Prevalence of Atypical Antipsychotic Drug Use Among Commercially Insured Youths in the United States

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Background: Use of atypical antipsychotic medications in pediatric populations is increasing. Although previous studies have presented data by age or sex, none has documented sex-specific prevalence by age group.

Objective: To estimate the 1-year prevalence of atypical antipsychotic use by age and sex among commercially insured youths in the United States.

Design: Period prevalence study, January through December 2001.

Setting: Administrative claims database of a large pharmaceutical benefit manager for 6,213,824 outpatients.

Main Outcome Measures: Period prevalence of outpatient prescription claims for atypical antipsychotic drugs among commercially insured, continuously enrolled youths.

Results: The prevalence of atypical antipsychotic use was 267.1 per 100,000 subjects aged 19 years and younger (16,599/6,213,824) and was more than twice as high for male patients as for female patients, although male and female patients were nearly equally represented in the overall population. Prevalence peaked at 594.3 per 100,000 subjects among male patients aged 10 to 14 years and 291.0 per 100,000 subjects among female patients aged 15 to 19 years. Nearly one fourth (3,830/16,599) of patients with a claim for an atypical antipsychotic were aged 9 years and younger, and nearly 80% of these (3,021/3,830) were boys.

Conclusions: Although evidence regarding the safety and efficacy of atypical antipsychotics in young children is limited, nearly one fourth of patients with claims for these drugs were aged 9 years or younger, and a large majority of these were boys. Understanding the long-term effects on the developing brain of early and prolonged exposure to atypical antipsychotics is crucial given their use in pediatric populations.


Use of Psychotropic Medications by Children and Adolescents Has Received Considerable Attention in the Scientific Literature and News Media. Previous studies have documented the use of central nervous system stimulants, serotonergic reuptake inhibitors, tricyclic and other antidepressants, and antipsychotics in selected pediatric populations. Although some of these studies predate the introduction of atypical antipsychotic drugs, most that report on the use of atypical antipsychotics note that their use is increasing in pediatric populations.

Atypical antipsychotic medications currently approved by the US Food and Drug Administration for the treatment of schizophrenia include risperidone, olanzapine, quetiapine, clozapine, and ziprasidone. In adults, atypical antipsychotics are as effective as traditional antipsychotics and have a much lower risk of extrapyramidal symptoms. In children and adolescents, however, data supporting the safety and efficacy of atypical antipsychotics are limited, and none of these drugs is approved for use in pediatric populations. Preliminary evidence suggests that adverse effects (eg, weight gain, sedation, and extrapyramidal symptoms) may be both more prevalent and more severe in children and adolescents than in adults.

Using a large national database of prescription drug claims in the United States, we examined the use of atypical antipsychotics by children and adolescents.

METHODS

We accessed the outpatient prescription claims database of AdvancePCS, the largest pharmaceutical benefit manager in the United States at the time of the study. Com-
commercial health insurance carriers contract with AdvancePCS to manage their formularies and adjudicate their prescription drug claims. AdvancePCS maintains a computerized pharmacy system that records data on each drug dispensed.

Our study included commercially insured patients whose insurance carriers required AdvancePCS to track claims at the patient level, excluding patients whose plans used a single identifier for multiple family members. The analysis data set included outpatient claims adjudicated for 6,213,824 patients aged 19 years and younger who were enrolled continuously from January through December 2001 and who filed at least one claim for any prescription drug during that period. Each patient’s claims were linked using a unique identifier encrypted to ensure confidentiality. A total of 1,171 insurers were represented, covering all 50 states as well as US territories. The institutional review board of Duke University Medical Center approved this study.

We evaluated claims for 5 atypical antipsychotic drugs—clozapine, olanzapine, quetiapine, risperidone, and ziprasidone. Period prevalence was defined as the number of children and adolescents per 100,000 with at least one prescription drug claim for an atypical antipsychotic in 2001. We calculated the period prevalence for each atypical antipsychotic individually, and we stratified the analysis by sex and age to explore differences in use of the drugs. We used $\chi^2$ or Fisher exact tests to test for differences in proportions and prevalence rates. All analyses were performed in SAS version 8.0 (SAS Institute Inc, Cary, NC).

### RESULTS

Table 1 shows characteristics of the overall study population. The population included more male patients than female patients, although sex-specific age distributions were similar. The geographic distribution of the study sample was consistent with that of the general US population.

In the data set including all ages, 810,911 patients had at least one claim for an atypical antipsychotic. Of those, 16,509 (20.5%) were aged 19 years and younger. The annual prevalence of atypical antipsychotic use was 267.1 per 100,000 patients aged 19 years and younger (16,509/6,213,824). Compared with the overall study population, patients with at least one claim for an atypical antipsychotic were more likely to be male (70.7% vs 51.2%; $P < .001$) and were older (76.9% vs 51.6% of patients aged 10 to 19 years; $P < .001$).

The period prevalence of atypical antipsychotic use was more than twice as high for male patients as for female patients. Patients aged 9 years and younger had an annual prevalence of 371.0 per 100,000 patients among male patients aged 9 years and younger. Prevalence peaked at 594.3 per 100,000 patients among male patients aged 10 to 14 years and at 291.0 per 100,000 patients among female patients aged 15 to 19 years. Risperidone was the most commonly used atypical antipsychotic among both male and female patients. Use of other atypical antipsychotics was similar for males and females, although female patients were more likely to have at least one claim for quetiapine.

Several studies have documented the use of psychotropic drugs in pediatric populations. Our findings highlight the outpatient use of atypical antipsychotics by sex and age in a large, commercially insured population of children and adolescents. Atypical antipsychotics warrant special study for several reasons. First, previous studies have documented the increasing use of atypical antipsychotics in selected pediatric populations. According to one estimate, the proportion of all pediatric psychotropic drug prescriptions accounted for by atypical antipsychotics more than doubled, from 2.4% to 5.1%, between 1997 and 2000. Second, as with all psychotropic medications, atypical antipsychotics work by altering brain chemistry—specifically, by blocking postsynaptic serotonin and dopamine receptors. While this specific action may enhance efficacy and reduce the likelihood of extrapyramidal symptoms, the long-term effects on the developing brain of early and prolonged exposure to atypical antipsychotics are unknown. Third, data regarding safety and efficacy of atypical antipsychotics in pediatric populations are limited. Finally, preliminary evidence suggests that even moderate doses of risperidone and olanzapine may be associated with weight gain, sedation, and extrapyramidal adverse effects that are more prevalent and more severe than those reported in adults.

In our analysis, 3 findings are particularly striking. First, nearly one fourth of children and adolescents with a claim for an atypical antipsychotic were aged 9 years and younger. To date, 9 randomized controlled trials have evaluated the safety and efficacy of atypical antipsychotics in children aged 10 years and younger. None of these trials included more than 120 patients and, more importantly, none had a follow-up period of longer than 26 weeks. The paucity of long-term data is of par-

### Table 1. Characteristics of Commercially Insured, Continuously Enrolled Youths*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male (No. (%))</th>
<th>Female (No. (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>3,184,077 (51.2)</td>
<td>3,029,747 (48.8)*</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>722,971 (22.7)</td>
<td>683,352 (22.6)</td>
</tr>
<tr>
<td>5-9</td>
<td>826,626 (26.0)</td>
<td>784,492 (25.9)</td>
</tr>
<tr>
<td>10-14</td>
<td>842,486 (26.5)</td>
<td>802,853 (26.5)</td>
</tr>
<tr>
<td>15-19</td>
<td>791,994 (24.9)</td>
<td>759,050 (25.1)</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>572,142 (18.0)</td>
<td>549,156 (18.1)</td>
</tr>
<tr>
<td>South</td>
<td>1,153,244 (36.2)</td>
<td>1,084,187 (35.8)</td>
</tr>
<tr>
<td>Midwest</td>
<td>896,725 (27.8)</td>
<td>856,387 (28.3)</td>
</tr>
<tr>
<td>West</td>
<td>571,966 (18.0)</td>
<td>540,017 (17.8)</td>
</tr>
</tbody>
</table>

* $P < .001$ for male vs female.

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ticular concern, because treatment with psychotropic drugs in clinical settings often continues for long periods due to the chronic nature of the underlying disorders.26

Second, male patients accounted for more than 70% of patients with a claim for an atypical antipsychotic. Of those aged 9 years and younger, nearly 80% were boys. Given that schizophrenia is seldom diagnosed before adolescence,39-41 it is likely that atypical antipsychotics are being prescribed to treat behavior disorders,16,42,43 which are identified more commonly in boys than in girls.44 In a study of low-income children and adolescents in Tennessee’s managed care program for Medicaid enrollees, Cooper et al17 found a 2.5-fold increase between 1996 and 2001 in incidence of antipsychotic use for attention deficit and disruptive behavior disorders. Managed care plans that provide almost complete coverage for drug therapy and only limited reimbursement for psychiatric evaluation may create strong incentives to treat behavioral problems using pharmacologic therapy.26

Third, the 1-year prevalence estimate in this commercially insured population is markedly lower than an estimate in the Texas Medicaid population.14 In 2002, 1.6% of Texas Medicaid enrollees aged 19 years and younger had a claim for an atypical antipsychotic, as compared with 0.3% of youths in our commercially insured population. The difference may reflect the fact that the AdvancePCS data include only prescriptions filled in outpatient pharmacies. Prescriptions filled in inpatient or institutional settings—facilities that provide care for seriously impaired youths—are not included. In addition, only oral dosage forms were included in our analysis, whereas all dosage forms were included in the study of Texas Medicaid enrollees.14

Off-label use of prescription drugs in children is not uncommon.45 According to one estimate, only one third of drugs used to treat children have been studied adequately in pediatric populations.46 Clinicians are left to extrapolate medication dosages and administration schedules for pediatric patients from clinical trials conducted in adults. Given how development can affect drug metabolism, extrapolating adult dosages to children and adolescents can have adverse consequences for both efficacy and safety.47,48 Recent federal legislation49,50 provides financial incentives for pharmaceutical companies to evaluate the safety and efficacy of their medications in children and mandates the National Institutes of Health to prioritize safety and efficacy studies of off-label uses of off-patent drugs in children. The impact of the legislation is unclear. Although the number of studies of medications prescribed to children has increased,51,52 important gaps in knowledge remain, especially for the treatment of mental health conditions in young children.53,54

Assessments of the safety and efficacy of atypical antipsychotic medications are complicated by the challenges of diagnosing psychotic illness in children55-57 and by the likelihood that many patients eligible for such studies are taking other psychotropic medications.58 Our findings suggest, however, that atypical antipsychotics are being used for more common problems for which safety, efficacy, and effectiveness can and must be evaluated.

Our study has some limitations. Although claims databases are reliable and valid for studies of drug use,57,58 they record only claims filed, not whether the drugs were taken. Also, patients may have had alternative sources of insurance; out-of-plan drug use was not captured in our analysis. Furthermore, the database likely underrepresents persons with lower socioeconomic status, a group that is less likely to have private prescription drug insurance. Also, as with many claims-based studies, clinical variables were not directly available in our data set. Thus, we were unable to explore interrelationships among clinical diagnoses and atypical antipsychotic drugs. Future studies in commercially insured, community-dwelling youths should examine the clinical diagnoses associated with the use of antipsychotic medications, the risks and benefits of these medications, and the concurrent use of other psychotropic drugs.

### Table 2. One-Year Prevalence of the Use of Atypical Antipsychotics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male</th>
<th></th>
<th></th>
<th>Female</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>Annual Prevalence, per 100 000†</td>
<td></td>
<td>No. (%)</td>
<td>Annual Prevalence, per 100 000†</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>11 728 (70.7)</td>
<td>368.3</td>
<td></td>
<td>4871 (29.3)</td>
<td>160.8</td>
<td></td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>0-4</td>
<td>223 (1.9)</td>
<td>30.8</td>
<td></td>
<td>48 (1.0)</td>
<td>7.0</td>
<td></td>
</tr>
<tr>
<td>5-9</td>
<td>2798 (23.9)</td>
<td>338.5</td>
<td></td>
<td>761 (15.6)</td>
<td>97.0</td>
<td></td>
</tr>
<tr>
<td>10-14</td>
<td>5007 (42.7)</td>
<td>594.3</td>
<td></td>
<td>1853 (38.0)</td>
<td>230.8</td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>3700 (31.5)</td>
<td>467.2</td>
<td></td>
<td>2209 (49.4)</td>
<td>291.0</td>
<td></td>
</tr>
<tr>
<td>Atypical antipsychotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>58 (0.5)</td>
<td>1.8</td>
<td></td>
<td>27 (0.6)</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>3151 (26.9)</td>
<td>99.0</td>
<td></td>
<td>1369 (28.1)</td>
<td>45.2</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>1849 (15.8)</td>
<td>58.1</td>
<td></td>
<td>1257 (25.8)</td>
<td>41.5</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>8121 (69.2)</td>
<td>255.1</td>
<td></td>
<td>2980 (61.2)</td>
<td>98.4</td>
<td></td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>398 (3.4)</td>
<td>12.5</td>
<td></td>
<td>264 (5.4)</td>
<td>8.7</td>
<td></td>
</tr>
</tbody>
</table>

*P < .001 for all characteristics.
†Number of enrollees with at least 1 claim for an atypical antipsychotic drug in 2001.
In summary, our study documents the prevalence of outpatient atypical antipsychotic medication use in a large, pediatric, commercially insured population. Although evidence regarding the safety and efficacy of atypical antipsychotics in young children is limited, nearly one fourth of patients with claims for these drugs were aged 9 years or younger, and a large majority of these were boys. Understanding the long-term effects on the developing brain of early and prolonged exposure to atypical antipsychotics is crucial given their use in pediatric populations.

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REFERENCES


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