ORIGINAL ARTICLE

National Trends in the Office-Based Treatment of Children, Adolescents, and Adults With Antipsychotics

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Context: Although antipsychotic treatment has recently increased, little is known about how this development has differentially affected the office-based care of adults and young people in the United States.

Objective: To compare national trends and patterns in antipsychotic treatment of adults and youths in office-based medical practice.

Design: Trends between 1993 and 2009 in visits with antipsychotics for children (0-13 years), adolescents (14-20 years), and adults (≥21 years) are described on a per population basis and as a proportion of total medical office visits. Background and clinical characteristics of recent (2005-2009) antipsychotic visits are also compared by patient age.

Setting: Outpatient visits to physicians in office-based practice.

Participants: Visits from the 1993-2009 National Ambulatory Medical Care Surveys (N = 484 889).

Main Outcome Measures: Visits with a prescription of antipsychotic medications.

Results: Between 1993-1998 and 2005-2009, visits with a prescription of antipsychotic medications per 100 persons increased from 0.24 to 1.83 for children, 0.78 to 3.76 for adolescents, and 3.25 to 6.18 for adults. The proportion of total visits that included a prescription of antipsychotics increased during this period from 0.16% to 1.07% for youths and from 0.88% to 1.73% for adults. From 2005 to 2009, disruptive behavior disorders were the most common diagnoses in child and adolescent antipsychotic visits, accounting for 63.0% and 33.7%, respectively, while depression (21.2%) and bipolar disorder (20.2%) were the 2 most common diagnoses in adult antipsychotic visits. Psychiatrists provided a larger proportion of the antipsychotic visits for children (67.7%) and adolescents (71.6%) than to adults (50.3%) ($P < .001$). From 2005 to 2009, antipsychotics were included in 28.8% of adult visits and 31.1% of youth visits to psychiatrists.

Conclusions: On a population basis, adults make considerably more medical visits with a prescription of antipsychotics than do adolescents or children. Yet antipsychotic treatment has increased especially rapidly among young people, and recently antipsychotics have been prescribed in approximately the same proportion of youth and adult visits to psychiatrists.

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Over the past several years, an increasing number of adults and children in the United States have been treated with antipsychotic medications.[1,2] Antipsychotics are now among the most commonly prescribed and costly classes of medications.[3] In adults, antipsychotic medications have demonstrated efficacy and have been approved by the Food and Drug Administration (FDA) as a primary treatment for schizophrenia[4,5] and bipolar disorder[6,7] and as an adjunctive treatment for major depressive disorder.[8] In children and adolescents, antipsychotics are indicated for irritability associated with autistic disorder (5-16 years), tics and vocal utterances of Tourette syndrome and bipolar mania (10-17 years), and schizophrenia (13-17 years).[9]

With increasing use of antipsychotic drugs, the range of mental disorders treated with these medications in practice has broadened.[10-15] As a result, the proportion of second-generation antipsychotic medications prescribed to treat schizophrenia has decreased from 51% (1995-1996) to 24% (2007-2008),[2] while antipsychotic treatment of anxiety disorders in adults and youths has roughly doubled.[12] In young people, attention-deficit/hyperactivity disorder and other disruptive disorders account for a substantial proportion (37.8%) of antipsychotic use.[11]

The metabolic safety concerns of antipsychotic medications[16,17] focus our attention on antipsychotic prescribing practices in the community, especially on the extent to which antipsychotics are used to treat disorders for which there is limited empirical evidence of efficacy.[15,18] Young people may be especially sensitive to the adverse metabolic effects of second-generation antipsychotics. As compared with adults, children may be more vulnerable to antipsychotic-induced weight gain[19] and perhaps even to antipsychotic-associated diabetes.[20,21]

Young people and adults vary in several important clinical respects[22] that might influence trends in antipsychotic use. Disruptive behavioral disorders, which are more commonly diagnosed in boys than in girls[23] and in nonwhite youths than in white youths,[24,25] occur in a substantial proportion of young people receiving outpatient mental health care.[26] Increasing clinical acceptance of antipsychotics for problematic aggression in disruptive behavior disorders[27] may have increased the number of children and adolescents (especially male youths and ethnic/racial minorities) being prescribed antipsychotics. The increase in the number of clinical diagnoses of bipolar disorder[28] and autistic spectrum disorders[29] among children and adolescents may have further increased antipsychotic use by youths, particularly by boys. With respect to adults, acceptance of antipsychotics as adjuvant treatment of major depressive disorder, even in the absence of psychotic features,[30] might have increased antipsychotic use. Because depressive disorders are significantly more common in women than in men,[31] such a trend might preferentially increase antipsychotic use among adult women. Increasing use of antipsychotics in adult anxiety disorders may have a similar effect.[12]

A comparison is presented of nationally representative survey data from adult and youth visits to office-based physicians. The analyses focus on trends and patterns of antipsychotic treatment. Prior to conducting these analyses, we predicted that the increase in the proportion of physician visits with a prescription of antipsychotic medications would be more pronounced for youths than for adults.

METHODS

Data were obtained from the National Ambulatory Medical Care Survey (NAMCS).[32] The NAMCS, which is conducted annually by the National Center for Health Statistics, samples a nationally representative group of visits to physicians in office-based practice. Following National Center for Health Statistics recommendations, data from contiguous survey years were combined to derive more stable estimates (1993-1998, 1999-2004, and 2005-2009). Across the 17 survey years, response rates varied between 58.9% (2006) and 73.1% (1993), with a mean of 66.1%.[33] For each visit, the treating physician or member of the physician's staff provided information about patient sociodemographic and clinical characteristics, as well as the medications prescribed or supplied to the patient.

DIAGNOSIS

Diagnoses were made according to the *International Classification of Diseases, Ninth Revision, Clinical Modification*. For the analysis of trends in antipsychotic use stratified by age groups, visits were grouped by occurrence of mood, anxiety, and psychotic disorders. In the analysis that compares the characteristics of antipsychotic visits across age groups (2005-2009), visits were classified by diagnoses of schizophrenia and related psychotic disorders, bipolar disorder, depression, anxiety, developmental disorders or mental retardation, disruptive behavior disorders, and other mental disorders (eTable, http://www.archgenpsychiatry.com).

PSYCHOTROPIC MEDICATIONS

Visits in which psychotropic medications were either supplied or prescribed were classified into 5 medication groups: antipsychotic medications, which are the primary focus of the analyses; stimulants and other attention-deficit/hyperactivity disorder medications; antidepressants; anxiolytics/hypnotics; and mood stabilizers. The antipsychotic medication group excluded prochlorperazine edisylate and promethazine hydrochloride because they are commonly used for nonpsychiatric indications. Anxiolytics/hypnotics included benzodiazepines and nonbenzodiazepine sedatives and anxiolytics. Mood stabilizers included lithium carbonate or lithium citrate, carbamazepine, divalproex sodium/valproate sodium/valproic acid, and lamotrigine. All antidepressants including those such as bupropion hydrochloride, duloxetine hydrochloride, and trazodone hydrochloride, which are also used for non–mental health indications, were included.

SOURCE OF PAYMENT

Data were collapsed into 3 nonmutually exclusive categories: (1) private insurance such as Blue Cross/Blue Shield and other commercial insurance; (2) public insurance, including Medicare, Medicaid, and other government insurance; and (3) a residual category ("self-pay/other") that combined patients with self-payment, no charge, workers compensation, those whose source of insurance was unknown, and those who received uncompensated care. In visits with more than 1 source of payment, assignment was hierarchical, with visits assigned to private, public, and self-pay/other insurance groups in descending order.

FDA-APPROVED INDICATION

One or more antipsychotics have been approved for schizophrenia or schizoaffective disorder, bipolar disorder, autistic disorder, Tourette syndrome, and major depressive disorder when coprescribed with an antidepressant. In the following analysis, FDA-approved visits include only those visits with a diagnosis for which the specific prescribed antipsychotic had been approved by the visit year for the age of the patient. This definition recognizes the substantial within-class heterogeneity in safety[34] and efficacy[35] that exists among antipsychotic medications and is consistent with the FDA's approach of drug indication approval at the level of individual drugs.

OTHER CHARACTERISTICS

Visits were also classified by patient sex, patient race/ethnicity (white, non-Hispanic, or other), specialty of the treating physician (psychiatrist or nonpsychiatrist), and whether psychotherapy was provided by the physician at the visit.

ANALYTIC STRATEGY

Population-based proportions and associated 95% CIs of office-based adult (≥21 years), adolescent (14-20 years), and child (0-13 years) visits with antipsychotic treatment (hereafter referred to as antipsychotic visits) were determined for the time periods of 1993-1998, 1999-2004, and 2005-2009. Denomi-

Table 1. Trends in National Annualized Population Estimates of Office-Based Physician Visits for Children, Adolescents, and Adults That Included Antipsychotic Treatment[a]

	Surveyed Antipsychotic Visits, No.			Antipsychotic Visits per 100 Population per Year, No. (95% CI)		
Time Period	Child	Adolescent	Adult	Children	Adolescents	Adults
1993-1998	36	68	1645	0.24 (0.09-0.40)	0.78 (0.46-1.10)	3.25 (2.73-3.76)
1999-2004	222	196	1978	1.41 (1.01-1.80)	2.71 (1.94-3.48)	4.51 (3.82-5.19)
2005-2009	270	257	2676	1.83 (1.27-2.39)	3.76 (2.78-4.73)	6.18 (5.06-7.30)

[a]Data are from the National Ambulatory Medical Care Survey (NAMCS) and the US Census Bureau (July 1, 1996; July 1, 2002; and July 1, 2007). Population-based proportions of office-based child (0-13 years), adolescent (14-20 years), and adult (≥21 years) visits with antipsychotic treatment (hereafter referred to as antipsychotic visits) per 100 population were estimated by dividing the mean annual weighted number of national antipsychotic visits determined from NAMCS data by the estimated population for the corresponding age group during each time period derived from intercensal estimates from the US Bureau of the Census.

Table 2. National Estimated Number of Office-Based Medical Visits by Children, Adolescents, and Adults That Included Antipsychotic Treatment (2005-2009)[a]

	Surveyed Antipsychotic Visits, No.			Antipsychotic Visits per 100 Population, Estimated No. (95% CI)		
Variable	Child	Adolescent	Adult	Children	Adolescents	Adults
Total	270	257	2676	1.83 (1.27-2.39)	3.76 (2.78-4.73)	6.18 (5.06-7.30)
Sex						
Male	207	162	1049	2.75 (1.84-3.67)	4.45 (3.19-5.70)	4.81 (3.87-5.75)
Female	63	95	1627	0.87 (0.53-1.21)	3.25 (2.17-4.33)	7.48 (6.10-8.85)
Race/ethnicity						
White, non-Hispanic	189	200	2081	2.25 (1.54-2.96)	4.99 (3.60-6.38)	6.93 (5.60-8.26)
Other	81	57	595	1.31 (0.81-1.81)	1.88 (1.01-2.75)	4.48 (3.40-5.55)

[a]Calculated using National Ambulatory Medical Care Survey (NAMCS) and US Census Bureau data. Population-based proportions of office-based child (0-13 years), adolescent (14-20 years), and adult (≥21 years) visits with antipsychotic treatment (hereafter referred to as antipsychotic visits) per 100 population were estimated by dividing the mean annual weighted number of national antipsychotic visits for the selected demographic groups determined from NAMCS data by the estimated population for the corresponding demographic groups during each time period derived from intercensal estimates from the US Bureau of the Census.

nators were derived from intercensal estimates from the US Bureau of the Census[36] of the corresponding demographic groups (**Table 1**). For years 2005-2009, population-based proportions of office-based antipsychotic visits with surrounding 95% CIs were determined for the 3 age groups (0-13, 14-20, and ≥21 years), sex, and broad race/ethnicity group (**Table 2**).

The proportions of youth (0-20 years) and adult (≥21 years) office-based antipsychotic visits were determined overall and stratified by patient sex, patient race/ethnicity, payment source, physician specialty, psychotherapy, broad mental disorder group, and FDA-approved indication for each time period (1993-1998, 1999-2004, and 2005-2009). Logistic regression models were used to assess time trends in the probability of antipsychotic visits. A study period variable was defined for each survey year running from 0 for 1993 to 1 for 2009. The outcome of interest is the odds of an antipsychotic across the entire period (1993-2009). For example, an odds ratio of 2.0 denotes twice the odds that a visit included an antipsychotic at the end (2009) as compared with the start (1993) of the study period. Separate regressions were constructed for each level of visit characteristics of interest. For example, one regression assessed the odds of antipsychotic visits over the study period for male visits and a separate regression for female visits. An interaction term was added to each regression to assess whether trends in antipsychotic use significantly differed across these groups. The *P* values associated with these interaction terms are presented in **Tables 3** and **4**.

For years 2005-2009, the difference in proportion test was used to compare the background and clinical characteristics of antipsychotic visits for children, adolescents, and adults during the period from 2005 to 2009. A separate analysis compared the clinical characteristics of youth and adult antipsychotic visits by specialty of the treating physician (psychiatrist vs nonpsychiatrist). The frequency distribution in the time period of 2005-2009 of the 4 most commonly prescribed antipsychotics in each age group was also determined.

Analyses were adjusted for visit weights, clustering, and stratification of data using design elements provided by the National Center for Health Statistics. When adjusted for these elements, survey data represent annual visits to US office-based physicians.[37] Analyses were conducted using SUDAAN software (Research Triangle Institute), all analyses were 2 sided, and α was set at .05.

RESULTS

TRENDS IN ANTIPSYCHOTIC VISITS ON A POPULATION BASIS

On a per capita basis, office-based antipsychotic visits increased among all 3 age groups but were consistently more prevalent for adults than for adolescents and were least prevalent for children (Table 1). During the 2005-2009 time period, the estimated number of antipsychotic visits per 100 adults was significantly greater for female than male patients, while the reverse was true for children (Table 2). For adolescents and adults, but not children, the corresponding proportion of antipsychotic visits was significantly greater on a per population basis for white non-Hispanics than for the other racial/ethnic group.

Table 3. Trends in Antipsychotic Prescribing Patterns in Youth and Adult Office-Based Visits, Stratified by Background Characteristics

Characteristic	Surveyed Visits, No.			Antipsychotic Visits per 100 Visits, %			OR[a] (95% CI)	Interaction *P* Value[b]
	1993-1998	1999-2004	2005-2009	1993-1998	1999-2004	2005-2009		
Total								
Youths	34 732	28 837	28 801	0.16	0.71	1.07	8.47 (5.37-13.35)	<.001
Adults	149 823	122 998	119 698	0.88	1.12	1.73	2.58 (2.05-3.24)	
Male								
Youths	17 549	14 715	14 486	0.19	0.94	1.46	9.87 (5.94-16.42)	<.001
Adults	59 486	51 014	48 214	0.96	1.17	1.69	2.26 (1.71-2.98)	
Female								
Youths	17 183	14 122	14 315	0.13	0.47	0.67	6.27 (3.54-11.08)	.005
Adults	90 337	71 984	71 484	0.83	1.09	1.76	2.80 (2.20-3.57)	
White, non-Hispanic								
Youths	24 153	17 434	17 881	0.16	0.85	1.21	9.80 (6.03-15.91)	<.001
Adults	116 642	84 494	89 215	0.86	1.15	1.79	2.72 (2.16-3.44)	
Other								
Youths	8519	6993	10 920	0.18	0.55	0.80	4.52 (1.65-12.36)	.03
Adults	25 125	19 922	30 483	1.13	1.41	1.56	1.54 (0.98-2.41)	
Private insurance								
Youths	21 117	20 045	16 449	0.10	0.41	0.77	10.07 (5.36-18.93)	.001
Adults	79 899	65 996	72 627	0.50	0.64	1.17	3.39 (2.50-4.58)	
Public insurance								
Youths	6367	5620	8966	0.36	1.36	1.50	4.44 (2.25-8.77)	.06
Adults	39 403	40 387	29 958	1.79	1.79	3.19	2.26 (1.59-3.22)	
Self-pay/other insurance								
Youths	7248	2848	2981	0.16	1.71	1.85	16.75 (7.46-37.64)	<.001
Adults	30 521	15 070	15 425	0.69	1.72	1.89	3.75 (2.54-5.54)	

[a] The odds ratio (OR) is associated with the transformed survey year variable: (survey year – 1993)/16, and therefore it estimates the change in odds of a visit with antipsychotic treatment (hereafter referred to as an antipsychotic visit) over the entire 1993-2009 study period.
[b] The interaction *P* value refers to the age group × time interaction.

TRENDS IN ANTIPSYCHOTIC USE AMONG ADULT AND YOUTH VISITS

During the study period, antipsychotic use increased among adult and youth visits, with a significantly greater increase by youths. Antipsychotic use increased especially rapidly among visits by young people who were male, non-Hispanic white in race/ethnicity, and who paid for their care with private insurance or other nonpublic sources. Antipsychotic use also significantly increased among visits by youths who were Hispanic or nonwhite. A corresponding increase did not, however, occur among adults who were Hispanic or nonwhite (Table 3).

Antipsychotic use was substantially more common in visits to psychiatrists than nonpsychiatrists (Table 4). Among visits to psychiatrists, antipsychotic use increased significantly more rapidly in visits by youths than adults. By 2005-2009, a similar proportion of youth and adult visits to psychiatrists included an antipsychotic medication. A marked increase also occurred in antipsychotic use among visits by youths to nonpsychiatrist physicians.

Throughout the study period, antipsychotic use was prevalent in visits by youths and adults with psychotic disorder diagnoses. There was a particularly marked increase in antipsychotics in visits by youths with mood disorder diagnoses. By 2005-2009, almost one-third of youth visits with a mood disorder diagnosis (31.3%) included an antipsychotic medication. A smaller, though nevertheless significant, increase also occurred in antipsychotic use by adult visits with mood disorder diagnoses. By contrast, antipsychotic use visits with anxiety disorder diagnoses increased in a roughly parallel manner among youth and adult visits (interaction $P = .66$) (Table 4).

CHARACTERISTICS OF CHILD, ADOLESCENT, AND ADULT ANTIPSYCHOTIC VISITS

In 2005-2009, several differences were evident in the demographic and clinical characteristics of antipsychotic visits by children, adolescents, and adults (**Table 5**). Male patients predominated among child and adolescent antipsychotic visits, while female patients predominated among adult antipsychotic visits. This was partially explained by a predominance of male patients (80.3% [95% CI, 73.8-85.4]) among child and adolescent antipsychotic visits with disruptive behavior disorders and a predominance of female patients (67.9% [95% CI, 63.6-71.6]) among adult antipsychotic visits with mood disorders (data not shown). Not surprisingly, schizophrenia, bipolar disorder, and depression accounted for a considerably larger percentage of adult than child antipsychotic visits, while disruptive behavior and developmental disorders accounted for a greater proportion of child than adult antipsychotic visits. Visits without a mental disorder diagnoses accounted for roughly one-third of adult antipsychotic visits. In a post hoc analysis, 96.5% of the adult antipsychotic visits without mental disorders were to nonpsychiatrist physicians, and 33.7% included a quetiapine fumarate prescription (data not shown).

Table 4. Trends in Antipsychotic Prescribing Patterns in Youth and Adult Office-Based Visits, Stratified by Clinical Characteristics

Characteristic	Surveyed Visits, No.			Antipsychotic Visits per 100 Visits, %			OR[a] (95% CI)	Interaction *P* Value[b]
	1993-1998	1999-2004	2005-2009	1993-1998	1999-2004	2005-2009		
Psychiatrists								
Youths	1006	1844	1250	8.80	20.31	31.13	6.58 (4.04-10.72)	<.001
Adults	8515	7392	5921	16.78	22.75	28.48	2.52 (1.87-3.39)	
Nonpsychiatrists								
Youths	33 726	26 993	27 551	0.05	0.13	0.33	11.14 (4.21-29.47)	.09
Adults	141 308	115 606	113 777	0.31	0.42	0.89	4.61 (3.39-6.28)	
Psychotherapy								
Youths	473	988	721	7.64	16.34	24.27	5.77 (2.44-13.64)	.12
Adults	4442	4941	3707	10.65	16.61	22.17	3.04 (2.06-4.49)	
No psychotherapy								
Youths	34 259	27 849	28 080	0.11	0.42	0.75	9.70 (5.50-17.12)	<.001
Adults	145 381	118 057	115 991	0.70	0.75	1.35	2.68 (2.05-3.50)	
Mood disorders								
Youths	463	988	748	6.62	15.86	31.32	11.01 (5.96-20.33)	<.001
Adults	7198	6737	6236	7.73	11.59	17.69	3.70 (2.76-4.97)	
No mood disorders								
Youths	34 269	27 849	28 053	0.12	0.41	0.57	6.56 (3.74-11.51)	.0002
Adults	142 625	116 261	113 462	0.60	0.66	1.04	2.08 (1.64-2.64)	
Anxiety disorders								
Youths	247	451	461	5.29	12.59	16.33	4.27 (1.75-10.44)	.66
Adults	2905	2904	3160	3.74	7.64	10.00	3.46 (2.30-5.20)	
No anxiety disorders								
Youths	34 485	28 386	28 340	0.14	0.61	0.91	8.34 (5.18-13.43)	<.001
Adults	146 918	120 094	116 538	0.82	0.99	1.54	2.41 (1.91-3.04)	
Psychotic disorders								
Youths	42	72	64	61.86	63.90	65.32	1.48 (0.43-5.16)	.19
Adults	1276	1243	1217	52.31	48.65	45.27	0.62 (0.42-0.91)	
No psychotic disorders								
Youths	34 690	28 765	28 737	0.13	0.64	0.99	9.75 (5.99-15.86)	<.001
Adults	148 547	121 755	118 481	0.54	0.8	1.41	3.86 (3.05-4.88)	

[a] The odds ratio (OR) is associated with the transformed survey year variable: (survey year – 1993)/16, and therefore it estimates the change in odds of a visit with antipsychotic treatment (hereafter referred to as an antipsychotic visit) over the entire 1993-2009 study period.
[b] The interaction *P* value refers to the age group × time interaction.

During 2005-2009, antidepressants and anxiolytics were more often prescribed in adult antipsychotic visits than in child and adolescent antipsychotic visits, while the reverse was true of stimulants. Mood stabilizers were prescribed in roughly one-quarter of adolescent and adult antipsychotic visits, but only about 1 in 10 child antipsychotic visits (Table 5).

Only a small proportion of child and adolescent antipsychotic visits included an FDA clinical indication (Table 5). For child antipsychotic visits without an FDA indication, the 3 most common specific mental disorder diagnoses were attention-deficit/hyperactivity disorder (17.0%), oppositional defiant disorder (11.3%), and disruptive behavior disorder not otherwise specified (10.5%). The corresponding diagnoses for adolescent antipsychotic visits were bipolar disorder not otherwise specified (14.9%), anxiety disorder not otherwise specified (12.6%), and attention-deficit/hyperactivity disorder (11.4%), and, for adults, the 3 most common diagnoses in antipsychotic visits without an FDA indication were anxiety disorder not otherwise specified (17.7%), depression not otherwise specified (10.9%), and bipolar disorder not otherwise specified (10.3%) (data not shown).

An evaluation by physician specialty revealed that, compared with visits to psychiatrists, visits to nonpsychiatrist physicians by youths and adults that included antipsychotic medications were more likely not to include a mental disorder diagnosis. As a result, antipsychotic visits to psychiatrists were far more likely than those to nonpsychiatrists to include several specific mental disorder diagnoses. For example, a significantly larger percentage of youth and adult visits to psychiatrists than nonpsychiatrists included a bipolar diagnosis. As compared with antipsychotic visits to psychiatrists, antipsychotic visits to nonpsychiatrists were also significantly less likely to be for an FDA-approved indication. Only a small minority of youth and adult antipsychotic visits to nonpsychiatrists included an FDA-approved indicated diagnosis (**Table 6**).

INDIVIDUAL ANTIPSYCHOTIC MEDICATIONS

The frequency distribution of antipsychotic medications varied across the 3 age groups (2005-2009). Among adult antipsychotic visits, the most commonly prescribed drugs were quetiapine (32.6%) followed by risperidone (16.9%), olanzapine (15.2%), and aripiprazole (13.8%). For adolescent visits, aripiprazole (29.0%), quetiapine (26.8%), risperidone (23.0%), and olanzapine (9.3%) were the 4 most common medications. Among child antipsychotic visits, the most commonly prescribed drugs were risperidone (42.1%), aripiprazole

Table 5. Demographic and Clinical Characteristics of Office-Based Physician Visits With Antipsychotic Treatment by Child, Adolescent, and Adult, 2005-2009[a]

Characteristic	Visits, %			χ^2 Statistic	*P* Value
	Children (n = 270)	Adolescents (n = 257)	Adults (n = 2676)		
Sex					
Male	76.8	60.8	37.7	20.84	<.001
Female	23.2	39.2	62.3		
Race/ethnicity					
White, non-Hispanic	68.5	80.1	77.9	3.73	.02
Other	31.5	19.9	22.1		
Source of payment					
Private insurance	38.4	52.5	43.8	2.85	.02
Public insurance	49.7	31.9	44.3		
Self-pay or other	11.9	15.6	11.8		
Mental disorder diagnosis					
Schizophrenia	6.0[b]	8.1[b]	15.8	9.03	<.001
Bipolar	12.2	28.8	20.2	6.29	.002
Depression	11.2[b]	20.9	21.6	4.54	.01
Anxiety	15.9	14.4	13.4	0.29	.75
Developmental disorders	13.1	5.0[b]	1.6	8.64	<.001
Disruptive behavior disorders	63.0	33.7	3.5	24.84	<.001
Other mental disorders	18.0	16.8	14.3	0.71	.49
Comorbidity group					
No mental disorders	12.0[b]	14.8	34.2	7.43	<.001
1 mental disorder	44.0	45.5	44.8		
≥2 mental disorders	44.0	39.7	21.0		
FDA antipsychotic indication status					
Approved indication	6.0[b]	12.9	28.4	28.34	<.001
No approved indication	94.0	87.3	71.6		
Other psychotropic medications					
Antidepressant	31.2	46.6	56.9	10.72	<.001
Mood stabilizer	9.6	26.4	24.6	12.92	<.001
Anxiolytic/hypnotics	3.4[b]	9.1[b]	38.7	26.34	<.001
Stimulant/ADHD medication	54.1	30.3	5.0	23.45	<.001
Psychotherapy provided	31.0	30.8	23.8	1.36	.26
Physician specialty of psychiatrists	67.7	71.6	50.3	8.77	<.001
Duration of visit, mean (SE), min	26.4	25.3	23.8	2.20[c]	.11

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; FDA, Food and Drug Administration.
[a] Results from the National Ambulatory Medical Care Survey data are presented as weighted percentages, except duration of visit (children, 0-3 years; adolescents, 14-20 years; and adults, ≥21 years).
[b] Estimates are based on 30 or fewer cases and therefore do not meet National Center for Health Statistics reliability standards for national estimation.
[c] *F* statistic.

(28.0%), quetiapine (19.2%), and olanzapine (4.4%). First-generation antipsychotics represented a greater proportion of adult (11.9%) than child (1.3%) or adolescent (1.8%) antipsychotic medications (data not shown).

COMMENT

Antipsychotic treatment in office-based practice has increased for children, adolescents, and adults. Compared with children and adolescents, adults make a substantially larger number of per capita office-based visits that include antipsychotic prescriptions. Increasing antipsychotic use by adults has also been reported from several other industrialized countries, although trends among youths have not been studied outside the United States.[38] When considered in the narrower context of US office-based care, antipsychotic treatment has increased more rapidly among youths than adults. By 2005-2009, antipsychotics were prescribed in roughly equal proportions of youth and adult visits to psychiatrists. Yet important differences exist in antipsychotic use across age groups. Although antipsychotic treatment of adults is concentrated among female patients and patients diagnosed with bipolar disorder, depression, or schizophrenia, antipsychotic treatment of children and adolescents predominantly involves male patients and is common among patients with disruptive behavior disorders.

Most of the youth and adult antipsychotic visits did not include a diagnosis for which the antipsychotic had FDA approval for the patient age group. The strength of evidence supporting efficacy for these "off-label" conditions varies considerably across psychiatric disorders and individual antipsychotics.[18] Almost two-thirds of child antipsychotic visits in 2005-2009 included a disruptive behavior disorder diagnosis, and there are currently no FDA-approved medications for the treatment of disruptive disorders. Across all child visits during this period, risperidone was by far the most commonly prescribed antipsychotic. Uncertainty surrounds the appropriate role of risperidone and other antipsychotic medications in the

Table 6. Clinical Characteristics of Office-Based Physician Visits With Antipsychotic Treatment of Youths and Adults by Physician Specialty, 2005-2009[a]

Characteristic	Youth Visits With Antipsychotic Medications, %			Adult Visits With Antipsychotic Medications, %		
	Visits to Psychiatrists (n = 379)	Visits to Nonpsychiatrists (n = 148)	*P* Value	Visits to Psychiatrists (n = 1540)	Visits to Nonpsychiatrists (n = 1136)	*P* Value
Mental disorder diagnosis						
Schizophrenia	8.5	3.8[b]	.17	26.0	5.6	<.001
Bipolar	26.7	7.2[b]	<.001	33.6	6.6	<.001
Depression	17.4	13.3[b]	.39	32.2	1.8	<.001
Anxiety	20.1	3.8[b]	<.001	22.1	4.5	<.001
Developmental disorders	8.5	9.9[b]	.72	1.7	1.5	.81
Disruptive behavior disorders	53.0	36.0	.03	6.4	.7	<.001
Other mental disorders	21.2	8.6[b]	.006	20.6	8.0	<.001
Comorbidity group						
No mental disorders	2.6[b]	38.5	<.001	2.4	66.4	<.001
1 mental disorder	46.3	41.3		59.7	29.7	
≥2 mental disorders	51.2	20.2		38.0	4.0	
FDA antipsychotic indication status						
Approved indication	11.3	5.5[b]	<.001	46.8	9.8	<.001
No approved indication	89.7	94.5		53.2	9.2	
Other psychotropic medications						
Antidepressant	42.0	32.4	.15	65.0	48.7	<.001
Mood stabilizer	21.0	12.0[b]	.03	30.1	19.0	<.001
Anxiolytic/hypnotics	6.8[b]	5.3[b]	.63	45.0	32.3	<.001
Stimulant/ADHD medication	39.6	46.7	.32	8.3	1.7	<.001

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; FDA, Food and Drug Administration.

[a] Results from the National Ambulatory Medical Care Survey data are presented as weighted percentages (children, 0-3 years; adolescents, 14-20 years; and adults, ≥21 years).

[b] Estimates are based on 30 or fewer cases and therefore do not meet National Center for Health Statistics reliability standards for national estimation.

management of disruptive behavior disorders. Although some have urged greater caution in the treatment of disruptive behavior disorders with antipsychotic medications given their uncertain effects on cognitive, social, and physical development,[39] others note that risperidone tends to be well tolerated and beneficial for conduct disorder and other disruptive behavior disorders, particularly when there are problematic aggressive behaviors.[40,41] Randomized clinical trials provide evidence of efficacy in the treatment of aggressive youths with subaverage intelligence,[41-43] although discontinuation related to lack of continued efficacy may be considerable over the longer term.[43]

Antipsychotic treatment in youth mood disorder visits increased especially rapidly during the study period. By 2005-2009, youth mood disorders visits, which were mostly for bipolar disorder, were more likely than their adult counterparts to include an antipsychotic medication. This pattern is consistent with pooled analyses indicating that the effect size of antipsychotics for bipolar mania, especially compared with mood stabilizers, is larger for youths than adults.[44] The trend in the prescribing of antipsychotics to youths occurred within the context of a dramatic increase in the clinical diagnoses of bipolar disorder among young people.[11,45] Concern exists, however, over the accuracy of community diagnoses of bipolar disorder in children and adolescents.[46,47]

A greater proportion of adult antipsychotic visits than child or adolescent antipsychotic visits do not include a diagnosed mental disorder. This is largely attributable to the proportionately greater role of nonpsychiatrist physicians in the treatment of adults with antipsychotics than in the treatment of young people. Nearly all of the adult antipsychotic visits without mental disorder diagnoses were provided by nonpsychiatrist physicians. Primary care physicians and other nonpsychiatrists sometimes deliberately mask their patients' mental health problems to minimize stigma, to prevent adverse legal or occupational consequences associated with seeking mental health treatment,[48] or to capture more health plan benefits than would be available by providing mental health treatment.[49] Because patient and physician identities are protected in the NAMCS, however, deliberately withholding mental disorder diagnoses from the survey data is unlikely to be widespread. The considerable degree to which antipsychotics are prescribed to adults and, to a lesser extent, young people without concomitant psychiatric diagnoses calls for further examination. It is possible that some of these patients have been treated with antipsychotic medications for an extended period of time and that, at the time of the survey visit, they were experiencing few psychiatric symptoms. Because the survey form captures only up to 3 diagnoses per visit, it may also not enumerate all mental disorder diagnoses. Alternatively, some physicians may prescribe quetiapine or other antipsychotics for insomnia,[50] agitation,[51] or other symptoms that do not rise to the threshold of a mental disorder.

Research on racial/ethnic variation in antipsychotic treatment has largely, but not exclusively,[52] focused on patients with schizophrenia[53-56] or bipolar disorder.[57,58] The present findings offer a somewhat broader perspective on trends in antipsychotic use by white and nonwhite pa-

tients. Nonwhite adults stand out from the other age-racial/ethnic groups as not experiencing a significant increase in antipsychotic treatment during the study period. This pattern is consistent with evidence that adult African Americans and Hispanics are less likely than white adults to find psychotropic medications acceptable.[59,60] The roughly parallel increase in antipsychotic use among nonwhite youths and white youths during the study period is broadly consistent with research indicating that the race/ethnicity of adults is not strongly related to their willingness to give psychiatric medications to their children.[61,62]

Several factors may account for the increase in antipsychotic treatment within office-based practice. One factor may be the availability of new antipsychotics, including olanzapine (1997), quetiapine (1997), ziprasidone hydrochloride (2001), aripiprazole (2002), and paliperidone (2006), during the study period. Food and Drug Administration approval of antipsychotics to treat bipolar disorder, schizophrenia, and irritability associated with autistic disorder in youths, as well as various FDA approvals of adult indications, may also contribute to the increase in antipsychotic treatment. Clinical trials[40] and clinical practice guidelines[63] supporting antipsychotic use for youths outside of FDA-approved indications may have encouraged antipsychotic treatment of young people. The previously mentioned increase in the community diagnosis of bipolar disorder in young people, as well as increasing diagnosis of autism spectrum disorders,[64,65] may have also played a role. Furthermore, lower rates of acute and chronic extrapyramidal adverse effects with second-generation antipsychotics compared with first-generation antipsychotics[66] may also have increased the general ease of prescribing antipsychotics to vulnerable pediatric patients, even despite generally greater weight gain and metabolic risk with the newer agents.[9,17] The proliferation of behavioral managed care[67] and the attendant limitations on psychotherapy reimbursement[68] may further shift practice toward psychopharmacological management.[69] Cultural factors may also be at work, including a lessening of the stigma associated with mental health care, which is especially pronounced among young adults,[70] and greater public acceptance of psychotropic medications.[60] Pharmaceutical marketing,[71] including the promotion of off-label use,[72] likely also contributes to community antipsychotic prescribing practices. Finally, some patients may respond but not remit to evidence-based treatments, and, as a result, physicians endeavor to achieve remission by using antipsychotics as an adjunctive treatment.[73,74]

These analyses have several important limitations. First, the NAMCS samples visits rather than patients. Because an unknown quantity of patient duplication occurs and because patients may make several visits to several physicians each year, it is not possible to derive from the survey data an estimate of the number of unique people who are treated in office-based practice with antipsychotic medications each year. However, because each physician is randomly assigned to 1 of 52 weeks in the survey year, this duplication is likely to have only a limited effect on national estimates of unduplicated visits. Second, diagnoses in the NAMCS are based on the independent judgment of the treating physician, rather than research diagnostic interviews. Some primary care physicians may rely on diagnoses made by psychiatrists or other mental health specialists. Third, information is not available concerning dosages and duration of the antipsychotic medications. Dosages of antipsychotics for youths with disruptive behavioral disorders are likely to be considerably lower than that for youths with schizophrenia and other psychotic disorders.[75] In addition, some patients with FDA-indicated disorders may receive subtherapeutic antipsychotic doses.[76] Fourth, physician nonresponse may have biased the observed pattern of antipsychotic prescribing. Fifth, sample size limitations constrain efforts to evaluate the independence of associations between patient characteristics and provision of antipsychotic treatment. Sixth, since 2009, several developments, such as the approval of new antipsychotics (including asenapine [2009], lurasidone [2010], and iloperidone [2010]), labeling revisions strengthening the metabolic risk section regarding hyperglycemia and diabetes, dyslipidemia, and weight gain, and new practice guidelines,[77] may have influenced antipsychotic prescribing patterns. Finally, the sample is restricted to office-based visits and therefore does not capture visits to community mental health centers, hospital outpatient clinics, or various other outpatient settings, nor does it capture visits to inpatient settings where mental health care is provided. In 2009, for example, there were approximately 54.8 million total antipsychotic prescriptions in the United States,[78] of which approximately 18.9 million (34.5%) were from office-based settings included in the NAMCS scope. For these reasons, the population-based results should not be interpreted as representing population-wide antipsychotic use.

In summary, over a 17-year period, antipsychotic medications became more commonly used in office-based practice. The increase, which has been broad-based, has been especially concentrated among children and adolescents, particularly among youths diagnosed with mood disorders and those treated by nonpsychiatrist physicians. A substantial majority of child antipsychotic visits are for young people diagnosed with disruptive behavior disorders. In light of known safety concerns and uncertainty over long-term risks and benefits, these trends may signal a need to re-evaluate clinical practice patterns and strengthen efforts to educate physicians, especially primary care physicians, concerning the known safety and efficacy of antipsychotic medications. At the same time, a new generation of clinical trials is needed to evaluate the safety and efficacy of antipsychotic medications in conditions for which they are commonly prescribed but for which the evidence base remains underdeveloped.

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