Treatment of Young People With Antipsychotic Medications in the United States

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Impact Importance Despite concerns about rising treatment of young people with antipsychotic medications, little is known about trends and patterns of their use in the United States.

Objective To describe antipsychotic prescription patterns among young people in the United States, focusing on age and sex.

Design, Setting, and Participants A retrospective descriptive analysis of antipsychotic prescriptions among patients aged 1 to 24 years was performed with data from calendar years 2006 (n = 765,829), 2008 (n = 858,216), and 2010 (n = 851,874), including a subset from calendar year 2009 with service claims data (n = 53,896). Data were retrieved from the IMS LifeLink LRx Longitudinal Prescription database, which includes approximately 60% of all retail pharmacies in the United States. Denominators were adjusted to generalize estimates to the US population.

Main Outcomes and Measures The percentage of young people filling 1 or more antipsychotic prescriptions during the study year by sex and age group (younger children, 1-6 years; older children, 7-12 years; adolescents, 13-18 years; and young adults, 19-24 years) was calculated. Among young people with antipsychotic use, percentages with specific clinical psychiatric diagnoses and 1 or more antipsychotic prescriptions from a psychiatrist and from a child and adolescent psychiatrist were also determined.

Results The percentages of young people using antipsychotics in 2006 and 2010, respectively, were 0.14% and 0.11% for younger children, 0.85% and 0.80% for older children, 1.10% and 1.19% for adolescents, and 0.69% and 0.84% for young adults. In 2010, males were more likely than females to use antipsychotics, especially during childhood and adolescence: 0.16% vs 0.06% for younger children, 1.20% vs 0.44% for older children, 1.42% vs 0.95% for adolescents, and 0.88% vs 0.81% for young adults. Among young people treated with antipsychotics in 2010, receiving a prescription from a psychiatrist was less common among younger children (57.9%) than among other age groups (range, 70.4%-77.9%). Approximately 29.3% of younger children treated with antipsychotics in 2010 received 1 or more antipsychotic prescriptions from a child and adolescent psychiatrist. Among young people with claims for mental disorders in 2009 who were treated with antipsychotics, the most common diagnoses were attention-deficit/hyperactivity disorder in younger children (52.5%), older children (60.1%), and adolescents (34.9%) and depression in young adults (34.5%).

Conclusions and Relevance Antipsychotic use increased from 2006 to 2010 for adolescents and young adults but not for children aged 12 years or younger. Peak antipsychotic use in adolescence, especially among boys, and clinical diagnosis patterns are consistent with management of developmentally limited impulsive and aggressive behaviors rather than psychotic symptoms.
During the past several years, antipsychotics have gained popularity as treatments for psychiatric disorders in young people. Clinical trials support the efficacy of several antipsychotics for child and adolescent bipolar mania, adolescent schizophrenia, and irritability associated with autism in adolescents and children as young as 5 (risperidone) and 6 (aripiprazole) years. Yet most office visits by children and adolescents that involve antipsychotic treatment do not include one of these clinical diagnoses. In this setting, the clinical diagnoses associated with antipsychotic treatment vary with patient age. For example, a larger percentage of child (63.0%) than adolescent (33.7%) visits with antipsychotic treatment include disruptive behavior disorder diagnoses, while the reverse is true of bipolar disorder diagnoses (child, 12.2% vs adolescent, 28.8%).

Concerns have been raised regarding the risks of antipsychotic medications to the cardiovascular and metabolic health of young people. Second-generation antipsychotics appear to pose a greater risk of weight gain and dyslipidemia to children than to adults. Within the Medicaid program, growth in the percentage of children and adolescents treated with antipsychotics who also receive other psychotropic medications has further raised concerns regarding adverse effect burden. In the general population, the extent to which young people who are treated with antipsychotics also receive other classes of psychotropic medications is not known.

Concern has particularly focused on the safety of antipsychotic treatment of young children. In preschool-aged children, a paucity of research on psychiatric diagnoses complicates patient selection, the known efficacy of antipsychotics is limited largely to irritability associated with developmental disorders, adverse metabolic and endocrine effects are pronounced, variation in drug metabolism complicates dosing, and animal studies raise concerns regarding antipsychotic safety on the developing mammalian brain. As a result, it is recommended that preschool-aged children presenting for mental health care should receive a comprehensive psychiatric assessment and a trial of a relevant psychosocial intervention before considering psychopharmacologic treatment. In this context, the frequency with which preschool-aged children receive antipsychotic prescriptions from nonpsychiatrists or do not receive a trial of psychotherapy suggests potential gaps in care.

The rate of antipsychotic treatment tends to be higher in young adults and adolescents than in children. However, sample size constraints have limited descriptions of antipsychotic treatment to broad age groups. Because disruptive behavioral disorders are recorded in a substantial proportion of youth who are treated with antipsychotics and treatment of these conditions declines in late adolescence, an overall decline in antipsychotic treatment during late adolescence would support the hypothesis that diagnoses of disruptive behavioral disorders make important contributions to antipsychotic treatment in this age group.

The national prevalence of antipsychotic use by young people is not known. In the Medicaid program and some private insurance plans, antipsychotic use increased among young people during the late 1990s and early 2000s. On a per-visit basis, office visits by youth that included antipsychotic prescriptions increased rapidly between 1993-1998 and 1999-2004 and then grew more slowly between 1999-2004 and 2005-2009. A growing awareness of increasing use and safety concerns may have tempered antipsychotic treatment of young people.

We provide, to our knowledge, the first description of patterns and trends in antipsychotic use by young people in the United States. We focus on age-related variations in antipsychotic use, the role of psychiatrists and child and adolescent psychiatrists in prescribing antipsychotics, coprescribed psychotropic medications, and clinical diagnoses.

**Methods**

**Data Sources**

From the IMS LifeLink LRx Longitudinal Prescription databases, we obtained data on filled prescriptions for all antipsychotics in 2006, 2008, and 2010, as well as the total population by sex and age covered by these databases who filled 1 or more prescriptions during the year. From the Medical Expenditure Panel Survey we derived the percentages of young people by sex and single year of age who did not fill any prescriptions in 2006, 2008, and 2010. We also received data from the IMS LifeLink LRx Longitudinal Prescription database on prescriptions for other psychotropic medications in 2008 but not in 2006 or 2010. The LRx data contain deidentified individual prescriptions from approximately 33,000 retailers. In 2010, IMS LRx data captured 63% of all retail prescriptions in the United States and were nationally representative with respect to age, sex, and insurance.

We also received the 2009 IMS Medical Claims Database, which includes more than 16 million service claims per month from more than 100,000 unique physicians across all 50 states. The 2009 database was merged with pharmacy claims from patients common to the 2009 LRx database. Approximately 5.8% of the 2009 LRx sample of young people treated with antipsychotics was included in the merged file. Because all of the data sets are deidentified, they were exempted from human subjects review by the Yale University and New York State Psychiatric Institute Institutional Review Boards.

**Statistical Analysis**

We conducted a population-level, retrospective, observational study of antipsychotic use in the United States, focusing on antipsychotic use among young people aged 1 to 24 years (eTable 1 in the Supplement). We adjusted the IMS denominators with Medical Expenditure Panel Survey data on the percentages of young people by sex and single year of age who did not fill any prescriptions in 2006, 2008, and 2010. This adjustment generalized the IMS prevalence estimates of antipsychotic use based on individuals filling 1 or more prescriptions of any medication during the year to the entire US population of young people, including those who did not fill a prescription. The age and sex composition of the IMS population that filled at least 1 prescription of any
kind closely resembled the composition of the corresponding population from the nationally representative Medical Expenditure Panel Survey.

We calculated the percentages of younger children (age, 1-6 years), older children (age, 7-12 years), adolescents (age, 13-18 years), and young adults (age, 19-24 years) who used an antipsychotic overall and by sex for each year (Table 1). Rates of any antipsychotic use in 2010 by single year of age were also plotted separately for males and females (Figure). Among young people with any antipsychotic use, we determined the percentages with 1 or more antipsychotic prescriptions from a psychiatrist and 1 or more antipsychotic prescriptions from a child and adolescent psychiatrist for each of the 4 age groups in 2006, 2008, and 2010 (Table 2). We also determined the percentage of youth in each age group among antipsychotic users who received 1 or more prescriptions for stimulants, antidepressants, mood stabilizers, and benzodiazepines during the same year (Table 3).

In the 2009 merged file, we examined the following diagnoses of patients treated with antipsychotics with 1 or more mental disorder diagnoses in any treatment setting: attention-deficit/hyperactivity disorder (ADHD), disruptive behavior disorders, bipolar disorder, schizophrenia, autism or mental retardation, anxiety, depression, adjustment-related disorders, substance use, and other mental disorder diagnoses. Frequency distributions of these mental disorders and any psychotherapy use (eTable 2 in the Supplement) were examined within the 4 age groups (Table 4).

**Results**

**Overall Use of Antipsychotic Medications**

The 2010 LRx database included 36 484 younger children, 226 914 older children, 335 737 adolescents, and 252 739 young adults with 1 or more antipsychotic prescriptions. Accounting for the scope in data coverage, these numbers correspond to approximately 58 000 younger children, 360 000 older children, 530 000 adolescents, and 400 000 young adults with 1 or more antipsychotic prescriptions nationwide.
There were approximately 270,000 antipsychotic prescriptions dispensed to younger children, 2.14 million to older children, 2.80 million to adolescents, and 1.83 million to young adults nationwide in 2010. Across the 4 age groups, almost all of the antipsychotic prescriptions (96.7%) were for second-generation medications.

### National Trends in Antipsychotic Use

Antipsychotic use among younger and older children increased between 2006 (younger children, 0.14%; older children, 0.85%) and 2008 (younger children, 0.16%; older children, 0.87%) before declining between 2008 and 2010 (younger children, 0.11%; older children, 0.80%). For adolescents and especially young adults, there was an increase in antipsychotic use between 2006 (adolescents, 1.10%; young adults, 0.69%) and 2010 (adolescents, 1.19%; young adults, 0.84%). The increase in antipsychotic use in the 2 older groups occurred for both males and females (Table 1).

### Age and Sex Patterns of Antipsychotic Use

The percentage of persons with any antipsychotic use in 2010 was determined by single year of age for males and females (Figure). The percentage of males with antipsychotic use sharply increased from ages 1 to 10 years, reached a plateau...
that continued until age 17 years, rapidly declined to age 19 years, slowly declined to a nadir at age 22 years, and gradually increased until age 24 years. For females, the increase was more gradual and reached a lower peak at age 16 years before declining and following a pattern that resembled the one for males (Figure and eFigures 1 and 2 in the Supplement).

Antipsychotic Prescriptions From Psychiatrists

Most young people treated with antipsychotics in each age group filled 1 or more antipsychotic prescriptions that were written by a psychiatrist (57.9% of young children, 71.9% of older children, 77.9% of adolescents, and 70.4% of young adults in 2010) (Table 2). However, only a minority filled 1 or more antipsychotic prescriptions from a child and adolescent psychiatrist (29.3% of young children, 39.2% of older children, 39.2% of adolescents, and 14.2% of young adults in 2010). Younger children treated with antipsychotics were proportionately the least likely of the 4 age groups to have filled 1 or more antipsychotic prescriptions from a psychiatrist. Within age groups, a similar percentage of males and females treated with antipsychotics filled 1 or more prescriptions from a psychiatrist. There was no consistent temporal trend in the percentage of young people treated with antipsychotics who filled prescriptions from psychiatrists (Table 2).

Other Classes of Psychotropic Medications:

During 2008, most young people who were treated with antipsychotic medications were also treated with other classes of psychotropic medications. Among younger and older children, stimulants were the most commonly prescribed other class of psychotropic medication (younger children, 58.7%; older children, 68.7%). For young adults, antidepressants were the most commonly co-prescribed psychotropic class at 59.1% (Table 3). Among male adolescents, stimulants were the most commonly co-prescribed class, while among female adolescents, antidepressants were the most commonly co-prescribed class.

Clinical Diagnoses and Psychotherapy Use

In the merged 2009 medical claims and LRx sample, most of the younger children (60.0%), older children (56.7%), adolescents (62.0%), and young adults (67.1%) treated with antipsychotics had no outpatient or inpatient claim that included a mental disorder diagnosis. Among antipsychotic-treated children and adolescents with mental disorder claims, the most common diagnosis was ADHD (younger children, 52.5%; older children, 60.1%; adolescents, 34.9%), while depression was the most common diagnosis among young adults (34.5%), followed by bipolar (26.6%) and anxiety disorders (22.9%). Less than one-fourth of the patients in each of the age groups had an outpatient claim for psychotherapy (younger children, 13.5%; older children, 20.4%; adolescents, 24.8%; young adults, 18.8%) (Table 4).

Discussion

In contrast with earlier reports9-9 of increasing antipsychotic treatment of US children through the early 2000s, the percentage of young people treated with antipsychotics who filled prescriptions from psychiatrists (Table 2). There was no consistent temporal trend in the percentage of young people treated with antipsychotics who filled prescriptions from a psychiatrist. There was a rise in antipsychotic use during childhood that extended into adolescence for females, followed by a plateau and a decline during the transition to early adulthood. This age profile refines earlier reports of steadily increasing rates of antipsychotic use across multiyear developmental categories of childhood to adolescence2,28 to early adulthood.29 A peak in antipsychotic use among males aged 11 to 17 years fits with treatment of conduct problems that commonly occur during adolescence.30 In the United States, the rate of arrests for simple assaults peaks at age 16 years before quickly declining.31 An important issue remains in determining the extent to which the benefits and safety demonstrated for risperidone in clinical trials of youth with severe conduct disorders and below-average intelligence32,33 generalize to other antipsychotics and the broader population of youth with conduct disorders. Much also remains to be learned about the community and clinical prevalence of explosive aggression in children and adolescents.

A decrease in conduct disorders during late adolescence has been linked to suppression of aggression and improved impulse control.34 During late adolescence and early adulthood, neurobiological systems responsible for self-regulation and control undergo a complex maturation. This maturation involves a decrease in prefrontal gray matter related to synaptic pruning, an increase in myelination within the prefrontal cortex, and a proliferation of white matter tracts between cortical and subcortical areas, especially including the prefrontal regions, amygdala, nucleus accumbens, and hippocampus.35 This normal maturation of neurobiological systems may underlie the decrease in antipsychotic treatment prevalence during late adolescence among youth who do not have enduring cognitive impairments and long-term severe behavioral disorders.

Social factors may also play a role in the age-related decrease in antipsychotic treatment in late adolescence. As young people reach the legal age of majority, which is 18 years in most states, they assume greater independence and control of their medical care and may increasingly refuse or self-discontinue use of antipsychotic medications. Because many young people also terminate their formal education during this developmental period, they may also lose a primary point of entry into physical and mental health care. An increase in the incidence of substance disorders during this period36 may further lower the perceived need for mental health care and reduce the likelihood of accessing mental health treatment.
Male children and adolescents were more likely than their female peers to be treated with antipsychotics. This sex difference is consistent with the known male predominance of ADHD and other disruptive behavior disorders during childhood and adolescence. The narrowing of sex differences in the rate of antipsychotic treatment among young adults may be related to a greater contribution of severe mood disorders to antipsychotic treatment decisions. Mood disorders tend to have a later age of onset than does ADHD and to be female predominant.

In accord with a prior analysis of US office-based medical practice, most young people treated with antipsychotics did not have evidence of a mental disorder diagnosis in the health care claims data. Some primary care physicians may withhold mental disorder diagnoses because they are not reimbursed for these codes or to reduce stigma. In other cases, antipsychotics may be used to treat insomnia, agitation, or other symptoms that do not meet criteria for a mental disorder.

High rates of coprescribing of antipsychotics with other psychotropic classes were observed across all age groups and several medication classes. Stimulants were the most commonly coprescribed psychotropic class during the preadolescent years. Age patterns of coprescribed psychotropic medications reflected corresponding clinical diagnoses. Stimulant prescriptions and ADHD diagnoses peaked among older children, while antidepressant prescriptions and depression diagnoses increased during adolescence.

Maladaptive aggression is a common feature of ADHD. It was present in nearly half of the children in the large National Institute of Mental Health Multimodal Treatment of ADHD trial. In support of antipsychotic and stimulant combinations, one recent trial of severely aggressive children with ADHD and either oppositional defiant disorder or conduct disorder found that youth who received risperidone augmentation following optimization of stimulants achieved significantly greater reductions in aggressive and disruptive behaviors than did similarly treated children who received placebo as the adjuvant. In our study, among adolescents treated with antipsychotics who had diagnosed psychiatric disorders, the most common diagnoses were ADHD (34.9%), followed by depression (24.4%) and bipolar disorder (20.5%). In the community, the prevalence of adolescents with severe impairment is 8.7% for depression, 4.3% for ADHD, and 2.6% for bipolar disorder. These proportions suggest that adolescents with severely impairing ADHD or bipolar disorder may be more likely than those with severely impairing depression to receive antipsychotic treatment.

Some adolescents and young adults treated with antipsychotics were diagnosed with mood or anxiety disorders. Building empirical support for the efficacy of antipsychotics for adolescent bipolar disorder, including US Food and Drug Administration approval of aripiprazole in 2008 for adolescent mania or mixed bipolar disorder, may have contributed to antipsychotic use trends during the study period. Although depressed adults who partially respond to antidepressants sometimes benefit from antipsychotics, it is not known whether antipsychotics confer similar benefits to treatment-resistant depression in young people. It is also not known whether anxiolytic properties of antipsychotics that have been observed in some studies of adults extend to young people with anxiety disorders.

Practice guidelines urge particular caution regarding the use of antipsychotics in young children. In preschool-age children with disruptive behavior disorders, consideration of antipsychotic medications should be limited to those who have severe, sustained, and intractable impairment in multiple settings or who pose safety risks. If antipsychotic therapy is initiated, frequent systematic reassessments should be used to minimize treatment duration. However, young children treated with antipsychotics commonly receive their prescriptions exclusively from nonspecialist physicians. Given the paucity of high-quality empirical evidence supporting the efficacy and safety of antipsychotic treatment in this age group, these treatment patterns raise potential safety concerns and underscore the importance of improving access for young children with severe mental health problems to high-quality, specialized child and adolescent mental health services.

Despite progress during the past several years in developing effective psychotherapies for disruptive behaviors, depression, and anxiety in young people, psychotherapy was provided to only a minority of young people treated with antipsychotics with claims for mental disorder diagnoses. Greater understanding is needed of the factors that impede access to psychosocial interventions for young people with significant psychological distress.

This analysis has several limitations. First, the IMS prescription data capture medicines purchased rather than consumed. Second, no data were available concerning the effectiveness or safety of the antipsychotics. Third, although the population denominator was adjusted for the percentage of the population by age and sex who reported not filling a prescription in the study year, it is not possible to estimate the precision of the derived estimates. Fourth, service claims data were available only for a subset of patients. Fifth, the diagnostic data were based on clinical assessments and were not subject to expert validation. Finally, the primary analyses were based on 2010 dispensing patterns; since that time, prescribing practices may have changed.

Conclusions

After several years of increasing rates of antipsychotic treatment of children and adolescents in the United States, the rate of antipsychotic use among children decreased between 2008 and 2010. In view of evidence of widespread antipsychotic prescribing outside of US Food and Drug Administration–labeled indications and concerns regarding the adverse metabolic effects of second-generation antipsychotics, this decline is a welcome development. Nevertheless, age and sex antipsychotic use patterns suggest that much of the antipsychotic treatment of children and younger adolescents targets age-limited behavioral problems. In older teenagers and young adults, a developmental period of high risk for the onset of psychiatric disorders, antipsychotic use increased between 2006 and
2010. Clinical policy makers have opportunities to promote improved quality and safety of antipsychotic medication use in young people through expanded use of quality measures, physi-
cian education, telephone- and Internet-based child and ado-
lescent psychiatry consultation models, and improved ac-
cess to alternative, evidence-based psychosocial treatments.

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