the treatment of approximately 1 in 7 adult patients who develop new episodes of depression that are not complicated by other psychiatric conditions for which antipsychotic medications are indicated. Although antipsychotic dosing was generally in line with clinical recommendations,[16] nearly three-quarters of antipsychotic-treated patients did not receive even minimally adequate antidepressant treatment prior to antipsychotic initiation. This pattern raises the possibility of premature or inappropriate initiation of antipsychotic medications.

Approximately 14% of patients with new depressive episodes initiated an antipsychotic medication within 1 year of onset. In over one-third of these patients, new diagnoses of alternative conditions with indications for antipsychotics were recorded after onset of the depressive episode, suggesting that, for these patients, depression was not the likely primary target for antipsychotic treatment. In the remaining patients, approximately 8% of those with new episodes of depression, the antipsychotic was considered to be intended for the treatment of depression.

One previous study has reported a somewhat higher rate of antipsychotic treatment by patients with depression. In a study[15] of veterans with major depressive disorder without comorbid schizophrenia, schizoaffective disorder, or bipolar disorder, approximately 1 in 5 patients (20.6%) was treated with an antipsychotic medication. The male predominance of the veteran patient population may help to account for their relatively higher rate of antipsychotic treatment. In addition, over 50% of antipsychotic medication use in the

Table 4. Duration and Dose of Antipsychotic Treatment Among Patients With New Depressive Episodes With and Without Alternative Antipsychotic Indications

Antipsychotic Treatment Variable	Without Alternative Indication		With Alternative Indication	
Duration[a]	n	Days, Mean (SD)	n	Days, Mean (SD)
Any antipsychotic medication	131,176	134.0 (108.4)	92,254	147.7 (110.0)
Quetiapine	63,001	121.6 (103.8)	39,310	122.9 (102.8)
Olanzapine	28,818	108.1 (99.0)	21,841	110.6 (99.4)
Risperidone	33,897	108.7 (99.0)	30,979	110.8 (98.9)
Aripiprazole	20,612	103.8 (92.1)	19,178	105.1 (92.7)
Ziprasidone	9,423	96.8 (93.2)	10,972	96.5 (92.1)
Dose[b]	n	mg, Mean (SD)	n	mg, Mean (SD)
Quetiapine	62,136	186.4 (184.1)	38,745	263.4 (223.8)
Olanzapine	28,332	10.3 (7.3)	21,371	13.3 (8.1)
Risperidone	33,298	2.0 (1.5)	30,295	2.7 (1.7)
Aripiprazole	20,245	11.5 (7.5)	18,779	14.0 (7.9)
Ziprasidone	9,249	95.3 (50.6)	10,723	109.1 (51.6)

[a]Total days of medication possession based on days' supply dispensed.
[b]In mg, based on the prescription fill with the highest dose dispensed; calculated as ([number dispensed × mg/dose]/d supply); dose analyses excluded 4,858 episodes (1.8% of all initiations; 1.6% of those without indication; 2.0% of those with indication) for which the highest calculated single dose was outside a clinically reasonable dosing range (see eAppendix 2).

VA study[17,18] was for patients with comorbid posttraumatic stress disorder, a condition for which antipsychotic treatment, despite limited evidence of effectiveness, is not uncommon. Demographic and clinical predictors of antipsychotic use were largely consistent between the present study and the VA study, with younger patients, men, patients with more psychiatric comorbidities, and patients with more intensive mental health services use being more likely to receive antipsychotic medications.

The present estimate of patients with a new episode of depression without evidence of alternative antipsychotic indications who initiated an antipsychotic (8.2%) is similar to findings in a report from a national survey of office-based practice that 8.6% of adult depression visits without alternative indications included a SGA.[8] In the national survey, publicly insured depressed patients, such as those in the present study, were significantly more likely than their privately insured counterparts to receive an antipsychotic, and antipsychotic use rates significantly increased from 1999–2002 to 2007–2010. However, due to its sampling frame and cross-sectional single visit design, the office-based survey did not provide a rigorous means of excluding patients who had alternative psychiatric indications for receiving antipsychotic treatment.

The pattern of antipsychotic treatment in adult depression reflects several markers of greater illness severity. Higher rates of major depressive disorder, a primary diagnosis of depression, and a history of greater mental health service use all point toward targeted use in patients with greater severity of illness. In this context, the average duration of antipsychotic treatment in patients with depression, approximately 3–4 months, was almost identical to the duration of antipsychotic treatment of depressed patients who presumably initiated an antipsychotic for other indications (Table 4, eAppendix 3).

Antipsychotic dosing was largely consistent with clinical guidelines for adjunctive treatment for major depressive disorder (eAppendix 4).[16,19] With the exception of quetiapine, for which the mean dose fell significantly below the lowest recommended dose for schizophrenia, the mean of the highest prescribed antipsychotic dose among episodes was generally at the lower end of the recommended dosing range for schizophrenia. The highest labeled dose for depression was exceeded in only 15% (quetiapine) to 27% (olanzapine) of patients initiating an antipsychotic for depression, and maximum doses almost never exceeded labeled schizophrenia doses. This finding is reassuring when compared with the higher degree of dosing above clinical recommendations reported in the VA study (ranging from 32% for quetiapine to 91% for ziprasidone).[15]

A clear majority of patients initiating an antipsychotic for depression failed to meet minimal requirements for appropriate prior antidepressant treatment, particularly regarding adequate prior duration of antidepressant therapy. This observation extends longstanding concerns over poor antidepressant adherence in community practice to adjunctive antipsychotic treatment that should be initiated only after insufficient response to antidepressant monotherapy.[20] Antipsychotic use that occurred without concurrent antidepressant use or before a >30 day antidepressant trial was particularly common among African Americans, younger individuals, and men. In light of the risk of adverse effects associated with antipsychotics,[9–14] careful attention should be given to ensuring that antipsychotics are generally reserved for situations in which treatment failure has been established with first-line antidepressant treatment. Despite limited evidence suggesting potential effectiveness of quetiapine monotherapy in patients with unipolar major depression,[21] such data are lacking for any other antipsychotic, and antipsychotic monotherapy for major depressive disorder is neither approved by the FDA nor endorsed by any guidelines.[5,22] Of note, while we considered any duration of prior antidepressant use exceeding 31 days as minimally adequate and did not impose a requirement regarding dosing of the antidepressant, guidelines typically recommend 6–12 weeks of antidepressant treatment titrated, as tolerated, to standard maximal doses.[19] Similarly, our definition did not require trials of more than 1 antidepressant prior to augmentation with an antipsychotic, although 2 trials are generally recommended.[19] The operational definition of minimally appropriate treatment used for this study was thus quite conservative because a stricter definition of minimally adequate treatment would have been failed by an even larger proportion of individuals initiating an antipsychotic for depression.

Our study spanned the period from 2001 to 2010 because in clinical practice antipsychotics had been used for the treatment of depression prior to receiving FDA approval for this indication.[8,15] Replication of the analyses limited to depressive episodes occurring after January, 1 2008, resulted in findings almost identical to those obtained from the full

Table 5. Predictors of Antipsychotic Use Without Minimal Antidepressant Treatment Among Adults With New Depressive Episodes and No Observed Alternative Clinical Indications for Antipsychotic Treatment

Variable	Minimal Antidepressant Treatment[a] n	%	No Minimal Antidepressant Treatment n	%	Adjusted Odds Ratio[b] (95% CI)
Overall	37,591	28.7	93,585	71.3	…
Demographic[c]					
Sex					
Male	9,369	24.9	30,803	32.9	1.32 (1.28–1.36)
Female	28,222	75.1	62,782	67.1	Reference
Age, y					
18–24	6,431	17.1	18,553	19.8	1.27 (1.20–1.34)
25–34	10,465	27.8	23,089	24.7	1.03 (0.97–1.08)
35–44	10,283	27.4	24,361	26.0	0.97 (0.92–1.02)
45–54	7,485	19.9	19,135	20.5	0.92 (0.88–0.97)
55–64	2,927	7.8	8,447	9.0	Reference
Race/ethnicity					
White, non-Hispanic	21,693	57.7	46,457	49.6	Reference
African American, non-Hispanic	7,463	19.9	24,970	26.7	1.59 (1.54–1.64)
Hispanic	4,832	12.9	12,192	13.0	1.24 (1.19–1.28)
Other	3,603	9.6	9,966	10.7	1.25 (1.19–1.30)
Medicaid eligibility					
Disability	14,634	38.9	48,674	52.0	Reference
Low income	14,947	39.8	27,262	29.1	0.56 (0.54–0.57)
Other	8,010	21.3	17,649	18.9	0.62 (0.60–0.64)
Managed care (not FFS)	13,218	35.2	31,021	33.2	1.05 (1.02–1.08)
Clinical and Utilization[d]					
Primary depression diagnosis[e]	29,883	79.5	75,579	80.8	1.04 (1.01–1.08)
Major depressive disorder[e]	16,589	44.1	43,484	46.5	1.08 (1.06–1.11)
Anxiety	3,887	10.3	9,176	9.8	0.96 (0.92–1.01)
Substance use disorder	5,754	15.3	16,290	17.4	1.06 (1.02–1.11)
Personality disorders	178	0.5	704	0.8	1.33 (1.12–1.58)
Self-harm	62	0.2	183	0.2	1.10 (0.82–1.48)
Diabetes	2,850	7.6	7,063	7.6	0.95 (0.91–1.00)
Cardiovascular disease	6,726	17.9	16,295	17.4	0.87 (0.84–0.90)
Cerebrovascular disease	663	1.8	1,736	1.9	0.95 (0.86–1.04)
Psychotherapy	1,206	3.2	3,073	3.3	0.97 (0.90–1.04)
Mental health emergency department visit[f]					
No visit	36,094	96.0	88,359	94.4	Reference
1 to 2 visits	1,388	3.7	4,810	5.1	1.25 (1.16–1.34)
3 or more visits	109	0.3	416	0.4	1.26 (1.02–1.57)
Mental health hospital admissions[f]					
No admission	37,005	98.4	91,250	97.5	Reference
1 or more admissions	586	1.6	2,335	2.5	1.31 (1.19–1.44)
Mental health outpatient visits[f]					
No visit	28,900	76.9	69,269	74.0	Reference
1 to 2 visits	4,731	12.6	12,767	13.6	1.04 (1.00–1.09)
3 or more visits	3,960	10.5	11,549	12.3	1.05 (1.00–1.11)

[a]Defined as antipsychotic initiation preceded by ≥ 31 days of antidepressant supply and active antidepressant supply on the antipsychotic index date.
[b]In addition to all variables shown in this table, the model was also adjusted for index year.
[c]At index date.
[d]During the 180-day baseline period including index date.
[e]Within the range of index date and index date + 30 days.
[f]Primary diagnosis.
Abbreviation: FFS = fee-for-service.
Symbol: … = not applicable.

study period (eAppendices 5–10). This suggests that use patterns were largely unaffected by FDA approval and labeling.

As a claims-based observational study, our work has several particular strengths and limitations. Using 10 years of near-national Medicaid data, it is the first longitudinal study of a large and diverse real-world population that examines the role of antipsychotic medications for depression in clinical practice. A focus on patients with new episodes of depression facilitates examination of antipsychotic use patterns that is not possible in cross-sectional studies or studies of patients with ongoing depression. However, inferring treatment intent of antipsychotic initiation solely from observed diagnostic claims for depression and alternative conditions with indications for antipsychotic initiation may result in misclassification. Nevertheless, our exclusion of patients diagnosed with many conditions for which antipsychotics are frequently used in practice helps to narrow the focus to patients in which it is likely that antipsychotics were used to treat depression.

The claims data do not provide information on drug samples. This lack of data might have resulted in misclassification of the initiation dates for both antidepressant and antipsychotic treatment. For antidepressant treatment, this misclassification would have led to an artificial reduction in the measured duration of treatment and could therefore have led to an underestimation of the proportion of individuals who received minimally adequate duration of antidepressant therapy. However, as discussed above, our definition of minimally adequate antidepressant treatment (≥ 31 days) was quite conservative and would be expected to be robust to underestimation of the duration of antidepressant treatment due to samples. In addition, our analyses underestimate the duration of antipsychotic treatment within the year following initiation because the inclusion criteria assure 365 days of Medicaid eligibility only following the date of onset of the new depressive episode, not following antipsychotic treatment initiation. Sensitivity analysis limited to patients with 365 days of eligibility following antipsychotic initiation (including 89% of antipsychotic initiators) showed an increase in follow-up ranging from 2.2% (ziprasidone) to 3.0% (quetiapine) (data not shown). Lastly, the study was limited to Medicaid-insured patients, and the described patterns may present differently in other patient populations.

Although our study provides reassurance concerning the overall rate and dosing patterns of antipsychotic medications for depression, the finding that nearly three-quarters of antipsychotic-treated patients did not receive even minimally adequate treatment with antidepressants prior to antipsychotic initiation is of concern. Minimizing premature or inappropriate initiation of medications with substantial adverse effects and medical risks should be a priority for physicians who are engaged in the pharmacologic management of adults with depression.

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Author contributions: Dr Gerhard had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Potential conflicts of interest: **Dr Gerhard** serves on an external safety review committee for a Merck study and has provided expert consultation to law firms on behalf of Roche and Pfizer. **Dr Stroup** serves as an investigator in a study sponsored by Auspex Pharmaceuticals. **Dr Correll** has received grant or research support from Takeda. He has served as a member of advisory boards/Data and Safety Monitoring Boards for Alkermes, Forum, IntraCellular Therapies, Lundbeck, Otsuka, Pfizer, and Sunovion. He has served as a consultant to Alkermes, the Gerson Lehrman Group, IntraCellular Therapies, Janssen/Johnson and Johnson, Lundbeck, Medscape, Otsuka, Pfizer, ProPhase, Sunovion, Supernus, and Takeda. He has presented expert testimony for Bristol-Myers Squibb, Janssen, and Otsuka. He has received travel expenses from Janssen/Johnson and Johnson, Lundbeck, Otsuka, Pfizer, Pro-Phase, Sunovion, and Takeda. **Dr Olfson** serves as principal investigator on a grant to Columbia University from Sunovion Pharmaceuticals. All other authors report no financial relationships with commercial interests. **Drs Huang**, **Tan**, and **Crystal** report no financial or other relationship relevant to the subject of this article.

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Supplementary material: Available at PSYCHIATRIST.COM.

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See supplementary material for this article at PSYCHIATRIST.COM.

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Supplementary Material

Article Title: Antipsychotic Medication Treatment Patterns in Adult Depression

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List of Supplementary Material for the article

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

eAppendix 1: Antidepressants and antipsychotics included in the study.

Antidepressants

SSRI
CITALOPRAM
ESCITALOPRAM
FLUOXETINE
FLUVOXAMINE
PAROXETINE
SERTRALINE
VILAZODONE
VORTIOXETINE

SNRI
DULOXETINE
VENLAFAXINE
DESVENLAFAXINE
LEVOMILNACIPRAN
MILNACIPRAN (FDA approved only for fibromyalgia, though occasionally used for depression)

MAOI
PHENELZINE
TRANYLCYPROMINE
ISOCARBOXAZID

TRICYCLIC ANTIDEPRESSANTS
AMITRIPTYLINE
CLOMIPRAMINE
DESIPRAMINE
IMIPRAMINE
TRIMIPRAMINE
NORTRIPTYLINE
PROTRIPTYLINE
DOXEPIN

OTHER
MIRTAZAPINE
AMOXAPINE
MAPROTILINE
NEFAZODONE
TRAZODONE
BUPROPION

Antipsychotics

FIRST GENERATION
CHLORPROMAZINE
FLUPHENAZINE
HALOPERIDOL
LOXAPINE
MESORIDAZINE
MOLINDONE
PERPHENAZINE
PIMOZIDE
THIORIDAZINE

THIOTHIXENE
TRIFLUOPERAZINE
TRIFLUPROMAZINE
CHLORPROTHIXENE

SECOND GENERATION
ARIPIPRAZOLE
CLOZAPINE
OLANZAPINE
PALIPERIDONE
QUETIAPINE
RISPERIDONE
ZIPRASIDONE
ASENAPINE
ILOPERIDONE
LURASIDONE

eAppendix 2: Clinically reasonable dose ranges for second generation antipsychotics (in mg/day). Prescription claims with daily doses outside of these dose ranges were excluded from analysis (affecting approximately 1.8% of patients who initiated an antipsychotic).

	Minimum Daily Dose (mg)	Maximum Daily Dose (mg)
Quetiapine	25	1200
Olanzapine	2.5	40
Aripiprazole	2	30
Risperidone	0.25	8
Ziprasidone	20	240

eAppendix 3: Characteristics of antipsychotic treatment among patients with new depressive episodes with and without alternative antipsychotic indications (duration >30 days; 95th percentile doses)

	Without Alternative Indication		With Alternative Indication	
Duration				
	N	Percent>30 days	N	Percent>30 days
Any APM	131,176	74.4	92,254	80.3
Quetiapine	63,001	70.6	39,310	72.5
Olanzapine	28,818	65.5	21,841	68.2
Risperidone	33,897	66.0	30,979	68.1
Aripiprazole	20,612	65.5	19,178	66.7
Ziprasidone	9,423	60.5	10,972	61.6
Dose[a]				
	N	mg at 95th percentile	N	mg at 95th percentile
Quetiapine	62,136	600	38,745	800
Olanzapine	28,332	20	21,371	30
Risperidone	33,298	6	30,295	6
Aripiprazole	20,245	30	18,779	30
Ziprasidone	9,249	160	10,723	160

[a]based on the prescription fill with the highest dose dispensed; calculated as [(#dispensed*mg/dose)/days supply]; dose analyses excluded 4,858 episodes [1.8% of all initiations; 1.6% of those without indication; 2.0% of those with indication] where the highest calculated single dose was outside a clinically reasonable dosing range (eAppendix 2).
APM: antipsychotic medication

eAppendix 4: FDA adult labeled dosage recommendations for second-generation antipsychotics by indication (mg/day)

	Major Depressive Disorder – Adjunct to Antidepressants		**Schizophrenia**	
	Recommended Dose Range	Maximum Dose	Recommended Dose Range	Maximum Dose
Quetiapine	150-300	300	400-800	800
Olanzapine	3-12	20	10-15	20
Aripiprazole	5-10	15	10-15	30
Risperidone	n/a	n/a	4-8	16
Ziprasidone	n/a	n/a	40-160	160

eAppendix 5: Characteristics of adult Medicaid beneficiaries with new depressive episodes by treatment with oral antipsychotic medications (2008-2010)

	Total Episodes N=409,265 (100%)	APM Initiators N=58,605 (14.3%)		Non APM Initiators N=350,660 (85.7%)		P(Chi-Square)
		N	%	N	%	
DEMOGRAPHIC[a]						
Sex						
Male	94,547	18,380	31.4	76,167	21.7	<.0001
Female	314,717	40,225	68.6	274,492	78.3	
Age (mean, SD)	34.5 (12.7)	36.1	12.4	35.4	12.8	
Age						<.0001
18-24	102,516	13,194	22.5	89,322	25.5	
25-34	113,840	15,331	26.2	98,509	28.1	
35-44	82,592	13,206	22.5	69,386	19.8	
45-54	69,860	11,877	20.3	57,983	16.5	
55-64	40,457	4,997	8.5	35,460	10.1	
Race Ethnicity						<.0001
White, non-Hispanic	214,910	29,002	49.5	185,908	53.0	
African American, non-Hispanic	96,511	16,678	28.5	79,833	22.8	
Hispanic	61,299	8,195	14.0	53,104	15.1	
other	36,545	4,730	8.1	31,815	9.1	
Medicaid Eligibility						<.0001
Disability	141,420	27,028	46.1	114,392	32.6	
Low income	174,453	19,892	33.9	154,561	44.1	
Other	93,392	11,685	19.4	81,707	23.3	
Managed care (not FFS)	194,947	25,776	44.0	169,171	48.2	<.0001
CLINICAL&UTILIZATION[b]						
Primary Depression dx[c]	289,617	47,197	80.5	242,420	69.1	<.0001
Major Depressive Disorder[c]	130,335	29,247	49.9	101,088	28.8	<.0001
Anxiety	36,234	5,901	10.1	30,333	8.7	<.0001
Substance use disorder	52,628	10,473	17.9	42,155	12.0	<.0001
Personality disorders	1,286	350	0.6	936	0.3	<.0001
Self-harm	610	148	0.3	462	0.1	<.0001
Diabetes	35,128	4,522	7.7	30,606	8.7	<.0001
Cardiovascular Disease	75,468	10,557	18.0	64,911	18.5	.0041
Cerebrovascular Disease	7,395	1,075	1.8	6,320	1.8	.5904
Psychotherapy	14,548	2,419	4.1	12,129	3.5	<.0001
MH ER visit[d]						<.0001
No visit	394,594	55,064	94.0	339,530	96.8	
1 to 2 visits	13,600	3,253	5.6	10,347	3.0	
3 or more visits	1,071	288	0.5	783	0.2	
MH hospital admissions[d]	3,481	1,134	1.9	2,347	0.7	<.0001
MH outpatient visits[d]						<.0001
No visit	333,011	43,662	74.5	289,349	82.5	

1 to 2 visits	45,227	8,355	14.3	36,872	10.5	
3 or more visits	31,027	6,588	11.2	24,439	7.0	

[a]at index date; [b]during 180 baseline period including index date; [c]within Index date and index date+30 days; [d]primary diagnosis.

APM: antipsychotic medication; FFS: fee-for-service; MH: mental health; ER: emergency room

eAppendix 6: Antipsychotic use in the year following a new depressive episode by antipsychotic indications diagnosed in the period from the new depressive episode to 45 days following the antipsychotic medication initiation (2008-2010)

	Antipsychotic Medication Initiators N=58,605	
	N	%
No alternative APM Indication[a]	33,546	57.2
At least 1 alternative APM Indication[a]	25,059	42.8
Schizophrenia	5,729	9.8
Bipolar Disorder	13,496	23.0
Depressed[b]	3,655	6.2
Manic[c]	1,846	3.2
Mixed[d]	1,940	3.3
Other[e]	9,394	16.0
MDD with psychotic features	9,456	16.1
Dementia	541	0.9
Other[f]	884	1.5

[a]from the index date to 45 days following antipsychotic initiation; [b]ICD-9-CM 296.5, 296.50-296.56; [c]ICD9-CM 296.01-296.06, 296.4, 296.40-46; [d]ICD-9CM 296.6, 296.61-296.66; [e]ICD-9-CM 296.7, 296.80, 296.89; [f]pervasive development disorder, delusional disorder, depressive type psychosis, cyclothymic disorder;
APM: antipsychotic medication

eAppendix 7: Characteristics of initiators of antipsychotic medications by presence of antipsychotic indication during the period from a new depressive episode to 45 days following an antipsychotic medication initiation (2008-2010)

	No alternative APM indication over follow-up N=33,546		At least 1 alternative APM indication over follow-up N=25,059		P(Chi-Square)
	N	%	N	%	
DEMOGRAPHIC[a]					
Sex					<.0001
Male	10,250	30.6	8,130	32.4	
Female	23,296	69.4	16,929	67.6	
Age (mean, SD)	36.1	12.4	36.2	12.3	
Age					.3834
18-24	7,536	22.5	5,658	22.6	
25-34	8,828	26.3	6,503	26.0	
35-44	7,591	22.6	5,615	22.4	
45-54	6,710	20.0	5,167	20.6	
55-64	2,881	8.6	2,116	8.4	
Race Ethnicity					<.0001
White, non-Hispanic	17,736	52.9	11,266	45.0	
African American, non-Hispanic	8,394	25.0	8,284	33.1	
Hispanic	4,674	13.9	3,521	14.1	
other	2,742	8.2	1,988	7.9	
Medicaid Eligibility					<.0001
Disability	14,203	42.3	12,825	51.2	
Low income	12,093	36.1	7,799	31.1	
Other	7,250	21.6	4,435	17.7	
Managed care (not FFS)	14,933	44.5	10,843	43.3	.0027
CLINICAL&UTILIZATION[b]					
Primary Depression dx[c]	26,651	79.5	20,546	82.0	<.0001
Major Depressive Disorder[c]	14,905	44.4	14,342	57.2	<.0001
Anxiety	3,635	10.8	2,266	9.0	<.0001
Substance use disorder	6,144	18.3	4,329	17.3	.0012
Personality disorders	177	0.5	173	0.7	.0114
Self-harm	70	0.2	78	0.3	.0144
Diabetes	2,591	7.7	1,931	7.7	.9359
Cardiovascular Disease	6,160	18.2	4,451	17.8	.1705
Cerebrovascular Disease	617	1.8	458	1.8	.9177
Psychotherapy	1,455	4.3	964	3.9	.0032
MH ER visit[d]					
No visit	31,701	94.5	23,363	93.2	<.0001
1 to 2 visits	1,679	5.0	1,574	6.3	
3 or more visits	166	0.5	122	0.5	

MH hospital admissions[d]					.3668
No admission	32,882	98.0	24,589	98.1	
1+ admissions	664	2.0	470	1.9	
MH outpatient visits[d]					<.0001
No visit	24,827	74.0	18,835	75.2	
1 to 2 visits	4,676	13.9	3,679	14.7	
3 or more visits	4,043	12.1	2,545	10.2	

[a]at index date; [b]during 180 baseline period including index date; [c]within Index date and index date+30 days; [d]primary diagnosis.

APM: antipsychotic medication; FFS: fee-for-service; MH: mental health; ER: emergency room

eAppendix 8: Duration and dose of antipsychotic treatment among patients with new depressive episodes with and without alternative antipsychotic indications (2008-2010)

	Without Alternative Indication		With Alternative Indication	
Duration[a]				
	N	**Days, mean (SD)**	**N**	**Days, mean (SD)**
Any APM	33,546	132.0 (106.2)	25,059	145.0 (107.5)
Quetiapine	17,268	120.7 (103.4)	11,277	122.5 (102.3)
Olanzapine	3,359	104.9 (95.5)	3,361	105.5 (95.6)
Risperidone	6,014	106.1 (96.6)	6,491	106.9 (95.4)
Aripiprazole	9,969	106.8 (92.7)	7,929	108.8 (93.5)
Ziprasidone	2,314	98.6 (94.6)	2,939	95.3 (96.9)
Dose[b]				
	N	**mg; mean, (SD)**	**N**	**mg; mean, (SD)**
Quetiapine	17,071	184.3 (170.3)	11,149	257.8 (208.2)
Olanzapine	3,307	10.0 (6.9)	3,302	13.1 (8.0)
Risperidone	5,908	2.0 (1.4)	6,375	2.6 (1.7)
Aripiprazole	9,833	9.5 (6.9)	7,792	12.2 (7.7)
Ziprasidone	2,274	95.5 (49.5)	2,884	107.1 (50.7)

[a]total days of medication possession based on days supply dispensed; limited to claims with >0 days supply ; [b]in mg, based on the prescription fill with the highest dose dispensed; calculated as [(#dispensed*mg/dose)/days supply]; APM: antipsychotic medication

eAppendix 9: Predictors of antipsychotic use without minimal antidepressant treatment among adults with new depressive episodes and no observed alternative clinical indications for antipsychotic treatment (2008-2010)

	Minimal antidepressant treatment[a] N=9,714		No minimal antidepressant treatment N=23,832		Adjusted Odds Ratio[b] (95% CI)
	N	%	N	%	
TOTAL	9,714	29.0	23,832	71.0	
DEMOGRAPHIC[c]					
Sex					
Male	2,314	23.8	7,936	33.3	1.389 (1.31-1.47)
Female	7,400	76.2	15,896	66.7	Reference
Age					
18-24	1,895	19.5	5,641	23.7	1.37 (1.23-1.53)
25-34	2,846	29.3	5,982	25.1	1.07 (0.96-1.19)
35-44	2,359	24.3	5,232	22.0	0.98 (0.88-1.09)
45-54	1,880	19.4	4,830	20.3	0.95 (0.85-1.05)
55-64	734	7.6	2,147	9.0	Reference
Race Ethnicity					
White, non-Hispanic	5,601	57.7	12,135	50.9	Reference
African American, non-Hispanic	1,955	20.1	6,439	27.0	1.53 (1.44-1.63)
Hispanic	1,393	14.3	3,281	13.8	1.13 (1.05-1.21)
other	765	7.9	1,977	8.3	1.11 (1.02-1.22)
Medicaid Eligibility					
Disability	3,186	32.8	11,017	46.2	Reference
Low income	4,390	45.2	7,703	32.3	0.53 (0.50-0.57)
Other	2,138	22.0	5,112	21.5	0.65 (0.61-0.70)
Managed care (not FFS)	4,540	46.7	10,393	43.6	1.02 (0.97-1.07)
CLINICAL&UTILIZATION[d]					
Primary Depression dx[e]	7,722	79.5	18,929	79.4	0.98 (0.92-1.04)
Major Depressive Disorder[e]	4,271	44.0	10,634	44.6	1.03 (0.98-1.09)
Anxiety	1,083	11.2	2,552	10.7	0.97 (0.89-1.06)
Substance use disorder	1,627	16.8	4,517	19.0	1.05 (0.97-1.13)
Personality disorders	32	0.3	145	0.6	1.44 (0.97-2.13)
Self-harm	17	0.2	53	0.2	1.10 (0.63-1.92)
Diabetes	753	7.8	1,838	7.7	0.94 (0.86-1.03)
Cardiovascular Disease	1,772	18.2	4,334	18.2	0.89 (0.83-0.96)
Cerebrovascular Disease	169	1.7	448	1.9	0.94 (0.78-1.13)
Psychotherapy	421	4.3	1,034	4.3	0.93 (0.82-1.06)
MH ER visit[f]					
No visit	9,294	95.7	22,407	94.0	Reference
1 to 2 visits	385	4.0	1,294	5.4	1.22 (1.07-1.39)
3 or more visits	35	0.4	131	0.6	1.25 (0.85-1.85)
MH hospital admissions[f]					

No admission	9,584	98.7	23,298	97.8	Reference
1+ admissions	130	1.3	534	2.2	1.33 (1.08-1.64)
MH outpatient visits[f]					
No visit	7,411	76.3	17,416	73.1	Reference
1 to 2 visits	1,285	13.2	3,391	14.2	1.05 (0.96-1.14)
3 or more visits	1,018	10.5	3,025	12.7	1.09 (0.98-1.20)

[a] defined as AP initiation preceded by ≥31 days of AD supply AND active AD supply on the AP index date;
[b]in addition to all variables shown in eAppendix 8, the model also adjusted for index year; [c]at index date;
[d]during the 180 day baseline period including index date; [e]within Index date and index date+30 days;
[f]primary diagnosis;.
APM: antipsychotic medication; FFS: fee-for-service; MH: mental health; ER: emergency room

eAppendix 10: Characteristics of antipsychotic treatment among patients with new depressive episodes with and without alternative antipsychotic indications (duration >30 days; 95th percentile doses) (2008-2010)

	Without Alternative Indication		With Alternative Indication	
Duration				
	N	Percent>30 days	N	Percent>30 days
Any APM	33,546	74.4	25,059	80.3
Quetiapine	17,268	69.7	11,277	72.4
Olanzapine	3,359	64.9	3,361	66.5
Risperidone	6,014	65.3	6,491	67.2
Aripiprazole	9,969	66.8	7,929	68.8
Ziprasidone	2,314	60.0	2,939	59.7
Dose[a]				
	N	mg at 95th percentile	N	mg at 95th percentile
Quetiapine	17,071	600	11,149	667
Olanzapine	3,307	20	3,302	30
Risperidone	5,908	4	6,375	6
Aripiprazole	9,833	25	7,792	30
Ziprasidone	2,274	160	2,884	160

[a]based on the prescription fill with the highest dose dispensed; calculated as [(#dispensed*mg/dose)/days supply]; APM: antipsychotic medication