Factors Influencing the Use of Second-Generation Antipsychotics in Children with Psychosis

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ABSTRACT

BACKGROUND: In 2011, the U.S. Department of Health and Human Services sent a letter to state Medicaid directors explaining the need for oversight of psychiatric prescriptions for children with mental health disorders. The National Committee for Quality Alliance proposed 3 quality measures for rating managed care organizations (MCOs) that involve use of second-generation or atypical antipsychotics in children. In order to ensure appropriate use and to effectively manage the use of second-generation antipsychotics in children, MCOs need to better understand the factors that influence medication treatment decisions for children.

OBJECTIVES: To (a) determine how patient-level and physician-level factors influence decisions to prescribe second-generation antipsychotics to children (aged under 18 years) diagnosed with psychosis and (b) evaluate how the influence of these factors may differ between primary care providers and psychiatrists.

METHODS: This study employed a cross-sectional survey of 193 primary care providers and psychiatrists. A web-based patient simulation survey using a fractional factorial design was administered via a commercial vendor. Respondents were presented with simulated patient profiles described by various levels of factors considered to be essential to decision making. Respondents were asked to make treatment recommendations for each profile evaluated. In addition to treatment recommendations, demographics and beliefs about products were measured. Modified Poisson regression accounting for multilevel data was used to identify the factors that significantly affect treatment recommendations.

RESULTS: Psychiatrists were more likely to recommend second-generation antipsychotics than primary care practitioners (unadjusted RR = 1.36, 95% CI = 1.23-1.51). Social factors such as foster status or parental concern were not found to be significant predictors of prescribing second-generation antipsychotics. The percentage of a provider's patients using second-generation antipsychotics (RR = 1.002, 95% CI = 1.0002-1.003), patient age (aged 4 years: RR = 0.75, 95% CI = 0.68-0.84; aged 10 years: RR = 0.94, 95% CI = 0.91-0.99; reference group: aged 15 years), and patient disease severity (severe: RR = 1.11, 95% CI = 1.04-1.18; moderate: RR = 1.10, 95% CI = 1.05-1.17; reference group: mild) significantly predicted prescription behavior among primary care providers and psychiatrists. Primary care providers were about twice as likely to recommend antipsychotics if they believed the use of antipsychotics was a labeled indication (RR = 2.16, 95% CI = 1.56-2.98) or a medically accepted use (RR = 1.88, 95% CI = 1.33-2.67), when compared with physicians who believed there was no evidence available. This effect was not significant among psychiatrists. Primary care providers, but not psychiatrists, were also significantly influenced by patient white blood cell (WBC) count. Patients with healthy WBC counts were 1.11 times as likely (95% CI = 1.05-1.17) to receive antipsychotics from primary care providers compared with those with low WBC count. Patient body mass index (BMI) was not found to significantly influence prescribing behavior. Nearly 50% of patients did not receive recommendations for psychosocial care. Primary care providers recommended antipsychotic polypharmacy in 23% of the patient profiles, while psychiatrists did so in 42% of the profiles.

CONCLUSIONS: This study provides valuable insight into physician-prescribing practices for antipsychotics. The lack of significance of foster status and parental concern, after controlling for other factors, shows that physicians base their decisions on clinical factors more than social factors. Results for patient BMI and frequency of recommendations of polypharmacy are concerning. The general lack of awareness of evidence supporting use of antipsychotics is also highly concerning. The effects of patient BMI, beliefs about evidence supporting use, and prescribing practices with regard to psychosocial care and antipsychotic polypharmacy provide actionable results for managed care programs looking to improve their quality metrics. The results of this study further demonstrate the need for the immediate implementation of the various proposed quality metrics in this area and for new practice guidelines to raise the current standard of care.

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What is already known about this subject

- The use of second-generation antipsychotics in children is steadily increasing for several conditions, including psychosis.
- The introduction of quality metrics and attention from the Centers for Medicare & Medicaid Services have highlighted the importance of the increased use of antipsychotics in children.
- Foster children are known to receive a disproportionately high percentage of second-generation antipsychotics when compared with other children.

What this study adds

- This study showed that factors such as foster status, parental concern, and patient body mass index do not influence physician decision making after controlling for other factors.
- Evidence was found for antipsychotic polypharmacy and lack of evidence-based prescribing behavior, which suggests a need for new treatment guidelines and improved physician education.

The use of second-generation or atypical antipsychotics in children and adolescents has increased substantially over the past few years.¹ Although there is limited evidence of the efficacy of these drugs in children, they are being prescribed for children to treat several different conditions. Up to 10% of antipsychotics used in children are prescribed for psychosis.^{1,2} Existing studies in this area point toward a range

of potentially serious adverse events such as weight gain, diabetes, hypertension, metabolic and endocrine abnormalities, hyperprolactinemia, and dyslipidemia in the short term and several other unknown long-term effects.³⁻⁶

With increasing safety concerns and budgetary constraints, payers such as Medicaid have sought to better understand the use of these drugs in children.^{7,8} In 2011, the U.S. Department of Health and Human Services sent a letter to state Medicaid directors making them aware of the growing problem of antipsychotic use among foster children.^{9,10} The National Committee for Quality Alliance has proposed a set of quality measures related to use of antipsychotics in children in the Healthcare Effectiveness Data and Information Set (HEDIS). These measures include use of first-line psychosocial care, metabolic monitoring of children who are prescribed antipsychotics, and antipsychotic polypharmacy in children.¹¹ An increasing number of payers, including state Medicaid programs, are considering using these measures to rate managed care programs as they transition to a quality-based payment strategy.^{12,13} It is imperative that managed care programs obtain a better understanding of the decisions behind antipsychotic prescriptions to help formulate strategies to improve their performance on these quality measures.

Antipsychotic prescription decisions can be influenced by factors related to the patient or the provider. Patient characteristics, such as patient age, gender, body mass index (BMI), insurance, foster status, parental consent, and white blood cell (WBC) count,^{1,3-6,9} and physician characteristics, such as type and size of practice, specialization, and evidence supporting use,¹⁴⁻¹⁶ have been shown to influence the decision to prescribe second-generation antipsychotics to children. Although some of these factors, such as age, gender, insurance, foster status, and physician specialization, can be examined in administrative claims data, others are generally not available, necessitating the collection of primary data.

The purpose of this study was to (a) determine how patient-level factors, such as age, race, sex, foster status, and concern about consent from parent/guardian, influence physician decisions to prescribe second-generation antipsychotics in children with psychosis; (b) determine how physician characteristics, such as specialization, mental health patient volume, and beliefs about drugs, influence physician decisions to prescribe second-generation antipsychotics in children with psychosis; and (c) evaluate whether the influence of patient-level factors and physician characteristics on physician decisions was different for primary care providers and psychiatrists.

Methods

Study Design and Data Collection

This study employed a cross-sectional survey using separate convenience samples of primary care providers and psychiatrists. General psychiatrists and child psychiatrists were classified

as psychiatrists, and family medicine, internal medicine, and general practice physicians and pediatricians were classified as primary care providers. The study sample was obtained through a national physician panel maintained by Reckner Healthcare,¹⁷ a commercial vendor, and data were collected over a 7-week period leading up to November 1, 2013. The physician panel was compiled using a combination of random dialing, purchased samples, and referrals from across the country. Physicians were required to go through a short set of screening questions to make sure they met the inclusion criteria for the study. To be eligible for the study, physicians had to be engaged in full-time active practice for at least 2 years after residency and had to spend a considerable portion of their time in the outpatient care setting (50% for primary care providers and 25% for psychiatrists). Physicians were eligible for the study if their practices included children diagnosed with psychosis and prescribed second-generation antipsychotics.

Survey Design

The survey included a short screener with demographics, a patient simulation section, and a final section that measured physician beliefs and practice attitudes. In the patient simulation section, each physician was presented with a set of patient cases/profiles with information about patient demographics, symptoms, clinical parameters, and other relevant information. Each profile presented a patient displaying symptoms of psychosis of varying severity. For the purpose of this study, *psychosis* was defined as having uncontrollable agitation, auditory hallucinations and lack of age-appropriate grooming in varying frequencies, depending on the severity of the disease. Psychosis was chosen because it could be represented in a concise profile, while still being broad enough to capture several indications for which second-generation antipsychotics are popularly used. After reviewing each patient profile, the respondents selected a treatment plan for the patient from an exhaustive list of treatment options. The information presented in each profile was carefully constructed from current literature and qualitative interviews to include variables that were expected to be relevant to decision making.^{1,3-6,9,14-16} Six one-on-one interviews were conducted with psychiatrists, pediatricians, and mental health pharmacists to finalize the patient attributes and survey questions and test the drafted profiles. The list of variables that were present in the profiles and their various levels are presented in Table 1.

A fractional factorial design was used to determine a combination of various levels of these patient attributes that would support statistical analysis of the effect of each attribute independently. Thirty patient profiles were created using the combination of variables listed (see the Appendix for a sample patient profile, available in online article). These 30 profiles were grouped into 3 subsets of 10 profiles each that were balanced with respect to the hypothesized major drivers of

TABLE 1 List of Patient Attributes

Variable Name	Variable Description	Variable Levels		
		0	1	2
Severity	Disease severity	Mild	Moderate	Severe
Adherence	Risk for nonadherence	Absent	Present	–
WBC	WBC count	Low	Normal	–
ANC	ANC	Low	Normal	–
Alcohol	Alcohol/substance abuse	No	Yes	–
BMI	BMI	Underweight	Normal	Overweight
Sex	Sex	Male	Female	–
Race	Race	Caucasian	Black	–
Age	Age	<5 years	6-12 years	13-17 years
Puberty	Puberty	No	Yes	–
Foster	Foster status	Nonfoster	Foster	–
Diabetes	Type 2 diabetes mellitus	No	Yes	–
Consent	Concern about consent	None	Medium	High

Note: Each profile was constructed as a combination of these 13 variables at one of the possible levels. For a sample patient profile, see the Appendix (available in online article).

ANC = absolute neutrophil count; BMI = body mass index; WBC = white blood cell.

use. Such methodology has been used by other researchers.¹⁸ Each physician respondent was shown 1 subset of 10 profiles in a randomized order. Using balanced subsets instead of a randomly selected group of 10 profiles helped ensure that respondents were exposed to an equal distribution of all major predicted factors.

The survey also contained the Evidence-Based Practice Attitude Scale (EBPAS) to assess physician attitudes toward adopting evidence-based practices (EBP). The EBPAS was developed and validated in a behavioral health provider population and contains 4 subscales: (1) Appeal of EBPs, (2) Requirements for the use of EBPs, (3) Openness to innovation, and (4) Divergence of EBP with usual practice (perceived).^{19,20} The EBPAS was administered after the patient profiles in order to avoid any response bias. Physician background, practice characteristics, and beliefs about evidence supporting use of second-generation antipsychotics in children with psychosis were also measured. Physician belief about evidence concerning use of second-generation antipsychotics in children with psychosis was measured by asking respondents their beliefs about the level of evidence that existed for use of 11 second-generation antipsychotics for 3 age categories (5 years or under, 6-12 years, and 13-17 years) presented in the patient profiles. The level of evidence categories were “labeled indication,” “medically accepted use but not a labeled indication,” or “no evidence supporting use.” “Medically accepted use” was defined in the survey as a case where the antipsychotic drug does not have an approved indication by the U.S. Food and Drug Administration, but it has considerable evidence supporting use. Respondents could also indicate that they “don’t know.” The maximum level of evidence found for any

second-generation antipsychotic was used for the corresponding age group. Approval for this study was obtained from the University of Mississippi’s Institutional Review Board before data collection.

Data Analysis

The primary outcome variable for this analysis was whether a second-generation antipsychotic was selected as a treatment option for each patient profile presented to respondents. Each physician responded to 10 treatment profiles, creating a multilevel (or hierarchical) data structure. To assess predictors of the use of second-generation antipsychotics, an extension of a modified Poisson regression model (using a log link and a Poisson distribution) was used to handle a multilevel data structure for binary data.²¹ An exchangeable correlation structure was used in estimating robust standard errors. Such a model results in exponentiated coefficients that can be interpreted as risk ratios.²¹ Model building was done in multiple steps because of the somewhat small sample size at the physician level (N=193).²² Potential physician and patient factors were tested in separate models for the primary care providers and psychiatrists. Factors found to be significant ($P \leq 0.1$) in either of these multivariable models were then introduced into the final model, which included both specialties and tested for interactions between physician specialty and the predictors. The inclusion of interactions assessed whether each predictor variable was differently associated with the use of second-generation antipsychotics for psychiatrists relative to primary care providers. For reasons of parsimony, nonsignificant interactions ($P > 0.05$) were dropped, and a common effect for psychiatrists and primary care providers was estimated for the variable of interest. IBM SPSS (SPSS, Chicago, IL) was

FIGURE 1 Sample Selection Flow Chart

used for data analysis; the GENLIN procedure in SPSS with the repeated subcommand was used for the modified Poisson regression models.

Results

The contracted vendor invited 1,873 physicians to participate. After eliminating incomplete responses and respondents who were screened out, 215 completed surveys were collected (Figure 1). The median time to complete the survey, including

those who were excluded after the screener, was about 19 minutes. A total of 193 respondents, or 1,930 (193×10) unique physician-patient combinations, were used in the analyses after deleting 22 respondents who showed response patterns that indicated lack of consistency in responding or a misinterpretation of survey instructions. Summaries of respondent demographics, beliefs, and practice characteristics are provided in Tables 2 and 3. The final dataset used for analysis contained 129 respondents classified as primary care providers and 64 classified as psychiatrists.

Respondent Characteristics

Compared with primary care providers, psychiatrists were significantly older, spent more years in active practice, had lower patient volume in a typical week, and had a higher percentage of patients who were foster children (Table 2). In line with expectations, primary care providers spent a significantly greater proportion of their time in outpatient care (92% vs. 80% for psychiatrists). A substantial proportion of respondents indicated that they did not know the level of evidence available for use of second-generation antipsychotics in children with psychosis (Table 2). Despite this, a substantial proportion of profiles were recommended second-generation antipsychotics.

Prescribing Patterns

Across all physicians and patient profiles, 1,374 (71%) patient profiles were recommended treatment with second-generation antipsychotics. Primary care providers were significantly more likely to refer their patients to another provider and less likely to prescribe second-generation antipsychotics or psychosocial therapy (Table 3).

Factors Influencing Prescribing Behavior

Modified Poisson regression models were used to identify factors that influence the use of second-generation antipsychotics. Overall, psychiatrists were more likely to recommend second-generation antipsychotics than primary care providers (unadjusted risk ratio [RR]=1.36; 95% confidence interval [CI]=1.23-1.51). The percentage of a provider's patients using second-generation antipsychotics, patient disease severity, and patient age significantly predicted prescription behavior among primary care providers and psychiatrists (i.e., significant common effect and no significant interaction between these variables and physician specialty; Table 4). Primary care providers and psychiatrists differed significantly in their prescribing behaviors, with changes in patient WBC count and beliefs about evidence supporting use of second-generation antipsychotics.

The percentage of patient population in a provider's clinical practice using second-generation antipsychotics (RR=1.002; 95% CI=1.0002-1.003) was found to significantly predict prescribing behavior in the simulation experiment. Patients with a severe indication were 1.11 (95% CI=1.04-1.18) times

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TABLE 2 Demographic and Practice Characteristics for Study Respondents

Variable ^a	Physician Specialty		P Value
	Primary Care Provider (n = 129)	Psychiatrist (n = 64)	
	% (n)	% (n)	
Females	17.1 (22)	17.2 (11)	0.982
Race			0.522
Caucasians	62.0 (80)	65.6 (42)	
Asian Americans	27.9 (36)	25.0 (16)	
African Americans	1.6 (2)	0 (0)	
Native Hawaiians	0.1 (1)	0 (0)	
Hispanics	2.3 (3)	0 (0)	
Others	5.4 (7)	9.4 (6)	
Physician belief about evidence for use of second-generation antipsychotics in children aged 5 years and under			0.152
Don't know	26.4 (34)	15.6 (10)	
No evidence	13.2 (17)	21.9 (14)	
Medically accepted use	34.9 (45)	42.2 (27)	
Labeled indication	25.6 (33)	20.3 (13)	
Physician belief about evidence for use of second-generation antipsychotics in children aged between 6 and 12 years			0.068
Don't know	18.6 (24)	9.4 (6)	
No evidence	6.2 (8)	9.4 (6)	
Medically accepted use	37.2 (48)	26.6 (17)	
Labeled indication	38.0 (49)	54.7 (35)	
Physician belief about evidence for use of second-generation antipsychotics in children aged between 13 and 17 years			0.185
Don't know	11.6 (15)	4.7 (3)	
No evidence	1.5 (2)	3.1 (2)	
Medically accepted use	27.9 (36)	20.3 (13)	
Labeled indication	58.9 (76)	71.9 (46)	
Evidence-Based Practice Attitude Scale (EBPAS), ^b mean [±SD]			
Requirement	1.8 [1.1]	1.9 [1.1]	0.572
Appeal	2.5 [0.8]	2.7 [0.6]	0.065
Openness	2.1 [0.9]	2.5 [0.8]	0.002
Divergence	2.4 [0.9]	2.3 [0.9]	0.400
Total	2.2 [0.5]	2.3 [0.5]	0.048
Age, mean [±SD]	50.3 [8.0]	54.2 [8.8]	0.002
Years in practice, mean [±SD]	18.0 [6.9]	20.2 [7.0]	0.042
Patient volume per week, ^c mean [±SD]	174.5 [122.6]	108.3 [74.5]	0.0001
Percentage of patients in foster care, ^c mean [±SD]	9.1 [11.8]	15.9 [17.1]	0.001
Percentage of patients using antipsychotics, ^a mean [±SD]	27.4 [26.5]	35.0 [24.4]	0.054
Proportion of time spent in, ^c mean [±SD]			
Inpatient care	6.4 [10.7]	14.8 [18.9]	0.0001
Outpatient care	92.0 [12.1]	80.0 [21.7]	0.0001
Administration	1.2 [2.6]	2.7 [4.8]	0.004
Teaching/research	0.5 [1.7]	2.5 [6.5]	0.001
Proportion of patients diagnosed with, ^c mean [±SD]			
Psychosis	10.8 [12.6]	18.3 [16.6]	0.001
Bipolar disorder	17.7 [16.2]	23.2 [13.0]	0.021
Conduct disorder	29.5 [27.0]	20.5 [14.6]	0.013
Autism	11.9 [13.4]	13.6 [11.9]	0.398
Proportion of age groups, ^c mean [±SD]			
5 years and under	4.0 [5.7]	4.6 [7.8]	0.562
6-12 years	8.5 [8.2]	13.7 [14.1]	0.002
13-17 years	15.8 [11.8]	18.0 [10.9]	0.205
18 years and over	71.7 [21.5]	63.8 [27.7]	0.030

^aThis table represents actual demographics and provider characteristics and not the distribution of patient factors in the profiles presented to the physicians.

^bEBPAS and subscales are scored on a scale of 0 to 4 with higher values indicating more evidence-based practice.

^cThese values represent actual practice characteristics of respondents.

SD = standard deviation.

TABLE 3 Prescribing Patterns Across All Profiles Displayed, by Age Group

Treatment	Physician Specialty				P Value
	Primary Care Provider		Psychiatrist		
	N ^a	% (n)	N ^a	% (n)	
Second-generation antipsychotics					
5 years and under	424	46.0 (195)	221	74.7 (165)	0.0001
6-12 years	479	67.2 (322)	227	91.2 (207)	0.0001
13-17 years	387	78.3 (303)	192	94.8 (182)	0.0001
All age groups	1,290	63.6 (820)	640	86.6 (554)	0.0001
Antipsychotic polypharmacy					
5 years an under	424	11.5 (49)	221	33.5 (74)	<0.005
6-12 years	479	25.0 (120)	227	43.2 (98)	<0.005
13-17 years	387	32.8 (127)	192	50.5 (97)	<0.005
All age groups	1,290	22.9 (296)	640	42.0 (269)	<0.005
Other pharmaceutical treatment					
5 years and under	424	30.4 (129)	221	31.7 (70)	0.744
6-12 years	479	45.5 (218)	227	40.5 (92)	0.213
13-17 years	387	46.0 (178)	192	41.7 (80)	0.324
All age groups	1,290	40.7 (525)	640	37.8 (242)	0.223
Psychosocial treatment					
5 years and under	424	38.9 (165)	221	60.2 (133)	<0.005
6-12 years	479	46.3 (222)	227	54.2 (123)	0.052
13-17 years	387	48.3 (187)	192	52.1 (100)	0.394
All age groups	1,290	44.5 (574)	640	55.6 (356)	<0.005
Referral to another physician					
5 years and under	424	59.9 (254)	221	23.5 (52)	<0.005
6-12 years	479	47.8 (229)	227	15.4 (35)	<0.005
13-17 years	387	42.6 (165)	192	10.4 (20)	<0.005
All age groups	1,290	50.2 (648)	640	16.7 (107)	<0.005

Note: Denominators are as follows: aged 5 years–424 primary care providers, 221 psychiatrists; aged 6-12 years–479 primary care providers, 227 psychiatrists; aged 13-17 years–387 primary care providers, 192 psychiatrists; all age groups–1,290 primary care providers, 640 psychiatrists.

^aAll numbers are expressed as a percentage of the total population in that age group.

as likely, and those with a moderate condition were 1.10 (95% CI=1.05-1.17) times as likely, to receive second-generation antipsychotics when compared with mild patients. When compared with the aged 15 years patient profile, the probabilities of receiving a treatment recommendation for second-generation antipsychotics were 25% (RR=0.75; 95% CI=0.68-0.84) and 6% (RR=0.94; 95% CI=0.91-0.99) lower for the profiles of a child aged 4 and 10 years, respectively.

Primary care providers were about twice as likely to recommend second-generation antipsychotics if they believed the use of second-generation antipsychotics was a labeled indication (RR=2.16; 95% CI=1.56-2.98) or a medically accepted use (RR=1.88; 95% CI=1.33-2.67) when compared with physicians who believed there was no evidence available. This effect was not found to be significant among psychiatrists, although the RRs indicate that psychiatrists also seemed somewhat more likely to prescribe second-generation antipsychotics if they believed there was evidence supporting use. Similarly, primary care providers, but not psychiatrists, were significantly influenced by patient WBC counts. Patients with healthy WBC

counts were 1.11 (95% CI=1.05-1.17) times as likely to receive a second-generation antipsychotic compared with those who had low WBC counts from primary care providers.

Discussion

This study uses survey research methods to study approaches used by physicians for the treatment of mental health in children. Many of the factors evaluated are not available in administrative claims datasets, thus, providing unique contribution to this literature. The results of this study demonstrate that psychiatrists were more likely than primary care providers to recommend second-generation antipsychotics for children with psychosis. This finding is similar to that of Cooper et al. (2006), who found that increase in frequency of antipsychotic use by “mental health providers” was more than twice the increase seen in “non-mental health providers.”¹⁶ Documented expert interviews corroborate the hypothesis that most primary care providers are likely to refer patients as soon as psychotic symptoms are identified.²³ Since a large percentage of children with mental health problems are treated by primary

TABLE 4 Comparison of Factors Influencing Physician Prescription of Second-Generation Antipsychotics

Characteristics	Primary Care Provider ^{a,b} (n = 129)			Psychiatrist ^{a,b} (n = 64)		
	RR	95% CI	P Value	RR	95% CI	P Value
Physician Factors						
Physician's belief about evidence supporting use						
Labeled indication	2.16	1.56-2.98	<0.001	1.11	0.93-1.33	0.230
Medically accepted use	1.88	1.33-2.67	<0.001	1.11	0.93-1.32	0.240
Physician race						
Asian American	1.07	0.95-1.20	0.270	1.07	0.95-1.20	0.270
Caucasian	0.98	0.88-1.10	0.773	0.98	0.88-1.10	0.773
Percentage of patients diagnosed with psychosis	1.00	0.99-1.00	0.273	1.00	0.99-1.00	0.273
Percentage of patients using second-generation antipsychotics ^c	1.00	1.00-1.00	0.031	1.00	1.00-1.00	0.031
Years spent in active practice	1.01	1.00-1.01	0.170	1.01	1.00-1.01	0.170
Patient Factors						
Patient severity						
Severe	1.11	1.04-1.18	<0.001	1.11	1.04-1.18	<0.001
Moderate	1.10	1.05-1.17	<0.001	1.10	1.05-1.17	<0.001
Patient age						
4 years	0.75	0.68-0.84	<0.001	0.75	0.68-0.84	<0.001
10 years	0.94	0.91-0.99	0.016	0.94	0.91-0.99	0.016
Patient WBC count (normal range)	1.11	1.05-1.17	<0.001	1.00	0.96-1.04	0.877
Patient ANC (normal range)	0.99	0.96-1.03	0.776	0.99	0.96-1.03	0.776

Note: Reference categories: Evidence supporting use—No evidence available; Physician race—Other; Patient severity—Mild; Patient age—15 years; Patient WBC count—Low WBC count; Patient ANC—Low ANC. Dependent variable: whether a second-generation antipsychotic was prescribed.

^aSeparate RRs and 95% CIs are provided for primary care providers and psychiatrists wherever the interaction between physician specialty and the predictor is significant at the 0.05 level (belief about evidence supporting use and patient WBC count). Wherever the interaction is not significant, the same RR, 95% CI, and P value have been shown under both columns.

^bThe effect of physician specialty, while not presented in this table, was also included in the model. This effect comparing primary care providers and psychiatrists in this model is conditional on patient WBC count being low and no evidence available supporting use (i.e., the reference categories for the variables involved in the interaction). For ease of interpretation it was excluded from the table.

^cFor percentage of patients using second-generation antipsychotics, the 95% CI does not include 1 with more than 2 decimal points.

ANC = absolute neutrophil count; CI = confidence interval; RR = risk ratio; WBC = white blood cell.

care providers, it is important to understand the differences between them and psychiatrists and how they might affect the quality of care received by children.

Patient Characteristics

Patient characteristics found to significantly predict recommendation of second-generation antipsychotics included age, WBC count, and disease severity. In line with expectations, patients were more likely to be recommended second-generation antipsychotics when their disease was severe or moderate, in comparison with mild severity.²⁴ Physicians were less likely to recommend second-generation antipsychotics to children aged 4 years and 10 years when compared with children aged 15 years. Pathak et al. (2010) also found that use of second-generation antipsychotics increases with increase in patient age.¹

The significance of WBC count in treating children with mental health disorders is not very common in published literature. However, WBC values are suggested for constant monitoring if the patient is using clozapine, which has a black box warning listed for agranulocytosis.^{25,26} While this effect

does not seem to exist across all antipsychotics, it still seems to drive prescribing behavior among primary care providers. In this study, it was not possible to determine if the significance of WBC count could be attributed solely to the presence of clozapine among the possible treatment options.

Not all second-generation antipsychotics have labeled indications for use in young children with psychosis; therefore, the level of concern on the part of parents or guardians when providing consent for their use was hypothesized to be a factor influencing decisions about prescribing second-generation antipsychotics.⁸ However, parental concern and whether a patient was a foster child were not found to be significant predictors. These factors failed to meet the alpha of 0.1 in the initial models for each physician type and thus were not included in the final models. Studies that highlight the disproportionately high use of antipsychotics in foster children suggest that this might be a result of greater exposure to trauma, frequent changes in foster placement, and varying state oversight policies.^{8,9,27} The finding that physicians are no more likely to recommend these drugs to foster children, after

controlling for other factors, provides evidence that the increased use of antipsychotics in foster children with psychosis may be driven more by clinical factors than foster status of the child. This is consistent with previous research documenting that the more frequent use of antipsychotics in foster children appears to be related to higher needs more so than disparities in care.⁹ A similar positive finding in this study is the nonsignificance of “parental concern.” The nonsignificance of social factors reinforces the belief that physician prescription decisions for treatment of psychosis in children are driven more by objective clinical criteria.

Patient sex, race, BMI, puberty status, alcohol use, and blood glucose levels also did not meet the criteria for inclusion in the models for each physician type. The nonsignificant effect of BMI is particularly concerning because it appears that physicians do not take into account metabolic functions before recommending second-generation antipsychotics. In addition to the quality measures that deal with metabolic monitoring, the monitoring of a patient’s BMI is recommended by several guidelines.^{25,27-30}

Physician Characteristics

The most important physician characteristic influencing prescribing behavior was specialty. Cooper et al. found similar results in their study on trends in the prescription of antipsychotics using data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey.¹⁶ Belief about evidence supporting use of second-generation antipsychotics was found to be a significant predictor among primary care providers but not among psychiatrists. It is possible that the lack of significance among psychiatrists was a function of the sample size in that group, but the direction of the effect was similar in both groups of physicians.

The finding with the most direct impact on managed care was physician awareness of evidence supporting use of second-generation antipsychotics in children. A substantial proportion of physicians believed second-generation antipsychotics were a labeled or medically accepted use among children aged 5 years and under (Table 2), while almost none of these drugs actually had any evidence to support that use. This behavior of off-label prescribing in mental health providers is not unexpected and has been demonstrated before.¹ These numbers suggest that physician education regarding second-generation antipsychotic use is the utmost priority. Further, the development of treatment guidelines might help improve prescription behavior.

In line with expectations, physicians whose clinical practice had a greater proportion of children using second-generation antipsychotics were more comfortable recommending these drugs in the simulation experiment. This effect did not vary significantly by physician specialty. Primary care providers recommended multiple second-generation antipsychotics in 23% of the profiles, and psychiatrists did so in 42% of the pro-

files, which is higher than that observed even in elderly populations in previous research.³¹ Antipsychotic polypharmacy is not recommended in any age group because of the increase in risk of metabolic syndrome.³² Use of multiple antipsychotics is also one of the HEDIS measures for children. Only about 50% of the patients were recommended psychosocial therapy. This finding, while not unprecedented,³³ is very concerning because the National Collaborative for Innovation in Quality Measurement identified access to psychosocial care as a “needed service associated with medication use,”³⁴ and use of psychosocial therapy is also a HEDIS measure used to evaluate health plans.

Limitations

This study provides valuable insights into decisions related to prescribing second-generation antipsychotics to children. As with any study, however, there are limitations that need to be considered. A summary of the study results was offered as the only incentive for participation. There exists a potential risk for nonresponse bias. The sample obtained was conveniently sampled and somewhat skewed in terms of the distribution for race (majority Caucasians and Asian Americans) and gender (majority male), which could further limit generalizability of the findings. The sample size, while sufficient, was somewhat small, especially for psychiatrists. This could have resulted in missing effects that might have been significant predictors of prescribing decisions. The location of a provider’s practice (urban vs. rural) could have also influenced prescribing practice. However, this information was not collected during this study. Physician treatment recommendations are also influenced by insurance restrictions. However, this study did not account for such effects. This study focused on patients diagnosed with psychosis. Generalizations to other mental health conditions in children must be made with caution. Respondent comfort and experience with use of second-generation antipsychotics might have influenced treatment recommendations, especially among primary care practitioners. However, respondents were not screened based on the number of patients with psychosis. The use of vignettes to simulate patients carries some drawbacks. Respondents were not able to acquire additional information that they may have felt was needed. While researchers have demonstrated that vignettes offer adequate validity in measuring quality of care, it should be noted that actual treatment decisions made by physicians might be different.³⁵⁻³⁷ Treatment patterns for the profiles may also have been influenced by social desirability.

Conclusions

This study tested the factors influencing the prescription of second-generation antipsychotics among children with psychosis by presenting patient profiles with factors of interest. The analysis provided insights in 5 main areas: (1) psychiatrists

were more willing to recommend second-generation antipsychotics, than general practitioners; (2) older children were more likely to receive these medications than younger ones; (3) there was no difference in prescription rates between children in foster care and those who were not; (4) parental concerns regarding the use of antipsychotics did not appear to have influenced physician decisions; and most significantly, (5) physicians were more likely to recommend second-generation antipsychotics if they thought there was evidence to support their use. Findings regarding patient BMI, recommendations of psychosocial therapy, belief about evidence supporting use, and antipsychotic polypharmacy provide insight into physician behaviors that may have serious effects on managed care quality ratings. These results can help managed care programs gain a better understanding of this therapeutic area and plan appropriate education and other interventions to ensure quality care.

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Study concept and design were contributed by Ramachandran, Banahan, West-Strum, and Bentley. Ramachandran, Banahan, and Patel collected data; data interpretation was performed primarily by Ramachandran, Banahan, and Patel, along with Bentley and West-Strum. The manuscript was primarily written by Ramachandran, along with Banahan and Bentley, and revised by Banahan, Bentley, West-Strum, and Patel.

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APPENDIX Sample Patient Profile

(102) Elizabeth:

Doctor, please assume that Elizabeth is a patient you have newly diagnosed with mild psychosis. Her history and your current evaluation notes are summarized below.

Demographics	Lab values	Symptoms
Age: 15 Gender: Female Height: 63.7 inches Weight: 119.5 pounds BMI: 20.7 (Normal) Pubescent Caucasian	WBC: 7300 (Normal) ANC: 1300 (Low) Fasting glucose: 85 mg/dL	Patient has displayed symptoms of mild psychosis: <ul style="list-style-type: none"> • Occasional uncontrollable agitation • Minimally intrusive auditory hallucinations • Mild lack of age-appropriate grooming

The patient's diagnosis is consistent with family history. You have informed the parent about the use of atypical antipsychotics. The patient can afford her drugs.

During the visit you determine that:

- The parent is willing to sign an informed consent and hasn't expressed any concerns about the use of antipsychotics.
- The patient has no history of alcohol abuse.
- The parent mentions that the patient takes his medications on time.

Treatment options: (Please check all that apply)

<p>Atypical Antipsychotics</p> <p>☐ Aripiprazole (Abilify)</p> <p>☐ Asenapine (Saphiris)</p> <p>☐ Clozapine (Clozaril, generic)</p> <p>☐ Iloperidone (Fanapt)</p> <p>☐ Lurasidone (Latuda)</p> <p>☐ Olanzapine (Zyprexa, Zyprexa Relprevv, generic)</p> <p>☐ Olanzapine & Fluoxetine (Symbyax, generic)</p> <p>☐ Paliperidone (Invega, Invega Sustena)</p> <p>☐ Quetiapine (Seroquel, Seroquel XR, generic)</p> <p>☐ Risperidone (Risperidal, Risperidal Consta, generic)</p> <p>☐ Ziprasidone (Geodon, generic)</p> <p>Conventional Antipsychotics</p> <p>☐ Perphenazine (Trilafon, generic)</p> <p>☐ Chlorpromazine (generic)</p> <p>☐ Others</p>	<p>Anti-convulsants</p> <p>☐ Lithium (Lithobid, generic)</p> <p>☐ Alpha agonists</p> <p>☐ Other</p> <p>☐ Anti-depressants</p> <p>☐ Anxiolytics</p> <p>☐ Mood stabilizers</p> <p>☐ Stimulants</p> <p>☐ Other (Please specify _____)</p> <p>☐ Psychosocial Intervention</p> <p>☐ Refer to another physician with experience in dealing with pediatric mental health</p> <p>☐ Refer to non-medical practitioner</p> <p>☐ Other non-pharmaceutical treatment</p>
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