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Quality Concerns in Antipsychotic Prescribing for Youth: A Review of Treatment Guidelines

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Abstract

Background—Antipsychotic prescribing for youth has increased rapidly, is linked with serious health concerns, and lacks clear measures of quality for pediatric care. We reviewed treatment guidelines relevant to 7 quality concepts for appropriate use and management of youth on antipsychotics: 1) use in very young children, 2) multiple concurrent antipsychotics, 3) higher-than-recommended doses, 4) use without a primary indication, 5) access to psychosocial interventions, 6) metabolic screening, and 7) follow-up visits with a prescriber.

Methods—We searched for clinical practice guidelines meeting the following criteria: developed or endorsed by a national body, published after 2000, and specific treatment recommendations made related to 1 or more of the 7 quality concepts. Sources included electronic databases, the American Academy of Child and Adolescent Psychiatry Web site, and stakeholder and expert advisory committee recommendations. Two raters reviewed the 11 guidelines identified, extracting treatment recommendations, including details that could support measure definitions, and ratings of strength of recommendation and evidence.

Results—All 7 quality concepts were strongly endorsed by 1 or more guidelines, and 2 or more guidelines assigned their highest strength of recommendation ratings to 6 of the 7 concepts. Two guidelines rated evidence, providing high strength of evidence for 2 quality concepts: psychosocial interventions and metabolic monitoring.

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SUPPLEMENTARY DATA.

Supplementary data related to this article can be found online at <http://dx.doi.org/10.1016/j.acap.2014.05.009>.

Conclusions—Guidelines provide support for 7 quality concepts addressing antipsychotic prescribing for youth. However, guideline support is often based on strong clinical consensus rather than a robust evidence base.

Keywords

adolescents; antipsychotic agents; children; practice guidelines as topic; quality indicators

Antipsychotic prescribing for children has increased 2- to 4-fold over the past 15 years,^{1,2} raising several public health concerns. The majority of antipsychotic prescribing in children is for nonpsychotic conditions such as attention-deficit/hyperactivity disorder and disruptive behaviors.³ Vulnerable child populations, including minorities,⁴ Medicaid enrollees,² and those in foster care,⁵ are more likely to be prescribed antipsychotics. Antipsychotics can have serious adverse effects with long-term health implications, including diabetes and hyperlipidemia, movement disorders, and hyperprolactinemia.^{6–8} Especially worrisome is the limited evidence on the long-term safety of antipsychotic prescribing in children.^{1,9} These concerns have prompted calls for monitoring antipsychotic use in children, especially those in foster care and others covered by Medicaid or the Children's Health Insurance Program (CHIP).^{5,10,11} Quality measurement is one approach to monitoring, but few pediatric mental health measures exist.¹²

The Children's Health Insurance Program Reauthorization Act of 2009 Pediatric Quality Measure Program (PQMP) focuses on development and dissemination of new pediatric measures for Medicaid and CHIP. The National Collaborative for Innovation in Quality Measurement (NCINQ), a PQMP Center of Excellence, was tasked by the Agency for Healthcare Research and Quality and Centers for Medicare and Medicaid Services (CMS) to develop antipsychotic quality measures for children and adolescents.¹³ Consistent with CMS's Blueprint,¹⁴ and as described in more detail elsewhere,¹³ early steps in measure development include a review of existing and related measures and obtaining guidance from multiple stakeholders on priorities. NCINQ invited input from federal officials (including from Medicaid and CHIP), clinicians, patient and family advocates, state officials, and subject matter experts on concepts, including earlier antipsychotic measure development efforts by multistate quality collaboratives.^{5,15,16} The stakeholder advisory committees (Online Supplement A) identified 7 high-priority measure concepts. Four concepts address appropriateness/overuse of antipsychotics in children: 1) use in very young children, 2) multiple concurrent antipsychotics, 3) higher-than-recommended doses, and 4) use without a primary indication. Three additional concepts address management of children receiving antipsychotic therapy: 5) access to psychosocial interventions, 6) metabolic screening, and 7) follow-up visits with a prescriber.

Clinical practice guidelines (CPGs) that summarize research and provide clinical recommendations have been used to develop guidance for states on psychotropic medications¹⁰ and can play a critical role in the information-gathering stage of quality measure development.¹⁴ First, CPGs can inform the decision to move forward with measure development. Ideally, measure concepts are supported by strong recommendations and high ratings of evidence by national guidelines. Second, guidelines may provide details that

refine measure concepts or inform measure definitions. Here we report on the NCINQ team's review of CPG recommendations relevant to the 7 quality concepts prioritized by stakeholders. We summarize relevant antipsychotic treatment recommendations, ratings of strength of recommendations (SOR) and evidence (SOE), and discuss implications for measure development. This information may be of clinical and policy interest, building on Administration for Children and Families' approach to developing guidance for states on psychotropic medications on the basis of endorsement by 2 or more guidelines¹⁰ in addition to contributing to NCINQ's measure development efforts.

Methods

The initial search was conducted April 2012 and was updated in September 2013. Guideline inclusion criteria were: 1) addressed measure concepts, 2) English-language publication in the United States since 2000, and 3) issued or used by a national organization, or developed with input from a national workgroup or advisory panel. First we conducted a search of the National Guidelines Clearinghouse and Guidelines International Network, PubMed, and PsychInfo using: "antipsychotic," "youth OR child* OR adolescen*," "guideline OR algorithm," yielding 5 guidelines meeting criteria.^{17,18,20–22} Second, the Web site of the leading child psychiatry professional association (American Academy of Child and Adolescent Psychiatry, AACAP) was examined, yielding 3 additional guidelines.^{23–25} Finally, 3 guidelines were recommended by the advisory panels: a Texas guideline²⁶ used by the national Medicaid Medical Directors Learning Network,⁵ a Canadian guideline¹⁹ considered highly relevant and methodologically rigorous, and the American Psychiatric Association's Choosing Wisely recommendations.²⁷ The 11 identified guidelines, including abbreviations used throughout, are summarized in Table 1. Two raters (EK, MF) reviewed the guidelines to extract relevant treatment recommendations and ratings of SOR and SOE. Seven guidelines provided formal ratings of their recommendations, but used different rating systems, and only two^{19,20} followed Institute of Medicine standards²⁸ for rating both SOR and SOE. To support comparisons across guidelines, the authors mapped CPG ratings to general categories of strong, moderate, or weak (Table 2).

Results

Table 3 summarizes guideline ratings for each quality concept, categorized as strong, moderate, or weak. Detailed treatment recommendations and ratings extracted from guidelines are summarized for each concept in Online Supplement B. Guideline recommendations and ratings for each quality concept are described below, highlighting similarities and differences.

Use of Antipsychotics in Very Young Children

Three guidelines (AACAP-AAA,²³ PPWG,²¹ and TX²⁶) address use of antipsychotics in very young children and highlight the lack of data on effectiveness and safety of antipsychotics in this population. AACAP-AAA strongly recommends caution, and a clinical review is triggered under TX guidelines. PPWG endorses psychosocial interventions as the treatment of choice in this age group, recommending antipsychotics only after

psychosocial interventions have failed. Guidelines vary in their definition of very young, with AACAP-AAA and PPWG using <6 years of age and Texas using <4 years of age.

Use of 2 or More Concurrent Antipsychotics

Four guidelines (AACAP-AAA,²³ AACAP-PsyMed,²⁴ T-MAY,²⁰ and TX²⁶) addressed the concurrent use of 2 or more antipsychotics as a practice to be avoided. AACAP-AAA rates this practice as “not endorsed,” and it triggers a clinical review in the TX parameters. SORs were strong for the 2 guidelines with ratings,^{20,23} while the 1 SOE rating was weak.²⁰ Guidelines clarify that concurrent use may be appropriate when transitioning from one medication to another, but did not specify duration.²⁴

High Doses of Antipsychotics

Five guidelines (AACAP-AAA,²³ AACAP-SZ,²⁵ TRAAY,²² T-MAY,²⁰ and TX²⁶) recommended conservative antipsychotic dosing strategies for children. Three guidelines endorsed a ‘start low and go slow’ approach,^{20,22,23} which AACAP-AAA rated with a moderate SOR. AACAP-SZ strongly recommended adequate dosing and reassessing dosing needs over time. Only 2 CPGs provided specific dose parameters,^{20,26} while AACAP-AAA states doses for children should not exceed the maximum recommended for adults.

Use of Antipsychotics Without a Primary Indication

Seven guidelines address use of antipsychotics in the absence of a primary indication such as psychotic disorder.^{18,20–23,26,27} Guidelines consistently recommend psychosocial treatments and safer medications before advancing to antipsychotics, with AACAP-AAA²³ rating the SOR as strong. Two other CPGs provide ratings of use of antipsychotics as second- or third-line treatment options, with SORs of strong to weak depending upon the child’s age and diagnosis.^{18,21}

Psychosocial Services

Seven guidelines address psychosocial services in the context of antipsychotic prescribing for children.^{17,18,20–23,25} Psychosocial services are recommended as first-line treatment for very young children,²¹ youth with aggression,^{20,22} and children with disruptive behavior disorders.¹⁸ In the absence of a primary indication, guidelines recommend psychosocial treatments before initiating an antipsychotic with strong SOR ratings,^{18,20,21,23} while concomitant psychosocial services for youth with schizophrenia²⁵ and bipolar disorder¹⁷ also had strong SOR ratings. Some guidelines recommended type and duration of psychosocial interventions.^{18,21,25}

Metabolic Screening

Eight guidelines recommend glucose and lipid screening for children prescribed antipsychotics.^{17,19–23,25,26} The specificity of recommendations for ongoing metabolic monitoring varies, with some guidelines recommending “appropriate” monitoring^{21,26} and others identifying specific tests and follow-up intervals.^{19,23} AACAP practice parameters^{17,23} endorse the consensus statement of the American Diabetes Association and American Psychiatric Association³¹ for fasting glucose and fasting lipid profile, while

CAMESA¹⁹ calls for more frequent monitoring in youth and additional monitoring of fasting insulin. Of the 5 guidelines with ratings,^{17,19,20,23,25} SORs are strong for baseline and ongoing monitoring, while CAMESA SOE ratings highlight higher evidence for baseline than follow-up, and differences among tests and medications.

Follow-up Visits

Six guidelines^{17,21,23–26} address follow-up with a prescriber for children and adolescents on antipsychotics, and the 3 guidelines that provide ratings characterize SORs as strong.^{17,23,25} Some guidelines specify visit content (assessment of medication efficacy and side effects, dose adjustments, medication adherence, and family support).^{24,25} Visit frequency is specified on the basis of severity of illness²⁵ and the need to monitor symptoms²¹ and side effects.^{17,23}

Discussion

To our knowledge, ours is the first study to summarize and compare recommendations and ratings for 11 guidelines addressing the use of antipsychotics in children. We build on earlier antipsychotic measure development efforts by multistate quality collaboratives^{5,15,16} by summarizing the level of guideline endorsement for stakeholders' high-priority quality concerns.

All 7 quality concepts were strongly endorsed by 1 or more guidelines, and 2 or more guidelines assigned their highest SOR ratings to 6 of the 7 concepts. Appropriate management concepts (psychosocial interventions, metabolic monitoring, and follow-up visits) had multiple guidelines consistently endorsing access to these services with strong SOR ratings. Appropriate-use recommendations focused on the sequence of treatments (eg, lower dose before higher doses, psychosocial interventions before antipsychotics in very young children or in the absence of a primary indication). Although 2 concepts (psychosocial interventions and metabolic screening) had both high SOR and SOE ratings, other guideline ratings were generally based on clinical consensus rather than scientific evidence. This reliance on consensus highlights both limitations in the evidence base and challenges in research, guideline, and measure development processes.

First, the current research paradigm in child psychiatry is focused on short-term efficacy and safety trials. Studies that test factors helpful to guidelines and quality measure development such as frequency of follow-up, timing of interventions, and choices and combinations of therapies are not priorities for most research funding agencies. Large health systems and pooled electronic health records may present new opportunities to examine a broader range of quality domains.

Second, guidelines are often generic in their recommendations for clinical care. Guidelines reviewed here offered some details that could inform measure definitions, including dosing parameters, age thresholds for “very young children,” allowing for concurrent use of multiple antipsychotics while changing medications, and reasons for medical follow-up that suggest frequency intervals. However, because of the heterogeneity of settings, patient populations, insurance and public health systems, and number and level of details needed,

guidelines cannot provide recommendations that fully meet the needs of measure developers. For example, guidelines recommend follow-up care but generally did not specify type or duration. A recent Institute of Medicine report²⁸ calling for clearer articulation of detailed recommendations may increase the utility of guidelines to support quality measure development.

Finally, the measure development process itself requires scientific evidence. The National Quality Forum has standardized domains of testing and review for proposed quality measures.³⁰ Moving from a quality concept to a fully specified measure requires multiple decisions on inclusion and exclusion criteria, periods of observation, and definitions of elements such as medication classifications, duration of medication trials, and visit type. A recent validation study of antipsychotic polypharmacy measures highlights the impact that varying definitions such as duration of concurrent use have on the operating characteristics of the measure.³² Evidence-informed consensus is needed on the types of standards most appropriate for different types of measure constructs, technical specifications, and testing domains. Guidance issued by the National Quality Forum³⁰ on evaluating evidence and measure testing may support development of measures that provide insight into population-based trends as well as individual prescribing practices.

Multiple stakeholders have identified the growing use of antipsychotics in children as an area of concern, but the lack of quality measures in this domain (as in other areas of child behavioral services¹²) complicates efforts to monitor and assess use. Robust quality measures are a critical tool for improving outcomes, increasing accountability, and aligning systems, providers, and patients toward common outcome and quality goals. On the basis of the guideline review presented here, NCINQ's multiple and diverse stakeholder advisory committees recommended moving forward with all proposed measure concepts, citing the importance of the topic and noting the measures address an opportunity to improve care for an area of urgent public health concern. The guideline review also helped inform measure definitions, which were refined through testing in Medicaid and managed care data and continued advisory panel reviews. As with other measures developed through the PQMP, the measures may be considered for implementation in national programs and will be made publicly available to support quality improvement and clinical decision making.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

National Guidelines Identified for Review Related to NCINQ Pediatric Antipsychotic Measure Concepts

Abbreviated Name	Sponsoring Organization and Guideline Title	Year	Population	Brief Description
AACAP-AAA	AACAP—Practice parameter for the use of atypical antipsychotic medications in children and adolescents ²³	2011 Web	5–18 y	19 recommendations on the use of atypical antipsychotics in children, rated using AACAP rating system.*
AACAP-PsyMed	AACAP—Practice parameter on the use of psychotropic medication in children and adolescents ²⁴	2009	18 y	13 best practice principles that underlie psychotropic medication prescribing for children (unrated).
AACAP-BP	AACAP—Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder ¹⁷	2007	18 y, bipolar disorder	11 recommendations on the treatment of bipolar disorder in children, rated using AACAP rating system.*
AACAP-ODD	AACAP—Practice parameter for the assessment and treatment of children and adolescents with oppositional defiant disorder ¹⁸	2007	18 y, oppositional defiant disorder	11 recommendations on the treatment of oppositional defiant disorder, rated using AACAP rating system.*
AACAP-SZ	AACAP—Practice parameter for the assessment and treatment of children and adolescents with schizophrenia ²⁵	2001	18 y, schizophrenia	Recommendations are embedded within a summary of the literature on treatment of schizophrenia in children, with some recommendations rated using AACAP system.*
CAMESA	CAMESA—Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children—Evidence-based recommendations for monitoring safety of second generation antipsychotics in children and youth ¹⁹	2011	18 y, on antipsychotic	Monitoring tests for children on antipsychotics are rated for SOR and SOE for 10 laboratory and 6 physical examination tests for each of 6 atypical antipsychotics, at 4 time points (baseline, 3, 6, and 12 mo) using the GRADE ^{29,33} system (total of 384 rated recommendations).
PPWG	AACAP-sponsored Preschool Psychopharmacology Working Group—Psychopharmacological treatment for very young children: Contexts and guidelines ²¹	2007	<6 y	9 treatment algorithms for the treatment of 9 diagnoses in preschool aged children with rated recommendations for each stage of the algorithm using an adaptation of the AACAP rating system.*
TRAAY	Center for the Advancement of Children's Mental Health—Treatment recommendations for the use of antipsychotics for aggressive youth ²²	2003	18 y, aggression	14 recommendations on the use of antipsychotics in the treatment of aggression in youth. Formal consensus methods are used and recommendations are unrated.
T-MAY	Center for Education and Research on Mental Health Therapeutics—Treatment of maladaptive aggression in youth ²⁰	2012	18 y, aggression	20 recommendations on the treatment of aggression in children, with ratings of SOE using Oxford Centre for EBM grading of evidence system ³⁴ and separate SOR ratings.
TX	Texas Department of Family and Protective Services—Psychotropic medication utilization parameters for foster children ²⁶	2013	Foster care	9 psychotropic prescribing practices that trigger a clinical review for children in foster care in Texas (unrated).
APA-CW	American Psychiatric Association—Choosing Wisely ²⁷	2013	Children and adults	5 questionable antipsychotic prescribing practices for children and adults, based on formal consensus methods (modified Delphi, >70% agreement).

NCINQ indicates National Collaborative for Innovation in Quality Measurement; AACAP, American Academy of Child and Adolescent Psychiatry; SOE, strength of evidence; and SOR, strength of recommendation.

* AACAP rating system is used for most AACAP guidelines (see Table 2 for definitions).

Table 2
Recommendation Rating Systems and Definitions Used by National Guidelines Related to Pediatric Antipsychotic Use

Guidelines*	Rating System	Rating Definition [†]			Not Endorsed [‡]
		Strong/Highest Rating	Moderate Rating	Weak Rating	
AACAP-AAA, AACAP-BP AACAP-ODD, AACAP-SZ	AACAP rating system [§]	Minimal standard/clinical standard: Rigorous/substantial empirical evidence (meta-analyses, systematic reviews, RCTs) and/or overwhelming clinical consensus; expected to apply more than 95% percent of the time	Clinical guideline: Strong empirical evidence (nonrandomized controlled trials, cohort or case-control studies), and/or strong clinical consensus; expected to apply in most cases (75% of the time)	Options: Acceptable but not required; there may be insufficient evidence to support higher recommendation (uncontrolled trials, case/series reports)	Not endorsed: Ineffective or contraindicated
CAMESA	GRADE ²⁹ system (includes SOR and SOE ratings)	SOR strong: 1A, 1B, 1C SOE high: 1A, 2A	SOE moderate: 2A	SOR weak: 2A, 2B, 3 SOE low: 1C, 2B, 3	
PPWG	Adaptation of AACAP rating system	A: Well-controlled RCTs, large meta- analyses, or overwhelming clinical consensus	B: Empirical evidence (open trials, case series) or strong clinical consensus	C: Single case reports or no published reports, recommendation developed by expert consensus (informal)	
T-MAY	Oxford Centre for EBM grading of evidence (A–D) system ³⁴ for SOE and separate SOR ratings	SOR very strong: 90% agreement SOE A: Consistent level 1 studies (eg, RCT)	SOR strong: 70–89% agreement SOE B: Consistent level 2 or 3 studies (eg, cohort or case control studies) or extrapolations from level 1 studies, B	SOR fair: 50–69% agreement SOE C: Level 4 studies (eg, case studies) or extrapolations from level 2 or 3 studies	SOR weak: <50% agreement SOE D: Level 5 evidence (eg, expert opinion without explicit critical appraisal) or troublingly inconsistent or inconclusive studies of any level

RCT indicates randomized controlled trial; SOE, strength of evidence; and SOR, strength of recommendation.

* See Table 1 for full names.

[†]To support comparisons of ratings across guidelines, ratings were grouped into the following categories: strong/highest, moderate, or weak.

[‡]Most guidelines used a “strong” recommendation against rather than “not endorsed” to indicate that a practice should be avoided.

[§] AACAP rating system is used for most AACAP guidelines.

Table 3
Strength of Recommendations and Evidence (When Available) Related to 7 Antipsychotic Measure Concepts

Strength of Recommendation and Evidence Ratings [‡] by Antipsychotic Measure Concept							
Guideline*	Use in Very Young Children	Multiple Concurrent Antipsychotics	Higher Than Recommended Doses	Use Without a Primary Indication	Access to Psychosocial Interventions	Metabolic Screening	Follow-up Visit With Prescriber
AACAP-AAA	Strong	Strong	Moderate	Strong	Strong	Strong	Strong
AACAP-PsyMed		Unrated					Unrated
AACAP-BP					Strong	Strong	Strong
AACAP-ODD				Moderate	Strong		
AACAP-SZ			Strong		Strong	Strong	Strong
CAMESA [†]						Strong (SOR) [‡] , high (SOE) [‡]	
PPWG [§]	Strong–weak [‡]			Strong–weak [‡]	Strong–weak [‡]	Unrated	Unrated
TRAAAY			Unrated	Unrated	Unrated	Unrated	
T-MAY		Strong (SOR), weak (SOE)	Unrated	Unrated	Strong (SOR), high (SOE)	Strong (SOR), high (SOE)	
TX	Unrated	Unrated	Unrated	Unrated		Unrated	Unrated
APA-CW				Unrated			
Totals							
CPG with recommendation	3	4	5	7	7	8	6
CPG with rated recommendation	2	2	2	3	6	5	3
CPGs with	2	2	1	2	6	5	3
SOR = strong							
CPGs with	0	0	0	0	1	2	0
SOE = strong							

CPG indicates clinical practice guidelines; SOR, strength of recommendation; and SOE, strength of evidence.

* See Table 1 for full names.

[‡] CAMESA provides ratings of both SOR and SOE and rate each antipsychotic medication, each time interval (0, 3, 6, 12 months) and each test separately. All combinations cannot be shown, but in general, testing is strongly recommended, and evidence is rated highest at 0 and 3 months.

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[‡] CPG ratings were categorized as strong/high, moderate, or weak to facilitate comparisons across guidelines (see Table 2). Most guideline rating systems did not rate strength of recommendation and evidence separately. To be conservative, we consider all ratings as SOR unless it is specified that the rating is for SOE.

[§] PPWG provides ratings for each step of treatment algorithms for 9 different diagnoses. All combinations cannot be represented; variation exists in ratings by diagnosis and age.