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Use of Antipsychotic Medications in Pediatric Populations: What do the Data Say?

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Abstract Recent reports of antipsychotic medication use in pediatric populations describe large increases in rates of use. Much interest in the increasing use has focused on potentially inappropriate prescribing for non-Food and Drug Administration-approved uses and use amongst youth with no mental health diagnosis. Different studies of antipsychotic use have used different time periods, geographic and insurance populations of youth, and aggregations of diagnoses. We review recent estimates of use and comment on the similarities and dissimilarities in rates of use. We also report new data obtained on 11 health maintenance organizations that are members of the Mental Health Research Network in order to update and extend the knowledge base on use by diagnostic indication. Results indicate that most use in

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pediatric populations is for disruptive behaviors and not psychotic disorders. Differences in estimates are likely a function of differences in methodology; however, there is remarkable consistency in estimates of use by diagnosis.

Keywords Antipsychotics · Children · Adolescents · Medicaid · Mental Health Research Network · Off-label · MarketScan · IMS Health · NAMCS · NDTI · NCS-A

Introduction

Prescriptions for antipsychotic medications among children are reported to have increased greatly in recent years [1, 2•]. Most antipsychotic medications prescribed to children are "second-generation" or "atypical" antipsychotic medications. These medications are argued to have milder side effect profiles (e.g., reduced extrapyramidal symptoms) than "first-generation" or "typical" antipsychotic medications. However, the side effects of second-generation antipsychotics (SGAs) can still be severe [3•, 4•]. The side effect profiles of individual medications in the same class differ significantly and their impact on the individual patients who take them are also known to differ [5•, 6, 7•]. Of the 10 SGAs approved by the Food and Drug Administration (FDA) for adults in the USA, four of these (risperidone, olanzapine, quetiapine, and aripiprazole) are approved as treatments for pediatric bipolar disorder (10–17-year-olds) and schizophrenia (13–17-year-olds). Only risperidone and aripiprazole are approved for the treatment of irritability in children with autism spectrum disorders (ASD); risperidone is approved for ASD patients aged 5–16 years and aripiprazole for those aged 6–17 years.

Much scholarly research has focused on potentially inappropriate prescribing for non-FDA-approved uses. For example, these medications have been prescribed for children, who exhibit disruptive behaviors and aggression [8, 9•], but who do not have any of the diagnoses for which the FDA has approved their use. Most antipsychotic medication use among children and adolescents is "off label", that is, for indications that are not approved by the FDA or used for children who are younger than the approved age ranges [10–12, 13•]. Such uses include (but are not limited to) sleep disorders, attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, conduct disorder, major depressive disorder, and post-traumatic stress disorder. SGAs are also prescribed to individuals with developmental delay to treat aggression and self-injurious behaviors [14–17]. Lack of FDA approval stems, in part, from the ethics of protecting vulnerable populations from clinical trial research during drug development. The risk of harm to children and adolescents, particularly in the developmental phase of new medications, deters drug developers from including pediatric populations in research. Also, drug developers have limited financial incentives to conduct safety and efficacy trials of antipsychotic medications among children because clinicians are prescribing the medications in the absence of pediatric-specific evidence. Pediatric randomized controlled trials usually lag availability by years, if they are conducted at all. By the time the results of such trials are known, clinical practice has become entrenched and the impact of the research on prescribing patterns is minimal—even when the newest and most expensive medications are found to be no more effective and no safer than older, cheaper medications.

Considering the increasing overall prevalence of off-label SGA use in children and adolescents, the goal of this study was to review recent research concerning use in this population by diagnostic category and to compare and contrast this use by indication across different population estimates. We were particularly interested in comparing estimates of use for approved and non-approved uses, and use among children and adolescents with no apparent mental health diagnosis. We also present new estimates of SGA use in a population of managed care enrollees across 11 sites in the Mental Health Research Network (MHRN).

Methods

We conducted a review of recently published studies regarding the prevalence of SGA use in pediatric populations. We searched Medline using the keywords "antipsychotic" and ("pediatric" or "children" or "adolescent"). We also searched on the generic name of each SGA approved by the FDA and "pediatric", "children", or "adolescent". The publication date was limited to be between January 2010 and August 2013. Our search yielded six studies reporting prevalence of use of antipsychotic medications by diagnostic category in children and adolescents. We provide a critical review of the methods and populations of patients included in these articles.

We also conducted a descriptive analysis of SGA utilization in 11 managed care organizations that are members of the MHRN—a subset of organizations that are members of the Health Maintenance Organization (HMO) Research Network and funded by the National Institute of Mental Health. We compared the rates of diagnoses within groups of patients using classes of psychotropic medications. These data offer new insights into rates of off-label use by diagnosis, including use among children and adolescents with no apparent diagnosis.

Population

The new data reported here are derived from the pharmacy claims data across the MHRN. These data are harmonized using a common data model so as to be in the same format at each site. The harmonized data are known as the Virtual Data Warehouse.

The MHRN rates reported are mental health diagnoses for all children aged less than 18 years as of 31 December 2011 who filled at least one prescription for a SGA medication in 2011. Individuals were required to have at least 10 months of continuous enrollment in a health plan that included prescription drug coverage at one of the MHRN sites. A single *International Classification of Diseases, 9th Revision, Clinical Modification* diagnosis code for any mental health condition (290–319) was counted as evidence of a diagnosis. All diagnosis codes in 2011 were counted. Individuals could have had more than one diagnosis and the corresponding rates of diagnoses among children and adolescents using SGAs sum to more than 100 %.

The total population of individuals meeting the enrollment criteria includes 258,597 individuals aged 0–5 years, 294,722 aged 6–11 years, and 331,388 aged 12–17 years. To provide a comparison to adult rates of diagnoses among SGA users, we also report on 3,767,365 individuals older than 18 years.

Review of Data on Antipsychotic Utilization in Pediatric Populations

Previous estimates of antipsychotic medication use rates generally fall into three categories—those based on Medicaid administrative claims, those based on commercial administrative claims data (e.g., Truven Health Analytics, Marketscan), and those based on nationally representative surveys of patients and clinicians. Each of these data sources has strengths and limitations.

Medicaid-based Estimates

A 2009 study by Crystal et al. [18•] estimated rates of antipsychotic medication use with Medicaid Analytic Extract Data (MAX) for seven states (California, Florida, Georgia, Illinois, New York, Ohio, and Texas) in 2004. The study included continuously enrolled children and adolescents aged 6–17 years. Use was defined as the occurrence of at least one prescription claim for an antipsychotic medication and reported among those aged 6–12 and 13–17 years. Mental health diagnoses were obtained from in- and outpatient MAX files. All claims for an individual in the MAX data can be linked by a unique Medicaid Statistical Information System identification number.

The overall rate of use in this sample of young people was 4.2 % (n=88,096). Of those using antipsychotic medication, about 3.3 % had a diagnosis of schizophrenia and 18.7 % had a diagnosis of bipolar disorder. Other notable prevalent diagnoses included ADHD (29.1 %), conduct disorder or disruptive behavior disorder without ADHD (8.9 %), anxiety or depression (9.1 %), and autism (4.9 %). Roughly 9.1 % had no mental health diagnosis.

The 2011 study by dos Reis et al. [19•] reported on antipsychotic use among children in foster care and insured by Medicaid in a mid-Atlantic state. The data in this study were from 2003 and identified 16,969 individuals aged < 20 years who were continuously enrolled, had a mental health diagnosis, and had at least one prescription claim for an antipsychotic. Unlike the study by Crystal et al. [18•], dos Reis et al. required two clinical encounters with a mental health diagnosis in order for the diagnosis to be considered valid. Also, the study by dos Reis et al. [19•] excluded cases where a prescription occurred but no mental health diagnosis was found.

The overall use of antipsychotics in this foster care population was 2.7 %. Only 5 % of youth using antipsychotics had a diagnosis of schizophrenia and 21 % had a diagnosis of bipolar disorder. Over 53 % of antipsychotic users had a diagnosis of ADHD, 33.8 % had a diagnosis of depression, 26.3 % had a diagnosis of conduct disorder, 26.8 % had a diagnosis of oppositional defiant disorder, and 5.4 % had a diagnosis of ASD.

Finally, a 2012 study by Matone et al. [20••] reported rates of antipsychotic medication use with MAX data from 50 states for 2002–2007. This comprehensive study included 15.2 million children aged 3–18 years with at least 10 months of continuous eligibility in each year. Young people were divided into three age categories (3–5, 6–11, and 12–18 years) and 10 diagnostic categories. Like other studies, a single diagnosis code was considered valid evidence of a mental health condition.

Of the 3.55 million children aged 3–5 years, the overall rate of SGA use was 0.4 % in 2007. The corresponding rates were 2.1 % in those aged 6–11 years (n=5.83 million) and 3.7 % in adolescents 12–18 (n=5.78 million). Detailed rates were also reported by age and diagnostic category. Among children aged 3–5 years in 2007 using SGAs, 0.93 % had a diagnosis of bipolar disorder alone (no comorbid mental health diagnoses), and none were diagnosed with schizophrenia. Across other diagnoses, 13.8 % had a diagnosis of ADHD alone, 5.5 % had a diagnosis of conduct disorder alone, and 4 % had a diagnosis of autism alone. Over 25 % had three or more comorbid mental health diagnoses, and 11.3 % had no mental health diagnoses.

In young people aged 6–11 years using antipsychotics, a diagnosis of schizophrenia appeared in 0.05 % of cases and bipolar disorder in 1.8 % of cases. A similar pattern of diagnoses was reported in those aged 6–11 years for other diagnoses with 19.6 % of young people in this category having a diagnosis of ADHD, 3.7 % having a conduct disorder, and 2.2 % having a diagnosis of autism. About 8.6 % had a diagnosis of ADHD and conduct disorder together. Over 26 % had three or more comorbid mental health conditions, and 10.1 % had no mental health diagnosis.

The distribution of diagnoses in those aged 12–18 years was similar to that for those aged 6–11 years, with 0.4 % of

users having a diagnosis of schizophrenia and 4 % having a diagnosis of bipolar disorder. Other select diagnoses included ADHD (10.5 %), conduct disorder (4.4 %), and autism (1.5 %). Over 29.4 % had three or more comorbid diagnoses, and 13 % had no mental health diagnoses. Table 1 provides estimates of antipsychotic medication use.

Strengths and Limitations of the Medicaid-based Estimates

One strength of the Medicaid-based rates is the large sample size used to generate estimates, which results in high precision. The multi-state studies are also important because a large number of children are insured by Medicaid in the USA, and these studies therefore have important policy implications for Medicaid budgets. Estimating rates for economically disadvantaged children and those at increased risk of mental health problems (e.g., children in foster care) is also important in order to evaluate potentially inappropriate use (e.g., use of antipsychotics rather than psychotherapy).

There are several limitations to the Medicaid-based rate estimates. First, it is not possible to determine the validity of the diagnoses (e.g., through chart review or structured clinical interview) for such a large population of young people. Diagnoses from primary care clinicians and mental health specialists likely have different positive predictive values. MAX data are often missing the rendering provider number and, even when present, it is necessary to contact states individually to obtain data on providers. In addition, access to mental health specialists has been a significant concern for children covered by Medicaid [21–24], making the likeliness of diagnosis by a provider that is not a mental health specialist more likely.

It is also not possible to determine the exact mental health disorder for which the antipsychotic medication was prescribed. In cases where there are multiple psychiatric diagnoses (e.g., bipolar disorder and ADHD) it is impossible to determine whether the prescription might be inappropriate. Further, none of the studies reported on the quantity of medication dispensed, so it is not possible, for example, to distinguish ongoing use of the medications from short-term acute use in the reported results. Ongoing use is more likely to be associated with the emergence of negative side effects (e.g., weight gain).

It is also difficult to reconcile the differences in diagnostic rates across the various estimates without standardizing the populations with respect to age, sex, race, and eligibility status (e.g., poverty, supplemental security income, foster care), and managed care. For example, the study by Crystal et al. [18•] used only seven states and reported on those aged 6–17 years, whereas Matone et al. [20••] reported on those aged 3–18 years in 50 states. Differences in the composition of the populations are likely responsible for some of the differences in estimated rates.

Finally, the MAX data are almost exclusively claims for providers billing Medicaid on a fee-for-service (FFS) basis. However, the majority of children insured by Medicaid in the USA are enrolled in managed care plans where a HMO receives capitated payments for enrollees. The FFS data likely capture claims for individuals who are more difficult to enroll in managed care plans, such as those with family and/or housing instability. It is possible that the MAX data are biased towards a population of youth with a higher disease burden and greater use of pharmacotherapy and less access to psychotherapy.

Pediatric Utilization Rates Estimated From Commercial Data

Alongside the Medicaid-based estimates, Crystal et al. [18•] reported on rates using 2006 Marketscan data from Truven Health Analytics. The Marketscan data include administrative claims information from a variety of commercial payers, as well as Medicaid. In these data, limited to privately insured youth, the overall antipsychotic utilization rate in children and adolescents was 0.21 %. Of these users, 2.2 % had a diagnosis of schizophrenia, 25.2 % had a diagnosis of bipolar disorder, 21.4 % had a diagnosis of ADHD, 16 % had a diagnosis of anxiety or depression, 4.5 % had a diagnosis of conduct disorder or disruptive behavior disorder, and 5.2 % had a diagnosis of autism. About 14.6 % had no mental health diagnosis.

Strengths and Limitations of the Commercial Data

Strengths of the Marketscan data include the large sample size and national representativeness of the population of Americans with employer-provided health insurance and Medicaid. Marketscan data also include inpatient medication dispensings which Medicaid pharmacy claims do not (although some of these data are derived from a proprietary projection methodology of unknown quality). Like the Medicaid data, diagnoses are not validated through chart review. Also, the data derived from large employers so small- and medium-sized firms are not represented. Finally, individuals (and their dependent children) in the Marketscan data have a unique identifier for every employer. Individuals can be easily followed over time so long as the primary insured person does not change employers. If the primary insured person moves to a different employer for whom Truven Analytics collects data then they are assigned a new identifier. Thus, an unknown amount of duplication in the rates of diagnosis and utilization occurs. The amount of duplication is likely to be small as a proportion of all claims; however, the effect of double counting may be greater for less common diagnoses (e.g., schizophrenia, bipolar disorder).

Table 1 Estimates of antipsychotic medication utilization [a]

Study	Database	Population	Overall rate of SGA Use	Select diagnoses	Rate (%) among users
Crystal et al. [18•]	2004 Medicaid MAX data (7 states)	Continuously enrolled young people aged 6–17 y	4.20 %	Schizophrenia,	3.3
				bipolar disorder	18.7
				ADHD,	29.1
				conduct disorder,	8.9
				anxiety/depression,	9.1
				autism,	4.9
				no MH diagnosis	9.1
Dos Reis et al. [19•]	2003 Medicaid data from mid-Atlantic state	Children in foster care < 20 y old	2.70 %	Schizophrenia,	5.0
				bipolar disorder,	21.0
				ADHD,	53.0
				conduct disorder,	26.3
				anxiety/depression,	33.8
				autism,	5.4
				no MH diagnosis	N/A
Matone et. al. [20••]	2002–2007 Medicaid data from 50 states	Continuously enrolled young people aged 3–18 y	Age 3–5 y: 0.4 %; age 6–11 y: 2.1 %; age 12–18 y: 3.7 %	Schizophrenia,	0.4
				bipolar disorder,	4.0
				ADHD,	10.5
				conduct disorder,	4.4
				anxiety/depression,	3.8
				autism,	1.5
				no MH diagnosis	13.0
Crystal et al. [18•]	2006 MarketScan data	Continuously enrolled young people aged 6–17 y	0.21 %	Schizophrenia,	2.2
				bipolar disorder,	25.2
				ADHD,	21.4
				conduct disorder,	4.5
				anxiety/depression,	16.0
				autism,	5.2
				no MH diagnosis	14.6
Olfson et. al. [2•]	2005–2009 NAMCS	Physician-reported prescribing, children aged 0–20 y		Schizophrenia,	8.1
				bipolar disorder,	28.8
				ADHD,	N/A
				conduct disorder,	33.7
				anxiety/depression,	35.3
				autism,	5.0
				no MH diagnosis	14.8
Merikangas et al. [25]; Olfson et. al. [26•]	NCS-A	Young people aged 13–18 y		Schizophrenia,	N/A
				bipolar disorder,	2.6
				ADHD,	1.5
				conduct disorder,	N/A
				anxiety/depression,	38.3
				autism,	7.6
				no MH diagnosis	0.1

SGA second-generation antipsychotic, *MAX* Medicaid Analytic Extract Data, *NAMCS* National Ambulatory Care Medical Survey, *NCS-A* National Comorbidity Survey, Adolescent Supplement, *ADHD* attention deficit hyperactivity disorder, *MH* mental health, *N/A* not applicable

[a] Some rates and labels have been aggregated from the original reports and may not be directly comparable. Readers should consult the original reports for exact rates and diagnoses

Survey-based Data

Alexander et al. [13•] reported on antipsychotic medication use between 1995 and 2008 using physician survey data from IMS Health. The National Diagnostic and Therapeutic Index (NDTI) data are generated from a stratified random sample of approximately 4,800 office-based physicians who report on two consecutive workdays per quarter. Respondents fill out an encounter form that details patients' diagnoses and medications prescribed. The authors reported on all visits where an antipsychotic medication was prescribed. Using the diagnosis at the same visit where the prescription occurred, the authors classified the evidence in support of that indication as either "on label", off-label with moderate or strong evidence, or off-label with uncertain evidence using the Drugdex drug compendium. The distribution of diagnoses was reported for all individuals, but not separately for young people. Nevertheless, the results regarding on- and off-label use are informative. Of the 4,216,000 individuals younger than 18 years using SGAs in 2008, 67 % had an off-label indication with uncertain evidence and 9 % had an indication with moderate or strong evidence. Only 24 % of use in this cohort was on-label.

Olfson et al. [2•] reported on antipsychotic use rates using National Ambulatory Care Medical Survey (NAMCS) data. Data across 2005–2009 were combined to stabilize estimates. The NAMCS data are nationally representative of visits to physicians in office-based settings. The physician or staff member reports information on visits and the authors report on those visits at which an antipsychotic prescription occurred. The weighted numerators for calculating rates are based on 270 actual visits for children and 257 actual visits for adolescents. The denominator for calculating rates of pediatric use was estimated from US Census Bureau data.

Of the children aged 0–13 years included in this sample, 6 % had a diagnosis of schizophrenia and 12.2 % had a diagnosis of bipolar disorder. Over 63 % had a diagnosis of disruptive behavior disorder. About 12 % had no mental health diagnosis. The authors reported that 94 % of use in this population had no approved indication. The distribution of rates in adolescents aged 14–20 years were somewhat similar, with 8.1 % having a diagnosis of schizophrenia and 28.8 % having a diagnosis of bipolar disorder. Roughly 34 % of individuals in this age group had a diagnosis of disruptive behavior disorder and 14.8 % had no diagnosis.

The final study identified was by Merikangas et al. [25]. The investigators used data from the National Comorbidity Survey, Adolescent Supplement (NCS-A). These nationally representative data were collected on 10,123 young people aged 13–18 years between February 2001 and January 2004. Unlike the claims- or visit-based estimates reviewed here, the NCS-A estimates were based on structured interviews conducted by professional (but lay) interviewers. Computerized algorithms were used to assign *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* diagnoses. However, in contrast to the other studies reviewed here, medication use was self-reported over the previous 12 months.

The rates reported in the study by Merikangas et al. [25] are not directly comparable to other data reviewed here because the rates are antipsychotic use among those diagnosed rather than the diagnoses among those using antipsychotics. Among those with a developmental disorder (e.g., autism), 7.6 % reported using an antipsychotic (the confidence interval, however, was 2.3–21.9 %). Of those with a diagnosis of bipolar disorder 2.6 % reported antipsychotic use; and of young people with ADHD, 1.5 % reported antipsychotic use. Only 0.1 % of those with no mental health diagnosis reported using an antipsychotic. Schizophrenia was not assessed.

In a companion paper, Olfson et al. [26•] reported on the diagnostic characteristics of the 51 children reporting use of antipsychotics in the NCS-A data. Of users, 59.1 % had any behavior disorder, 38.3 % had any anxiety disorder, and 24.8 % had any mood disorder.

Strengths and Limitations of the Survey-based Data

While the results of the study by Alexander et al. [13•] appear to be generally similar to the rates reported using Medicaid data, there are limitations to the NDTI-based estimates. First, the authors extrapolated the national estimates from the sample data for visits by patients of all ages. And while the authors cite previous studies of the comparability of the NDTI and NAMCS, it is not clear that the NDTI is representative of mental health care or antipsychotic prescriptions. Aside from the statistical methodology, the estimates are also based on visits and particularly on visits where the diagnosis and prescription occurred together. Like the NDTI-based estimates, the NAMCS-based estimates are visit-based rather than patient based. Diagnoses from other clinicians (e.g., consulting psychiatrist) or from previous visits are missing. There is also no diagnostic information from inpatient settings available. Further, Olfson et al. [2•] acknowledge that they cannot derive unique patients and an unknown amount of patient duplication occurs in the estimates.

Encounter reports completed by physicians likely do not capture ongoing medication use prescribed by other clinicians or diagnoses given by other clinicians at separate encounters contemporaneously or in the recent past prior to the index encounter.

MHRN Data

Recent estimates of antipsychotic use in youth reviewed above are based on somewhat old data. This study was conducted, in part, to provide updated estimates on the use of these medications. Table 2 provides detailed estimates of diagnoses among children, adolescents, and adults who used SGAs in 2011.

Table 2 Rates of diagnoses among second-generation antipsychotic users in the Mental Health Research Network (%)

Age (y)	Sex/ race	Anxiety disorders	Attention disorders	Bipolar disorder	Depressive disorders	Disruptive behaviors	All mood disorders	Schizophreniform diagnoses	Nonorganic psychoses	Other organic psychoses	Other psychoses	Other psychoses of childhood	Paranoid states	Tourette disorder	Other tic disorders	Autism	Developmental delay	Specific developmental delays	Other mental health	No mental health diagnosis
0–5	F	12.3	40.4			56.1	22.8									19.3		14.0		
	M	8.9	41.4			49.7	12.0									37.2		32.2		
	NW		38.9			52.8										22.2				
	UN	28.0	26.7			37.8										15.6		22.2		
	WH	13.8	45.5			48.3	19.3									36.6		31.7		
6–11	F	34.0	54.4	11.2	10.6	40.3	40.4		4.4			2.9		1.3		16.5	4.4	16.7	21.6	8.1
	M	28.5	66.9	7.5	6.1	43.1	31.5		2.1	0.4		4.3		3.3	5.0	32.0	3.6	15.7	16.2	5.6
	NW	15.1	57.9	3.9	4.6	39.9	24.3		3.4					1.9	2.0	23.5	5.0	15.8	14.3	11.9
	UN	34.0	63.8	8.0	8.3	42.7	35.9		2.1			4.6		2.3	1.8	27.2	3.4	14.1	18.9	4.6
	WH	31.6	65.6	9.1	7.0	43.6	34.5		2.7	0.4		4.2		3.1	4.3	29.4	3.2	16.7	17.6	4.9
12–17	F	49.5	29.7	27.6	43.5	28.3	62.3	3.3	11.6	0.3		1.2		0.8	0.8	9.2	3.1	7.0	41.4	4.4
	M	34.8	48.9	18.8	24.0	34.0	43.6	3.3	10.6	0.7		2.8	0.8	3.5	3.1	25.2	3.8	9.1	30.8	6.8
	NW	29.7	34.6	18.5	28.4	31.6	45.2	4.4	14.7			1.7		2.0	2.0	19.3	5.0	7.5	31.7	8.3
	UN	41.8	39.8	23.0	34.8	29.6	51.1	2.7	12.2	0.8		1.9	0.5	1.8	1.3	17.3	2.3	8.4	33.7	5.8
	WH	42.4	43.9	22.8	30.8	32.6	51.9	2.8	9.6	0.8		1.8	0.4	2.5	2.7	19.3	3.5	8.4	36.0	5.0
18+	F	44.4	5.2	32.2	44.8	2.3	29.9	10.3	8.2	14.1	3.8	0.1	2.4	0.1	0.1	0.6	1.0	0.6	37.9	6.0
	M	36.2	7.3	26.6	35.7	4.5	27.5	16.1	11.7	13.2	3.3	0.3	2.9	0.6	0.3	3.3	1.8	1.3	40.9	7.1
	NW	32.8	3.2	24.9	35.7	3.5	25.2	21.6	13.5	13.3	3.2	0.2	3.5	0.2	0.2	1.9	1.8	1.0	36.3	7.1
	UN	43.1	8.1	31.5	43.0	3.3	34.2	11.3	9.8	6.7	2.6	0.2	2.1	0.2	0.2	2.1	1.1	0.9	35.8	7.4
	WH	42.6	6.1	30.8	42.0	3.0	28.5	10.9	8.7	15.6	3.9	0.2	2.5	0.4	0.2	1.5	1.2	0.8	40.5	6.0

F female, *M* male, *NW* non-white *UN* unknown race, *WH* white

Cells with with missing values have counts < 5 and are suppressed

What is striking about the MHRN rates is many youth using SGAs have disruptive behavior disorders, attention disorders, and mood disorders. These diagnoses are frequently comorbid with bipolar disorder and ASD. The absence of a mental health diagnosis among antipsychotic users is also notable because they are much lower than in the studies reviewed above. Only 8.1 % of girls aged 6–11 years and 4.4 % of girls aged 12–17 years had no mental health diagnosis. Among boys, the comparable rates were 5.6 % and 6.8 %, respectively.

The MHRN data also have limitations. The HMO population of children is more likely to be composed of dependents of employed parents. And similar to any claims-based analysis, the diagnoses could not be individually validated owing to the large number of youth.

What do the Data Say?

Despite the demographic differences in study populations and methodologic difficulties with claims- and visit-based approaches to estimating rates of antipsychotic use, some important conclusions can be drawn by assessing similarities in the results reported. First, it is clear that the vast majority of antipsychotic medication use in children and adolescents is for disruptive behavior. Only a small percentage, perhaps 3–4 %, of antipsychotic use appears to be for children with schizophreniform disorders or psychoses. This is not terribly surprising considering that these disorders are much less prevalent than attention disorders and mood disorders.

It is also clear that there is a heavy burden of comorbid mental health problems in youth using antipsychotic medications. One striking example is in the MHRN population of boys aged 6–11 years. In this group, 66.9 % had an attention disorder, 28.5 % had an anxiety disorder, 32 % had an ASD, 43.1 % had a disruptive behavior disorder, and 31.5 % had another mood disorder. Another interpretation of these data is that there is a large degree of diagnostic uncertainty in children and adolescents with behavioral health problems. The specific diagnosis in each child or adolescent using an antipsychotic medication may not be clear and individuals may therefore accrue diagnoses such as ADHD and conduct disorder before ultimately being diagnosed with schizophrenia or bipolar disorder. More research is needed to identify the degree to which disruptive behaviors are prodromal symptoms of serious mental illness.

Where the estimates differ is likely attributable to differences in methodology. The large claims-based samples offer stronger evidence of prescription use than self-reported use because a prescription claim record exists, but the validity of the diagnoses for these young people is unknown. In contrast, estimates based on NCS-A data have high diagnostic validity and weaker evidence of antipsychotic use. The self-reported use of medication over the last year likely underestimates use. In a study by Simon et al. [27], people queried about the effectiveness of their antidepressant could not accurately recall their treatment response compared to their depression scores in the medical record, even after it was verified that the patient filled the prescription and the patient was shown a picture of the pill. Other evidence on medication recall is mixed, with some studies reporting good recall compared to pharmacy records and others poor agreement [28–31]. We are somewhat more confident in the rates of antipsychotic use derived from claims-based data.

Another important difference in the estimates of antipsychotic utilization rates is that the NCS-A study diagnosed youth at home and in school settings, not in a health care setting. In contrast, not all youth in the NCS-A study were engaged with the health care system for behavioral health problems.

These data cannot reliably be used to comment on the appropriateness of antipsychotic medication use. Without detailed chart review, we cannot know from the claims data or visit-based data what symptoms the clinicians were trying to treat. In addition, we cannot be certain of the original setting of diagnoses (e.g., primary care consultation with psychiatry), or whether the patient had tried previous medications that were ineffective. Future studies using detailed chart reviews of electronic medical records or surveys of providers prescribing these medications might facilitate valid studies of appropriateness in the future; however, these analyses would be very expensive to conduct.

Conclusion

All the estimates of antipsychotic use among youth follow a similar distribution of diagnoses, regardless of the populations studied. The data support the conclusion that most use is not for psychotic disorders. Whether young people with other diagnoses are experiencing prodromal symptoms of psychosis is unclear. It is likely that distressed parents and family members of children with severe behavior problems are willing to try antipsychotic medications as a last resort, lack of FDA approval notwithstanding. It is also possible that children with no mental health diagnosis whatsoever are being treated by clinicians who are unsure of what diagnosis to give or reluctant to give a diagnosis with high stigma. The differences in antipsychotic utilization rates are likely a combination of practice variation in diagnosing young people, as well as in the propensity to prescribe these medications.

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- • Of importance
- •• Of major importance

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