

Evidence-Based Use of Second-Generation Antipsychotics in a State Medicaid Pediatric Population, 2001–2005

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Objective: The purpose of this study was to identify children in a state Medicaid population who were newly treated with second-generation antipsychotics from 2001 through 2005, to classify each use of these agents as evidence based or not depending on the child's diagnoses, and to identify factors associated with the likelihood of evidence-based use of the medication. **Methods:** A Medicaid claims database was used to retrospectively identify enrollees receiving initial outpatient treatment with a second-generation antipsychotic between 2001 and 2005. To capture all relevant treatments and diagnoses, claims were examined from January 2000 through December 2006. The final sample included 11,700 children under age 18. The primary measure of interest was the proportion for whom use of the antipsychotic was based on evidence. Evidence-based use (categorized as strong, plausible, or weak evidence) was defined as any use of the agent for a diagnosis supported by a clinical trial published before the end of 2005. Trend analysis and logistic regression were used. **Results:** The number of children newly treated with second-generation antipsychotics increased from 1,482 in 2001 to 3,110 in 2005. Of the new users of these agents during the study period, 41.3% had no diagnosis for which such treatment was supported by a published study. The medication with the highest level of non-evidence-based use was aripiprazole (77.1%), and risperidone had the lowest (30.6%). **Conclusions:** The number of children receiving second-generation antipsychotics doubled in this Medicaid population between 2001 and 2005, and a large proportion of the treatments were not supported by evidence from clinical studies. (*Psychiatric Services* 61:123–129, 2010)

Use of antipsychotic medications in office-based clinical practice has increased significantly in adult populations since the 1990s, and numerous studies have reported evidence of increasing use of these medications among children and adolescents (1–9). The increase has been most dramatic for newer, second-generation antipsychotics compared with first-generation agents.

For adults, the U.S. Food and Drug Administration (FDA) has approved use of second-generation antipsychotics for treatment of schizophrenia, bipolar and mood disorders, and selected other conditions (10–13). The upward trend in use of second-generation antipsychotics among children and adolescents has alarmed some authorities, partly because the FDA has approved limited use of only two of these agents in pediatric populations. In October 2006 risperidone was first approved for limited pediatric use—for irritability in autistic disorder in populations aged five to 16 years. Approval was given the following year for its use in the treatment of adolescents with schizophrenia and bipolar disorders. In 2007 aripiprazole was approved for treatment of schizophrenia among adolescents, and approval was expanded to include use for children with bipolar I disorder on the basis of a four-week trial involving patients aged ten to 17 (14). As of December 2009, several other sec-

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ond-generation antipsychotic medications were approved by the FDA for short-term use in certain pediatric groups and for serious mental health conditions.

Although most use of second-generation antipsychotics in pediatric populations has not been reviewed by the FDA, there is body of clinical trial evidence about use of these medications by children. These published trials have shortcomings in terms of sample size and study duration, which underlines the necessity for further study in this area. Nevertheless, clinicians may view favorable results of such clinical trials as evidence supporting use of second-generation antipsychotics by their pediatric patients. Use of a medication to treat a patient with a diagnosis for which some clinical trial evidence exists may be considered “evidence based.” Conversely, use of a medication to treat a condition or a type of patient when there has been no effort to systematically study safety and effectiveness can be considered “not evidence based.”

The purpose of this study was to describe use of second-generation antipsychotics in a pediatric population. Specifically, the study had three objectives. First, the study identified new users under age 18 who received second-generation antipsychotics in a state Medicaid population from 2001 through 2005. Second, for each child treated, the study classified use of the agent as either evidence based or not depending on the child’s diagnoses. This approach followed a concept used in a study of anticonvulsants in the Georgia Medicaid population (15). Third, the study identified factors associated with the likelihood of receipt of drug treatment categorized as evidence based.

Methods

Medicaid data

This project was reviewed and approved by the University of Arkansas for Medical Sciences Institutional Review Board. The study involved a retrospective analysis of data from a state Medicaid administrative claims database. The database allowed examination of all medical claims and diagnoses and of all outpatient med-

ication claims. The study population consisted of children who were new users of second-generation antipsychotics. A new user was operationally defined as receiving his or her first prescription for one of these agents—the index prescription—between January 1, 2001, and December 31, 2005, with no antipsychotic use during the 12 months before the date of service associated with the index prescription. The participant was required to be under age 18 on the index date and to have been continuously eligible for Medicaid one year before and one year after the index date.

Relevant information from pharmacy, inpatient, outpatient, and nursing home claims and from enrollment records was collected from January 2000 to December 2006. Information from before the study period was used to ensure that patients were excluded if they had been treated with an antipsychotic in the year before the index date. Because a time lag may occur between initial treatment and establishment of a definitive psychiatric diagnosis, medical claims data were obtained for the 12 months after the study to ensure the maximum likelihood of capturing all relevant diagnoses for children who started treatment late in the study period.

All prescription claims indicating that clozapine, olanzapine, risperidone, quetiapine, ziprasidone, or aripiprazole was dispensed for a child were extracted from the pharmacy claims database on the basis of specific generic codes for the medications. Outpatient and inpatient medical claims for 365 days before and after the index prescription date were obtained. All diagnosis codes from a participant’s medical claims were documented. By use of a scheme similar to those found in other studies (16–20), participants were classified on the basis of their diagnoses into different disease groups for which antipsychotics may be used. We used a list of *ICD-9-CM* codes for identifying different disease groups in the sample. The codes were first identified from the literature and then validated by using the sixth edition of *ICD-9-CM*.

Levels of evidence for antipsychotic use

During the study period, none of the second-generation antipsychotics had been reviewed and approved by the FDA to treat children with any condition, and thus all use was considered off label. Off-label use—that is, use for conditions other than the approved indications—is not prohibited. It may be supported by a robust data set of clinical trial information or may have no support in peer-reviewed literature or clinical practice experience. Therefore, characterizing a particular use of a medication as off label is not especially informative. Although the appropriateness of various off-label uses may be debated, there is a line of thinking that justifies such use when it is based on rational scientific theory or evidence from controlled clinical trials (21). Thus it has been suggested that compared with off-label use for which no scientific data are available, off-label use for which evidence exists is justifiable to some extent.

We used the approach of assigning hierarchical levels of evidence on the basis of research design. This approach is based on guidelines developed by the Agency for Healthcare Research and Quality (AHRQ) and by two of the AHRQ Evidence-based Practice Centers (1,22). Use of a specific second-generation antipsychotic for a particular condition was classified as “strong evidence-based use” if it was supported for that condition by at least one published randomized clinical trial with a sample size of more than 30 individuals in a population under 18 years of age. Use was classified as “plausible evidence-based use” if it was supported for the specific condition by at least one published nonrandomized trial with a comparison group and a sample size of more than 30 individuals in a population under 18 years of age. Finally, use was classified as “weak evidence-based use” if use for the condition was based on published reports of studies involving individuals less than 18 years of age, including open-label studies, retrospective studies with a sample size of less than 30, or nonrandomized trials with a sample size of more than 30 but without a com-

parison group. Any other specific use of a medication that did not fall into one of these categories was classified as “non-evidence-based use.”

A MEDLINE literature search identified clinical trials of second-generation antipsychotics in pediatric populations. All trials published before December 31, 2005, were considered. However, the date of publication was not considered in assigning the medication uses to the evidence categories, which allowed assignment in the most liberal fashion as well as consistent assignment of specific medication uses for the entire period of analysis. This approach acknowledges that certain findings may be disseminated among clinicians before studies are published. Studies were not considered if any of the participants were aged 18 years or older, if the study had three or fewer total participants, and if the results were not favorable for the antipsychotic.

The MEDLINE search identified 86 unique clinical studies. Most were open-label studies involving risperidone. All identified studies were reviewed to compile a comprehensive list of medications and uses (*ICD-9-CM* diagnosis codes) along with the level of evidence to support each use (strong, plausible, or weak evidence).

Because patient charts were not examined, it was difficult to establish a direct link between a specific diagnosis and the decision to initiate treatment with a second-generation antipsychotic. Thus we elected an approach that increased the likelihood of including a diagnosis for which use of a second-generation antipsychotic would be classified as evidence based. As noted, all diagnosis codes assigned to a study participant in the year before and after the study period were available. If a recipient was assigned at least one diagnosis that was associated with some level of evidence support, the medication use for that recipient was considered evidence based. Use of a medication was assigned to the no-evidence category when there was no published support for use of the medication with any of the diagnoses assigned to a patient during the observation period.

A sensitivity analysis was conducted that included diagnoses given to the

children only in the six months before and after their prescription index date. A second sensitivity analysis included 24 additional studies identified in the MEDLINE search that were published after the cutoff date of December 31, 2005; these included nine for risperidone and six for quetiapine.

Data analysis

To determine the trend of new users of second-generation antipsychotics in the state Medicaid population under age 18 from 2001 through 2005, we calculated the number of new users in each year. Trend graphs and ordinary least-squares regression were used to determine whether the trend was significant. For each second-generation antipsychotic, the number and percentage of new users in each disease category were determined over the five-year study period.

We used a logistic regression model to determine which groups were more or less likely to have an evidence-based use of a second-generation antipsychotic. This model used age as a continuous independent variable; categorical independent variables were gender, race, geographic location, metropolitan county status, receipt of psychotherapy, psychiatric hospitalization, and long-term care. For the model, evidence-based use was defined as meeting the standard for strong evidence-based use, and plausible and weak evidence-based use were considered to be non-evidence-based use. The significance level was set at .05. Log of odds (logit) as a linear function of the independent variables was employed, and the maximum likelihood estimation procedure was used to obtain the parameter estimates. SAS, version 9.1, was used for all data manipulations and statistical analyses.

Results

Of the 52,521 Medicaid-covered children with at least one prescription claim for a second-generation antipsychotic from 2001 to 2005, a total of 11,700 met the inclusion criteria. Table 1 presents data on demographic characteristics of the sample. Compared with the Arkansas Medicaid pediatric population, the sample was

much older and had a larger proportion of females.

Table 2 shows the number of children who initiated therapy over five years with each of the second-generation antipsychotics. The denominator used to calculate the percentages was the number of children continuously enrolled in Medicaid each year, which was fairly constant across the five years. None of the children received initial treatment with clozapine. For most children, therapy was initiated with risperidone (51.2%). The agent least used for initial treatment was ziprasidone (2.5%). Of interest, .5% of the sample received more than one second-generation antipsychotic prescription on their index date. Results of the regression analysis indicated that, on average, 431 children each year initiated treatment with a second-generation antipsychotic ($p < .001$).

The disease categories to which diagnoses obtained from the children's medical claims were assigned are

Table 1

Characteristics of 11,700 Medicaid recipients under age 18 who became new users of second-generation antipsychotics between 2001 and 2005

Characteristic	N	%
Age		
0–3	276	2.4
4–5	1,104	9.4
6–9	3,020	25.8
10–13	3,684	31.5
14–18	3,616	30.9
Gender		
Male	3,980	34.0
Female	7,720	66.0
Race ^a		
White	7,127	60.9
Black	3,226	27.6
Other	1,347	11.5
Mean number of claims ^b		
Outpatient	40.2	
Inpatient	1.0	
Long-term care	.4	
Second-generation antipsychotic prescription	9.9	
Recipients with at least one claim in two years		
Outpatient	11,695	99.9
Inpatient	5,152	44.0
Long-term care	50	.4

^a As reported in the Medicaid eligibility file

^b Mean number of claims per recipient over a two-year period (SDs not available)

Table 2

New users of second-generation antipsychotics among 11,700 Medicaid recipients under age 18 who became new users between 2001 and 2005

Year	Aripiprazole (N=2,108)		Olanzapine (N=1,147)		Quetiapine (N=2,097)		Risperidone (N=5,989)		Ziprasidone (N=297)		Multiple agents (N=62)		Total (N=11,700)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
2001	0	—	247	21.5	87	4.1	1,083	18.1	56	18.9	9	14.5	1,482	12.7
2002	1	<.1	293	25.5	219	10.4	1,264	21.1	56	18.9	4	6.5	1,837	15.7
2003	261	12.4	273	23.8	438	20.9	1,339	22.4	63	21.2	8	12.9	2,382	20.4
2004	884	41.9	181	15.8	597	28.5	1,161	19.4	48	16.2	18	29.0	2,889	24.7
2005	962	45.6	153	13.3	756	36.1	1,142	19.1	74	24.9	23	37.1	3,110	26.6

shown in Table 3, along with the *ICD-9-CM* codes that define the categories. It should be noted that a child with two or more diagnoses could be counted in more than one category. The most common condition identified was attention-deficit

hyperactivity disorder, followed by depression, conduct disorder, oppositional defiant disorder, and adjustment reactions.

At the time of the study there were four conditions for which treatment with risperidone was well supported

on the basis of the reports published before December 31, 2005: conduct disorder, developmental disorders, pervasive developmental disorders, and psychoses. Plausible evidence for risperidone use was found for the treatment of mania and bipolar dis-

Table 3

Assignment of 11,700 Medicaid recipients under age 18 to disease categories on the basis of diagnoses in 2000–2006 medical claims, by initial prescription for a second-generation antipsychotic^a

Category (<i>ICD-9-CM</i> code)	Aripiprazole		Olanzapine		Quetiapine		Risperidone		Ziprasidone		Multiple agents		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Adjustment reactions (309)	577	4.9	305	2.6	635	5.4	1,574	13.5	105	.9	19	.2	3,215	27.5
Anxiety (300.0, 300.2, 313.0)	252	2.2	128	1.1	300	2.6	635	5.4	41	.4	7	.1	1,363	11.6
Attention-deficit hyperactivity disorder (314)	1,256	10.7	681	5.8	1,142	9.8	3,940	33.7	125	1.1	31	.3	7,175	61.3
Conduct disorder (312, 314.2)	963	8.2	477	4.1	851	7.3	2,626	22.4	114	1.0	25	.2	5,056	43.2
Depression (296.2, 296.3, 300.4, 300.5, 311)	1,017	8.7	613	5.2	1,166	10.0	2,231	19.1	215	1.8	32	.3	5,274	45.1
Developmental disorders (314.1, 315, 317–319)	468	4.0	255	2.2	425	3.6	1,888	16.1	70	.6	12	.1	3,118	26.6
Eating disorders (307.1, 307.5, 783.0)	41	.4	19	.2	33	.3	55	.5	10	.1	1	<.1	159	1.4
Epilepsy (345)	52	.4	38	.3	63	.5	266	2.3	13	.1	3	<.1	435	3.7
Mania and bipolar disorders (296.0–296.1, 296.4–296.8)	415	3.5	220	1.9	452	3.9	600	5.1	83	.7	23	.2	1,793	15.3
Obsessive-compulsive disorder (300.3)	35	.3	22	.2	39	.3	120	1.0	2	<.1	0	—	218	1.9
Oppositional defiant disorder (313.81)	818	7.0	442	3.8	710	6.1	2,117	18.1	122	1.0	19	.2	4,228	36.1
Personality disorders (301)	53	.5	28	.2	47	.4	91	.8	14	.1	3	<.1	236	2.0
Pervasive developmental disorders (299)	75	.6	43	.4	81	.7	498	4.3	12	.1	3	<.1	712	6.1
Posttraumatic stress disorder (308)	10	.1	13	.1	19	.2	43	.4	3	<.1	1	<.1	89	.8
Psychoses (295, 297, 298)	267	2.3	124	1.1	174	1.5	505	4.3	52	.4	15	.1	1,137	9.7
Tic disorder (307.2)	19	.2	10	.1	10	.1	67	.6	4	<.1	1	<.1	111	.9
Substance abuse (291, 292, 303–305)	192	1.6	92	.8	215	1.8	240	2.1	52	.4	5	<.1	796	6.8
Other (290.00–319.99 and not elsewhere classified)	822	7.0	382	3.3	707	6.0	1,737	14.8	115	1.0	26	.2	3,789	32.4

^a A child could be assigned to multiple categories depending on the number of diagnoses.

Table 4

Evidence for use of second-generation antipsychotics to treat disorders among 11,700 Medicaid recipients under age 18 who became new users of these agents between 2001 and 2005

Level of evidence ^a	Aripiprazole (N=2,108)		Olanzapine (N=1,147)		Quetiapine (N=2,097)		Risperidone (N=5,989)		Ziprasidone (N=297)		Multiple agents (N=62)		Total (N=11,700)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Strong	0	—	124	10.8	452	21.6	3,842	64.2	0	—	0	—	4,418	37.8
Plausible	0	—	186	16.2	0	—	213	3.6	0	—	0	—	399	3.4
Weak	482	22.9	334	29.1	962	45.9	102	1.7	169	56.9	0	—	2,049	17.5
None	1,626	77.1	503	43.9	683	32.6	1,832	30.6	128	43.1	62	100.0	4,834	41.3

^a Evidence categories are based on studies published through 2005.

orders. Weak evidence supported use of risperidone for three disease categories—epilepsy, obsessive-compulsive disorder, and tic disorder. For olanzapine, strong evidence was found for use in treating psychoses and plausible evidence was found for mania and bipolar disorders. For quetiapine, strong evidence was found for use in treating mania and bipolar disorders. No strong or plausible evidence was found for use of aripiprazole and ziprasidone to treat any condition.

Table 4 shows the proportion of use of the five medications in each of the evidence categories. Among users of risperidone, 64.1% of use was in the category of strong evidence-based use—the largest percentage for any of the five medications. Among users of aripiprazole, 77.1% of use was not supported by any published evidence.

Almost half of the children in the sample (41.3%) appeared to have received a second-generation antipsychotic without having a diagnosis associated with any supporting evidence (Table 4). On the basis of this finding, we further investigated the diagnoses of these 4,834 participants. Over half of them (N=2,790, 58%) had a diagnosis of hyperkinetic syndrome of childhood with hyperactivity. Other frequently observed diagnoses among these 4,834 children were oppositional defiant disorder (N=1,617, 34%), depressive disorder (N=1,354, 28%), hyperkinetic syndrome of childhood without mention of hyperactivity (N=955, 20%), and unspecified disturbance of conduct (N=692, 14%).

Table 5 presents the results of the

logistic regression model that focused on factors associated with strong evidence-based uses of the medications. All the variables used in the model were significantly associated with strong evidence. Participants who had received psychotherapy were nearly twice as likely as those who had not to have an index prescription that was evidence based (odds ratio [OR]=1.92). Having a previous psychiatric hospitalization significantly increased the odds of receipt of an evidence-based prescription (OR=1.92).

We conducted a sensitivity analysis that included diagnoses given to children in only the six months before and after their index prescription date. In this analysis the percentage of children given prescriptions that were not based on any evidence increased from 41.3% to 55.1%. Another

sensitivity analysis included evidence from clinical studies that were published after the cutoff date of December 31, 2005. In this analysis the overall percentage of uses supported by weak evidence increased from 17.5% to 33.5%; the proportion of strong evidence-based use was not affected.

Discussion

These results add to the evidence that treatment of children with second-generation antipsychotic medications increased dramatically in the early years of this new century. Although prevalence is not a focus of this report, the number of children who received an initial prescription for a second-generation antipsychotic doubled between 2001 and 2005 in the Medicaid population that we examined. Because Medicaid enrollment

Table 5

Logistic regression model of predictors of evidence-based use of second-generation antipsychotics in a state Medicaid pediatric population

Variable	OR	95% CI	p
Age	.88	.87–.89	<.001
Female (reference: male)	.75	.69–.81	<.001
Race (reference: other)			
White	.62	.55–.70	<.001
Black	.76	.66–.87	<.001
Location of county in state (reference: Northwest)			
Northeast	1.18	1.04–1.34	.01
Central	.94	.83–1.07	.385
Southwest	.77	.67–.89	<.001
Southeast	.86	.74–.99	.035
Metropolitan county (reference: nonmetropolitan county)	1.18	1.07–1.29	.001
Received psychotherapy (reference: did not receive)	1.92	1.77–2.09	<.001
Long-term care claim (reference: none)	1.84	1.17–2.90	.009
Psychiatric hospitalization claim (reference: none)	1.92	1.77–2.09	<.001

grew more slowly than the number of patients initiating such treatment, we conclude that use of these medications in this population is increasing. Further studies are needed to determine whether this trend is evident in other pediatric populations, especially among children not enrolled in Medicaid.

It was not surprising that for every year examined most new users of second-generation antipsychotics were given an initial prescription for risperidone. Risperidone had been commercially available for several years before the study period. In addition, of the five second-generation medications examined, at the time of the study risperidone was supported by the largest base of evidence for use among children and adolescents. Risperidone accounted for the highest number of new users each year, and the proportion of new users who were prescribed risperidone as an initial treatment was consistent throughout the study period.

The growth in aripiprazole use is of particular interest. We identified five studies of its use in pediatric populations, and all of them offered only weak evidence; thus it is not surprising that our results revealed that 77% of its use was not evidence based. Nevertheless, the number of new pediatric users of aripiprazole, which was introduced in 2002, increased dramatically over the study period. New users increased by 338% between 2003 and 2004 and by 368% between 2003 and 2005. It is notable that in 2005 the proportion of children who received aripiprazole as an initial therapy (8.2%) was almost equal to the proportion who received initial therapy with risperidone (9.8%).

It is apparent that the increased acceptance of second-generation antipsychotics in the treatment of children during the study period was independent of a comparably robust expansion of the medical literature supporting their use. There continue to be only a limited number of specific conditions among children for which use of second-generation antipsychotics is supported by any evidence. The conditions for which there is current FDA approval for

pediatric use—for aggressive or self-injurious behavior among autistic children, for schizophrenia, and for bipolar I disorder—are rare for children. In our sample of children treated with second-generation antipsychotics between 2001 and 2005, these conditions were apparently present in only a small minority. Nevertheless, clinicians seem to be finding an increasing role for these agents in clinical settings.

Little information has been published about the clinical indications for which clinicians prescribe second-generation antipsychotics for children. This study identified diagnoses given to children who received these agents. In addition, we attempted to determine the proportion of use of these medications that could be described as evidence based. Our literature review of articles published through March 2007 identified 110 clinical studies of second-generation antipsychotic use in pediatric populations. Only 19 of the 110 studies were randomized placebo-controlled clinical trials, of which 12 studied risperidone. On the basis of our criteria, only ten clinical studies provided strong evidence for use of a second-generation antipsychotic in a pediatric population and four provided plausible evidence. This finding emphatically underlines the scarcity of well-designed, high-quality clinical studies to inform clinicians about the safety and effectiveness of these medications for conditions affecting children.

On the one hand, despite the relatively thin base of evidence, we found that 38% of the children in the sample had a diagnosis for which use of a second-generation antipsychotic was supported by strong evidence. Most was attributable to use of risperidone to treat children with diagnoses of conduct disorder and oppositional defiant disorder. However, use of other agents to treat children in this sample lacked substantial evidence.

On the other hand, 62% of children who started treatment with a second-generation antipsychotic during the study period did not have a diagnosis for which such treatment was supported by strong evidence. Examination of the diagnoses given to children

in this sample reveals important information about the clinical applications of these medications. Clearly, behavioral problems, including oppositional and conduct disorders and hyperkinetic-hyperactivity symptoms, were frequently seen among the children treated with second-generation antipsychotics. If the primary off-label uses for these medications are for children with behavioral problems, there is an obvious and urgent need to compare the safety and effectiveness of these agents and of other treatment approaches that are effective in modifying children's behaviors.

Other conditions that appear to be frequently diagnosed among children receiving second-generation antipsychotics include depression and adjustment disorder. It is not clear in our sample whether these conditions were primary diagnoses or comorbid conditions. In addition, because of the design of this analysis, these diagnoses may have been given after initiation of treatment with second-generation antipsychotics. Therefore, the possibility that treatment of maladaptive behaviors with second-generation antipsychotics may lead to high rates of depression cannot be discounted and should prompt urgent assessment.

As with all studies, a number of limitations bear consideration. A significant limitation is that the design could not establish a link between initiation of second-generation antipsychotic treatment and a specific triggering diagnosis. Administrative claims data can help to establish a temporal relationship between the start of a treatment and a new or changed diagnosis, but this relationship may or may not reflect the clinical reasons for a change in therapy. Obviously, this analysis was dependent on the diagnosis data that were recorded, and we did not have access to the working diagnoses that a clinician might have been considering with a trial of a medication. The validity of diagnoses is also a concern, particularly because—for younger children especially—certain psychiatric conditions may be difficult if not impossible to establish. Another concern is that we may have overestimated the number of evidence-

based users because we grouped specific diagnoses into broad disease categories and classified evidence-based used on the basis of the broad categories.

Clearly, further research is needed to understand prescribing of second-generation antipsychotics in pediatric populations. The questions to answer are numerous, and the answers should be informed by an awareness, which is highlighted in this report, that much of the use of these medications is unrelated to the current FDA-approved indications. Further, pediatric use of second-generation antipsychotics may be only marginally related to the specific conditions that have previously been studied. Important considerations include specific sequelae of such treatment in terms of patients' mental and social well-being as well as their overall physical health. Certainly, the most useful studies would compare these powerful new agents with other medications that have established uses and with behavioral and psychosocial interventions.

Conclusions

The results of this study indicate that use of second-generation antipsychotics in the treatment of children and adolescents increased considerably from 2001 to 2005 in a state Medicaid population. Much of the growth was attributable to rapid adoption of aripiprazole as an initial treatment, despite a paucity of evidence from clinical trials supporting use among children at the time of the study. Fewer than half of the children initiating treatment were given a diagnosis—either before or after treatment initiation—for which strong clinical evidence supported use of the second-generation agent. Children who were treated with psychotherapy and those who had been admitted to psychiatric hospitals before the index date of their initial treatment with a second-generation

medication were more likely to have a diagnosis for which medication use was supported by strong clinical evidence. Further research is needed to understand the prescribing of second-generation antipsychotics in the pediatric population.

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