

Practice Parameter on the Use of Psychotropic Medication in Children and Adolescents

ABSTRACT

The purpose of this practice parameter is to promote the appropriate and safe use of psychotropic medications in children and adolescents with psychiatric disorders by emphasizing the best practice principles that underlie medication prescribing. The evidence base supporting the use of psychotropic medication for children and adolescents with psychiatric disorders has increased for the past 15 to 20 years, as has their use. It is hoped that clinicians who implement the principles outlined in this parameter will be more likely to use medications with the potential for pharmacological benefit in children safely and to reduce the use of ineffective and inappropriate medications or medication combinations. The best practice principles covered in this parameter include completing a psychiatric and medical evaluation, developing a treatment and monitoring plan, educating the patient and family regarding the child's disorder and the treatment and monitoring plan, completing and documenting assent of the child and consent of the parent, conducting an adequate medication treatment trial, managing the patient who does not respond as expected, establishing procedures to implement before using medication combinations, and following principles for the discontinuation of medication. *J. Am. Acad. Child Adolesc. Psychiatry*, 2009;48(9):961–973. **Key Words:** practice parameter, psychopharmacology, multiple medications, treatment.

During the past 15 to 20 years, there has been a marked increase in our understanding of childhood psychiatric disorders and a developing evidence base for both psycho-

pharmacological and psychosocial treatments. Children are commonly affected by psychiatric disorders, and without treatment, they can experience short- and long-term distress

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AACAP practice parameters are developed by the AACAP Work Group on Quality Issues (WGQI) in accordance with American Medical Association policy. Parameter development is an iterative process between the primary author(s), the WGQI, topic experts, and representatives from multiple constituent groups, including the AACAP membership, relevant AACAP components, the AACAP Assembly of Regional Organizations, and the AACAP Council. Details of the parameter development process can be accessed on the AACAP Web site. Responsibility for parameter content and review rests with the author(s), the WGQI, the WGQI Consensus Group, and the AACAP Council.

The AACAP develops both patient-oriented and clinician-oriented practice parameters. Patient-oriented parameters provide recommendations to guide clinicians toward best treatment practices. Recommendations are based on empirical evidence (when available) and clinical consensus (when not) and are graded according to the strength of the empirical and clinical support. Clinician-oriented parameters provide clinicians with the information (stated as principles) needed to develop practice-based skills. Although empirical evidence may be available to support certain principles, principles are primarily based on expert opinion derived from clinical experience. This parameter is a clinician-oriented parameter.

The primary intended audience for the AACAP practice parameters is child and adolescent psychiatrists; however, the information contained therein may also be useful for other mental health clinicians.

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and impairment. The current evidence base to address the treatment needs of these children comes from high-quality randomized controlled trials for most psychotropic medication classes (e.g., stimulants, antidepressants, antipsychotics) and for a number of manual-based psychotherapeutic approaches.¹

Despite the advances of the past 2 decades, the vast majority of children with mental health problems still do not receive appropriate evaluative and treatment services.² Reports of the increased use of psychotropic medications in children^{3,4} suggest that prescribers, parents, and patients view pharmacological treatment as an important intervention to reduce the symptoms of childhood psychiatric disorders. However, reports of increased psychotropic medication use has also led to concerns that some children and adolescents are being overdiagnosed with psychiatric disorders and are being treated with medication/s that are not appropriate for them. Strategies to address the overuse or inappropriate use of medications (e.g., the Food and Drug Administration advisory “black box” warning for antidepressants) may actually create barriers to care (e.g., decreased antidepressant prescription rates⁵) and may result in unintended negative consequences (e.g., increased teen suicide rate⁶). Rather than advocating for restricting access to medication treatment, this parameter advocates for high-quality assessment and prescribing practices to enhance outcomes for children and to address societal concerns about how children with psychiatric disorders are treated.

There is a great range of appropriate psychopharmacological practice, reflecting the range of medical specialties, levels of expertise, and clinical settings of today’s prescribers. The principles highlighted in this parameter are not intended to create a uniform approach for all prescribers. A single approach for all prescribers would not be applicable or practical and could inadvertently restrict children in need from access to effective treatments. By focusing on the decision-making principles that underlie optimal psychopharmacological practice, it is hoped that more children will have the opportunity to receive appropriate treatment with medication and reduce the exposure of children to medication interventions that may not be appropriate. Given the focus in this parameter on the best practice principles for using psychotropic medications in children and adolescents, there is limited discussion of the details of the psychiatric evaluation and details about medication and psychosocial treatments for specific disorders. The American Academy of Child and Adolescent Psychiatry (AACAP) practice parameter for psychiatric assessment⁷ addresses specific guidelines for the evaluation of children and adolescents, and the AACAP practice parameters for the assessment and treatment of specific disorders^{8–13} address the evidence base for psychopharmacological and psychosocial treatments in children and adolescents.

This parameter is divided into five sections: assessment, development of the treatment and monitoring plan, psychoeducation and assent/consent, implementation of the treatment and monitoring plan, and management of complex pharmacological interventions including medication discontinuation.

Prescriber refers to any clinician who has the capacity to evaluate children for and treat children with psychotropic medications (e.g., child and adolescent psychiatrists, general psychiatrists, pediatricians, family doctors, nurse practitioners). *Parents* refer to biological parents or legal guardians. *Disorder* refers to the target of treatment, whether it is a disorder or symptom cluster. *Psychoeducation* refers to the process of imparting information about a disorder and its treatment, both the generic information and information of specific relevance to an individual child and family.

METHODOLOGY

A literature review of relevant articles pertaining to psychopharmacology in children and adults was completed using the PubMed database. In addition, textbooks on pediatric psychopharmacology were reviewed as were their reference lists. In addition, a PubMed search on quality medical care and the overuse of medical testing (e.g., routine laboratory or radiological testing), other medical procedures considered to be used excessively (e.g., cesarean section), and other medical conditions that have historically been overdiagnosed or misdiagnosed and treated inappropriately (e.g., patients with viral infections treated with antibiotics) provided background for this parameter.

GENERAL BACKGROUND

The increased use of psychotropic medications^{3,4} and psychotropic medication combinations^{14,15} to treat childhood psychiatric disorders reflects a deservedly larger role for medication treatment of childhood psychiatric disorders. A number of factors have likely influenced this increased use including increased support for the biological basis of some childhood psychiatric disorders, a developing evidence base demonstrating the efficacy of psychotropic medications in children and adolescents, advocacy efforts to identify and treat the large number of children with psychiatric disorders, reductions in funding and changing patterns of reimbursement for mental health care, and the marketing efforts of pharmaceutical companies to prescribers and consumers.

Advances in neuroscience suggest that childhood psychiatric disorders can be associated with abnormalities in neurotransmitters and/or structural or functional abnormalities of specific brain regions and/or the circuitry that interconnect

affected brain regions. These abnormalities may be caused by environmental factors, genetic factors, or their combination. Neurobiological explanations of childhood psychiatric disorders are often used to support the use of psychotropic medications for childhood psychiatric disorders (see Martin et al.¹⁵ for a review).

The current evidence base in child psychopharmacology includes basic and clinical research, which supports the safe and effective use of psychotropic medications (e.g., randomized controlled trials, studies of what the body does to the medication [pharmacokinetics], and what the medication does to the body [pharmacodynamics]). Efficacy and safety data are available for single pharmacological agents in the short-term treatment of a number of childhood psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD)¹⁶; major depressive disorder^{17–20}; obsessive-compulsive disorder (OCD)^{21–25}; other anxiety disorders including separation anxiety disorder, social phobia, and generalized anxiety disorders^{26–32}; and mania and tic disorders.³³ There is also evidence supporting the use of medications for aggression and serious problems with impulse control in children with disruptive behavior disorders^{34,35} and autism.³⁶ For disorders that present similarly in childhood, adolescence, and adulthood (e.g., schizophrenia), data from adult studies¹² and from extensive clinical practice⁸ can guide medication choices for children and adolescents. The evidence for short-term safety and efficacy is complemented by increasing information about the longer term safety and usefulness of some medications in children and adolescents.^{37–39}

In contrast to what is known about treatment with a single psychotropic medication, there is a smaller evidence base supporting the efficacy of medication combinations.⁴⁰ Psychotropic medication combinations are commonly used to address complex comorbid presentations,^{41–43} to enhance outcome for treatment-refractory or partially responsive patients,^{43,44} to manage side effects of an effective agent (e.g., anticholinergic medication for extrapyramidal symptoms), or to address symptoms hypothesized to be associated with multiple underlying neurotransmitter abnormalities (e.g., dopamine agonists for hyperactivity and serotonin agonists for anxiety⁴⁵). Although the design of studies of a single medication is relatively straightforward (e.g., randomized controlled trials), studies of medication combinations, combining medication and psychotherapy,^{18,32,46} and studies to address the sequence of treatment for complex presentations require more complex study designs⁴⁷ and are more costly to implement (e.g., Sequenced Treatment Alternative to Relieve Depression). The cost and complexity of these studies may partially explain the lack of such studies in children and adolescents.

The evidence base on which prescribers depend to make treatment decisions includes a medication's product infor-

mation as well as the larger medical literature. The product information for a specific medication, developed cooperatively by the pharmaceutical manufacturer and the Food and Drug Administration, generally reflects the evidence from studies sponsored by the pharmaceutical manufacturer, is geared toward marketing for a specific indication, and does not always reflect the evolving evidence base that may include investigator-initiated and federally funded postmarketing studies. Consequently, prescribers may have to rely on the reports of randomized controlled trials in the medical literature, consensus guidelines, and practice parameters, as well as the product information to effectively practice evidence-based psychopharmacology. For some psychiatric disorders, prescribers may use psychotropic medications "off-label" (e.g., selective serotonin reuptake inhibitors [SSRIs] for non-OCD anxiety disorders^{26–28,32}) or inconsistent with the product labeling (e.g., stimulants for children with ADHD and tic disorders⁴²) to best address the treatment needs of children and adolescents and to be consistent with the standard of care.

Advocacy efforts by the federal government such as Surgeon General Satcher's National Action Report,² practitioner organizations (e.g., AACAP, American Academy of Pediatrics, American Psychiatric Association), and family and patient support groups (e.g., National Alliance on Mental Illness, Children and Adults with Attention-Deficit/Hyperactivity Disorder) have educated the public regarding the need for evaluation and treatment services for childhood psychiatric disorders. Advocacy has likely resulted in decreased stigma and increasing interest in and use of mental health care, including pharmacotherapy.

For the past 10 to 15 years, significant changes in mental health services, including a shortage of child and adolescent psychiatrists, limitations in insurance coverage for inpatient and partial hospital programs, and fewer outpatient psychotherapy services by psychiatrists, may have also contributed to increase in psychotropic medication use.^{48,49}

Finally, the increased use of psychotropic medications has been attributed to the direct financial role of the pharmaceutical industry in funding clinical trials,⁵⁰ financial support to investigators,⁵¹ for resident training and continuing medical education,⁵² and direct-to-consumer advertising.⁵³ Although it has been repeatedly asserted that financial support for research and medical education at all levels has increased the use of psychotropic medications, it is difficult to quantify and to prove conclusively.⁵⁴ Direct-to-consumer advertising on television, which increased dramatically in the mid-1990s, has been posited as eliciting inappropriate demand that leads to inappropriate prescribing, yet direct-to-consumer advertising has also been demonstrated to be a helpful educational tool to increase awareness of treatment options for disorders that are undertreated or stigmatized, such as depression.⁵⁵

The purpose of this practice parameter is to promote the safe and appropriate use of psychotropic medications in children and adolescents with psychiatric disorders by emphasizing the best practice principles that underlie medication prescribing. There are multiple steps involved in the use of psychotropic medication in children and adolescents. First, the prescriber is responsible for completing an evaluation of the patient and family. The evaluation leads to a diagnostic formulation and the development of a psychosocial and psychopharmacological treatment plan based on the best available evidence. The pharmacological treatment plan includes not only an adequate medication trial but also strategies for preparing the patient and family and monitoring outcome and side effects. Before initiating the medication treatment plan, the patient and family need to be educated about the child's problem, treatment options, and the treatment and monitoring plan. The education of the patient and parent sets the stage for obtaining assent for treatment from the child and consent from the parents. Treatment is initiated according to the treatment plan with strategies to monitor for both benefits and side effects. Once the patient is stabilized on medication, monitoring visits occur regularly and predictably enough to enhance the patient's and family's confidence in the treatment and prescriber and to ensure effective management of longer term treatment and safety issues. Finally, if clinically indicated, the clinician, patient, and family identify a time for a medication discontinuation trial and have a plan for follow-up that will allow children to discontinue medication with minimal risk for an unmonitored relapse/recurrence of symptoms.

The prescriber establishes procedures to implement these tasks and uses them routinely to provide high-quality care that integrates the psychopharmacological evidence base, state-of-the-art clinical skills, and the patient's and family's needs and values. The clinician who establishes a high-quality approach to assessment and treatment will hopefully practice more consistently and have patients and families who understand, adhere to, and actively participate in the intervention and assessment of outcome. A proactive and positive approach may also decrease the stigma that some children and their parents experience from participating in psychiatric care. For clinicians who do not use a rigorous consistent approach to assessment and treatment, it is possible that they will introduce unacceptable variability into the pharmacological treatment of children, underuse psychosocial and pharmacological treatment approaches, and succumb to the use of ineffective treatment approaches or inappropriate medications or medication combinations. Children and families who do not receive high-quality mental health care may become demoralized by their care experience and may drop out of treatment or not seek treatment in the future. It is also possible that poor quality of psychiatric care may affect the

public's perception of prescribers of psychotropic medications and lead to a loss of public support for psychiatric treatment services.

PRINCIPLES

Assessment

Principle 1. Before Initiating Pharmacotherapy, a Psychiatric Evaluation Is Completed. The psychiatric evaluation⁷ is comprehensive enough to identify symptoms best addressed pharmacologically and best addressed with psychosocial treatments and to identify psychosocial factors that may impede an adequate and safe medication trial or confound the assessment of outcome. A comprehensive evaluation increases the likelihood that medication interventions will be well conceptualized and hopefully reduces the likelihood of treatment failure and poor adherence. Attention to psychosocial factors in the evaluation helps to ensure that psychosocial approaches are included in the treatment plan.

The psychiatric evaluation includes interviews with both the child and parents. During the assessment, the confidentiality needs of both the child and parents are balanced against the need for all involved to have a common information base on which to make treatment decisions. A review of previous records to assess past successful and unsuccessful treatments can enhance the likelihood that proposed intervention will be the next logical treatment step and reduce the chance that previously ineffective treatments will be used again.

Principle 2. Before Initiating Pharmacotherapy, a Medical History Is Obtained, and a Medical Evaluation Is Considered When Appropriate. Because a medication intervention in a child is a significant medical event, it is prudent to complete a medical evaluation to ensure that the child has no medical problem accounting for the psychiatric presentation and is healthy enough to participate in a medication trial with minimal risk. For example, the medical history helps to determine whether the child has any current or past medical problems; is taking any medications including prescribed medications, over-the-counter medications, complementary/alternative treatments, or illicit substances; has medication allergies; or has a personal or family history of medical problems associated with increased risk for side effects (e.g., a personal history of a structural cardiac abnormality before starting stimulants or family history of malignant arrhythmias or sudden cardiac death before starting atypical antipsychotics).

Targeted medical testing may be appropriate to establish a medical baseline before initiating medications with known risks (e.g., height and weight for stimulants¹³; height, weight, and lipid testing for antipsychotics⁵⁶). Although a routine history,

physical, and laboratory testing completed by a pediatric specialist is not necessary before starting most psychotropic medications, completing such an evaluation just before starting medication may be useful to document that a child is healthy and establishes a normal baseline. Such a medical screening evaluation may also put the patient, family, and prescriber at ease and thereby facilitate the initiation of the medication trial. Specific recommendations regarding medical screening are included in specific AACAP practice parameters for disorders for which medication treatments have proven benefit (e.g., ADHD, anxiety disorders, mood disorders).

Principle 3. The Prescriber Is Advised to Communicate With Other Professionals Involved With the Child to Obtain Collateral History and Set the Stage for Monitoring Outcome and Side Effects During the Medication Trial. Good communication and coordination among medical, mental health, and education professionals involved in the child's life is important for the safe and effective use of psychotropic medications. Communicating with these professionals during the evaluation process ensures that the evaluation is complete and sets the stage for subsequent interactions during treatment. Early communication also elicits the support of key professionals for the treatment plan (e.g., pediatricians who provide ongoing medical care, school nurses who may dispense medication, teachers who may be involved in evaluating the outcome) and may reduce the chance of misunderstandings during treatment. Follow-up among professionals during treatment enables all professionals involved to be up to date with the treatment plan and that treatment is well coordinated.

Treatment and Monitoring Plan

Principle 4. The Prescriber Develops a Psychosocial and Psychopharmacological Treatment Plan Based on the Best Available Evidence. After completing the evaluation, the prescriber organizes the case material into a diagnostic formulation that considers biological, psychological, and social etiologies for the patient's problems. The treatment plan will include strategies to ready the patient and family for treatment, the specific pharmacological and psychosocial treatments necessary to address the various targets of treatment, the timing and sequencing of psychosocial and psychopharmacological interventions, and the strategies for monitoring outcome and side effects. Pharmacological treatments can be initiated before, concurrent with, or after psychosocial treatments, depending on the evidence base and needs of the patient.

Treatment with medication can be considered to have three phases: an acute phase, which includes the initiation of medication treatment and subsequent dose adjustments to maximize response and minimize side effects; the mainte-

nance phase, during which responders to treatment consolidate their gains and remission or recovery occurs; and a discontinuation phase during which, if clinically indicated, medication is successfully tapered with minimal risk for relapse/recurrence.⁵⁷ The initial discussion of the treatment plan with the patient and family includes a discussion of the goals and approaches used in all phases of treatment.

At the beginning of the acute phase of treatment, psychosocial interventions to address patient and family factors that may impede the medication trial (e.g., inadequate supervision of medication adherence) or the assessment of outcome (e.g., parental lack of an understanding of target symptoms or common side effects) are initiated. Most clinicians will address this as part of the psychoeducation of the patient and family.

The plan for the medication trial is specific: starting dose, timing of dose changes, estimated maximum dose or blood level, strategies for monitoring and managing medication side effects, duration of the trial, assessment strategies (e.g., self-reports, parent reports, teacher reports), and alternative treatment strategies if the child is partially responsive or the trial is not successful. The AACAP practice parameters for specific disorders referenced above describe the detailed strategies for choosing a medication, starting doses and adjustment schedules, trial duration, and monitoring outcome and common side effects.

Traditionally, psychosocial treatment is recommended before pharmacological treatment. However, data are increasingly available from comparative treatment trials to guide the selection of first-line treatment. To date, randomized controlled trials suggest that medication management for ADHD is the first-line treatment¹⁶ and that medication combined with behavioral treatment may be required for optimal outcome in children with more complex problems.⁵⁸ For OCD, beginning with cognitive-behavioral therapy, especially if delivered by expert psychotherapists, or combined treatment is the best first option.⁴⁶ In contrast, the Treatment of Adolescent Depression Study demonstrated efficacy for combination therapy and medication management but not for cognitive-behavioral therapy alone at 12 weeks, suggesting that beginning with psychotherapy only in moderate to severe depression may not be the best first step.¹⁸

Prescribers are guided by the evidence base in developing their treatment plan. However, the evidence base for pediatric psychopharmacology is far from complete⁴⁰ and may not be specifically applicable or adequate to maximizing outcome for the child. For example, when the severity of the child's problem is such that the disorder precludes active participation in targeted psychosocial treatment (e.g., OCD with psychotic symptoms), beginning with medication and supportive psychological treatment may be a reasonable approach. Also, although empirically supported psychosocial treatments may

be first line as in OCD, many communities lack skillful providers of such treatments. In these communities, starting treatment with medication may be the only evidenced-based intervention practically available.

At some point in the transition from the acute phase to the maintenance phase of treatment, the prescriber reviews the progress to date and discusses the plan for maintenance treatment. The discussion of maintenance treatment goals is often easier for patients and parents than the discussion of initiating treatment, as moving into the maintenance phase suggests that the patient has experienced some benefit and satisfactorily has passed through the period for acute side effects. The frequency of visits during the maintenance phase reflects the goals of maintaining response and adherence, reducing functional impairment, and monitoring for late-onset side effects (e.g., tardive dyskinesia) or side effects of accumulating significance (e.g., weight gain, slowed growth) and the development of co-occurring conditions.

If the patient has evidenced a sustained period of remission or recovery and the prescriber believes that the medication may no longer be necessary, a discontinuation trial may be clinically indicated. Before initiating a discontinuation trial, the plan for discontinuation is reviewed with the patient and family focusing on the risks of discontinuation (e.g., the risks for withdrawal symptoms and the risk for relapse or recurrence of symptoms) and the treatment plan if symptoms return. This is especially important if the patient was significantly impaired or suicidal before medication treatment. A specific plan for tapering and discontinuing medication and appropriate frequency of monitoring visits prevents withdrawal effects of medication and allows the clinician to identify early relapse/recurrence of symptoms. Monitoring children for a period of time after they are off medication allows for early identification of relapse/recurrence before symptoms become too severe.

The AACAP practice parameters, consensus guidelines, and treatment algorithms (e.g., Texas Medication Algorithm Project, <http://www.dshs.state.tx.us/mhprograms/TMAPover.shtml>) provide detailed information about treatment approaches to patients with various disorders at the various phases of treatment.

Principle 5. The Prescriber Develops a Plan to Monitor the Patient, Short and Long Term. Many factors are involved in determining a monitoring strategy for children on psychotropic medications including the type of medication, the risk for and timing of onset of side effects, the patient's need for ongoing psychological support, the patient's and family's risk for nonadherence, and the phase of treatment. Discussion of the monitoring plan with the patient and family includes the frequency of visits and methods used to assess outcome and side effects. The frequency of visits is determined by the need

for dose titration, by the timing of onset of side effects, and to maintain the doctor-patient-family relationship. For example, medications that require multiple upward adjustments in dose may require more frequent visits initially than medications with fewer dosing adjustments. Monitoring medications with significant early-onset side effects (e.g., appetite suppression and insomnia on stimulants) would lead to more frequent early visits; monitoring for late-onset side effects (e.g., change in growth trajectory on stimulants) require at minimum the frequency of visits to ensure that side effects are detected. Follow-up visits are also an opportunity to provide psychosocial support, to address stressors and problems with adherence. Using rating scales in follow-up visits can be helpful to follow symptom severity; similarly, systematically documenting information on drug-specific side effects (e.g., weight gain, height, blood pressure) may be useful. The AACAP practice parameters for specific disorders (referenced above) offer guidelines on appropriate monitoring strategies. The clinician, patient, and family should develop an individualized monitoring plan appropriate to the needs of the patient and family and consistent with the prescriber's role in treatment.

During the maintenance phase, visits may not need to occur frequently. For example, children and adolescents with stable high-quality response and good adherence can be seen as infrequently as two to four times per year. Children and families under psychosocial stress or who have problems with adherence may need more frequent visits to maintain a high-quality outcome.

During the discontinuation phase, patients may actually need to be seen more frequently than during the maintenance phase. Close monitoring as the dose of medication is being lowered and, for a period of time thereafter, ensures that withdrawal symptoms and early signs of relapse/recurrence are identified quickly.

There are few data to help determine how long to monitor a child after the discontinuation of medication; however, the duration of follow-up reflects the risk for relapse in the short term and risk for recurrence of illness over the longer term. For example, in children with anxiety disorders, a monitoring period off medication of up to 6 months may be reasonable, given the time and financial burden of such follow-up and the low risk for relapse/recurrence for children who remain asymptomatic 6 to 12 months after treatment has been discontinued.⁵⁹ After discontinuation, visits may occur more frequently in the first few months and less frequently thereafter. It may be useful to schedule such follow-up visits before high-stress periods (e.g., the start of school for children with separation anxiety) or periods of known risk for recurrence (e.g., winter for seasonal affective disorder). For major depressive disorder and other disorders with a high risk for recurrence, it may be prudent to monitor children who

have discontinued medication at low frequency into adulthood.

Principle 6. Prescribers Should Be Cautious When Implementing a Treatment Plan That Cannot Be Appropriately Monitored. Implementing a pharmacological intervention requires extra caution in clinical situations in which there are barriers to monitoring the patient for outcomes and side effects. For example, a pharmacological trial is more challenging to implement when there is inadequate adult supervision, limited patient and family investment in treatment, or a high risk for nonadherence. Barriers to monitoring outcome and adherence increase the risk that the medication trial may be deemed unsuccessful or incomplete and increase the risk for inappropriate dosing, frequent medication switches, or the use of medication combinations. For example, if a prescriber is unaware that medications are not provided as planned, the prescriber may unknowingly increase the dose or add a second medication.

Assent and Consent for Treatment

Principle 7. The Prescriber Provides Feedback About the Diagnosis and Educates the Patient and Family Regarding the Child's Disorder and the Treatment and Monitoring Plan. After completing the evaluation and developing the treatment and monitoring plan, the prescriber educates the patient and the family about the child's problems, treatment options, and the treatment/monitoring plan. Such psychoeducation of the patient and family prepares them to assent and consent for treatment. The psychoeducation of the patient and family addresses the target of treatment, including the disorder's signs and symptoms; the course, including common complications (e.g., risk for oppositional behavior in children with ADHD) or potential for evolution of symptoms over time (e.g., recurrent depression may ultimately evolve into bipolar disorder); and the long-term prognosis (e.g., tic severity generally improves in late adolescence).⁶⁰ Specific risk factors (e.g., poor parenting skills) and protective factors (e.g., academic ability) that may affect the outcome of treatment also can be discussed. Negative attitudes about medication and the risk for adverse psychological reactions to taking medications in some children and their families are to be addressed directly.⁶¹ The specifics of the medication treatment plan are provided: generic and trade name of the medication, starting dose, timing of dose changes, estimated peak dose or blood level, strategies for monitoring and managing medication side effects, duration of the trial, assessment strategies (e.g., self-report, parent report, teacher report), alternative treatment strategies, and the plan if the child does not respond as expected. Providing high-quality printed information from reliable sources about the proposed medication (e.g., U.S.

Pharmacopoeia handouts) can be a useful adjunct to in-person psychoeducation.

To put the specific child's treatment plan into context, the prescriber discusses how his or her plan for the patient and family reflects the evidence base and relates to the usual care in the local community (i.e., the plan is more or less intensive than usual care or consists of medication management only or psychotherapy only). This information provides the patient and family an opportunity to evaluate the prescriber's plan vis-à-vis the evidence base and the practice pattern of other prescribers. Although the spectrum of clinical practice is broad, the prescriber should be familiar with the standard of care within his or her community and be able to communicate how he or she practices pharmacotherapy. As pharmacological treatment of childhood psychiatric disorders is increasingly a topic in the media, the prescriber's understanding of recent controversies (e.g., SSRIs and suicidality) and how they have an impact on treatment planning is critical to prescribing psychotropic medications to children.

Extended psychoeducation to address specific attitudinal or psychological issues regarding medication and/or specific psychosocial interventions to stabilize the home environment may be necessary to ready some patients and families to effectively implement or monitor a pharmacological treatment trial.⁶² For example, some teenagers may see taking medication as making them only "different" but not "better." Similarly, some families may not understand their child's difficulties from a psychopharmacological point of view (e.g., "He doesn't need medication, he just won't listen."), have difficulty understanding how medication may be useful (e.g., "Aren't all teenagers moody?"), have too high (or too low) expectations for medication treatment, or worry excessively about side effects.

For the effective implementation of the trial, prescribers need to clarify who is responsible for the various elements of the treatment plan. The responsibility for some elements may fall to the family and some to other professionals involved with the child (e.g., teacher ratings during stimulant treatment). Parents are ultimately responsible for storing medication safely and monitoring medication adherence, benefits, and side effects. Empowering the child to identify and communicate benefits and problems with the medication trial is also important. Although there can be variability in how children and families choose to implement pharmacological treatment (e.g., older teens taking more responsibility for taking their medication), being clear with the patient and family regarding their specific roles and responsibilities in treatment and strategies for managing his or her medication may improve adherence and enhance outcome. The prescriber also needs to be clear with the family about his or her role in treatment. Some prescribers restrict their role to pharmacotherapy only, others will prescribe medication only

if they are also responsible for the psychotherapy, and some who can prescribe may restrict their practice to assessment/consultation or psychotherapy only. Patients and their families may not always understand that prescribers can delimit their role in these ways and may expect the prescriber to function more comprehensively. Clinicians who limit the range of interventions provided may unwittingly implement a treatment plan that does not address the complexity of the patient's problems. For example, it is possible that patients who receive medication management only may not have their psychosocial needs assessed or treated and run the risk of being given medications to address problems that might be better addressed through psychosocial interventions. Similarly, clinicians who only practice psychotherapy may not use medications when clinically appropriate.

Principle 8. Complete and Document the Assent of the Child and Consent of the Parents Before Initiating Medication Treatment and at Important Points During Treatment. Assent and consent is considered an ongoing process of relationship building with both the patient and the family that begins with the evaluation and continues after treatment has been initiated. A specific assent/consent discussion before initiating a new medication treatment provides an opportunity for the prescriber to summarize the findings from the assessment, for the prescriber to present the treatment/monitoring plan, and for the child and parent to have their questions and concerns addressed. The assent/consent procedure also provides the clinician an additional opportunity to assess what the patient and family understands of the child's problems and their readiness and commitment to participate in treatment. After treatment has begun, the prescriber continues to assess whether the family and patient truly understand the process in which they are involved and determines whether the family is providing ongoing assent/consent for the care they receive.

As assent/consent is an ongoing process; it is recommended that before initiation of any additional psychotropic medications, at the transition to the maintenance phase, and before a discontinuation trial, the prescriber, patient, and family review the rationale for treatment; the past treatment experience; and the benefits, risks, and alternative treatments for each additional medication or the next phase of treatment.

Prescribers should document in the patient's medical record the initial assent/consent procedure as well as ongoing assent/consent during treatment. The documentation does not have to be extensive, but it does need to reflect adequately what occurred in the discussion with the patient and family. It is also useful for the prescriber to document that the patient and family had an opportunity to ask questions and have them answered and that the family understood the nature of the target of treatment and the specific risks and benefits of treatment.

The duration of the assent/consent procedure will vary, depending in part on how well the prescriber has prepared the patient and family. Many of the issues to be addressed during assent/consent are part of the prescriber's psychoeducation of the patient and family. The assent and consent discussion for most patients and families can be completed in a single session.

Principle 9. The Assent and Consent Discussion Focuses on the Risks and Benefits of the Proposed and Alternative Treatments. The content of assent/consent discussion should meet the current ethical and medical-legal standards. As consent standards evolve over time, and are tailored to meet the needs of the patient and family, it is critical for prescribers to be aware of the standard of care in their specialty, their community, and more specifically what patients and families need to know to actively participate in the treatment. A variety of resources are available to clinicians about the standards for consent; however, most published information concerns informed consent for research. For more specific information about the consent standard for prescribers in clinical practice, a discussion with the prescriber's malpractice carrier may be helpful.

Basic information provided during assent/consent would include the target of treatment, that is, signs and symptoms present in a particular child; the potential for benefit and side effects; the risks of not treating with medication; the timing and method of assessing outcome and side effects; the time commitment for treatment and monitoring; a description of the usual care in the community, including treatment alternatives (e.g., both medication and psychosocial alternatives) and their respective benefits and risks; a clear expectation that the family and patient will participate actively in the trial; and what to do if problems develop in treatment or the child does not respond as expected.

The prescriber has the responsibility to place the benefits and risks of the medication trial into perspective for the patient and family. For example, it can be helpful for parents to understand that the goal of the acute phase of treatment is to know how well their child responds to a medication and that the vast majority of side effects encountered during the acute phase (e.g., stomachaches, sedation, insomnia) respond to dose reduction or discontinuation and have little lasting significance. If the child responds, then the parents have to decide whether to transition to the maintenance phase of treatment. Thus, at the end of a successful short-term trial, patients and parents are weighing the observed benefit of medication against the acute side effects and potential for any longer term risks of the medication. Reassuring patients and parents that the prescriber will discontinue medications that are not useful or have unacceptable side effects may increase patients' and parents' comfort with starting medication.

Although it is not possible to provide a full and complete description of all the potential benefits and risks of the

proposed treatment and alternative treatment options, patient and parents should understand that some children respond well to medication treatment, and some do not respond at all. Common and expectable risks of the medication as well as patient- and family-specific risks (e.g., the potential for added risk for antipsychotic-induced weight gain in a child with obesity and a family history of type II diabetes) are discussed. Adverse events that may have prognostic significance (e.g., switching to mania on antidepressants) are rare, but clinically important adverse events (e.g., development of suicidal ideation during the medication treatment of depression) are also discussed. It may also be useful to discuss with patients and families that unexpected, unique, and perhaps even life-threatening events may occur during the course of treatment that may or may not be related to medication (e.g., sudden unexpected cardiac death). Although general information about the medication plan are shared, issues of specific relevance to the patient and family are also discussed (e.g., alcohol use and unprotected sex during medication treatment for at-risk teenagers) and addressed (e.g., problems with pill swallowing in younger children and teenagers' concerns about taking medication at school or on overnight activities). As many families may learn about medication benefits and risks in the popular media, specifically addressing the controversies regarding the use of medication for childhood psychiatric disorders may be useful (e.g., suicidality associated with antidepressant use and the cardiac risks of stimulants). Much of the information discussed during assent/consent may not be retained by the patient and family, and periodic review of the goals of treatment, as well as risks and benefits of treatment, may be required.

Clinicians should confidently provide information regarding risks and benefits and then put the treatment recommendation into context: How important is it to consider medication? What is a reasonable time frame for patients and parents to deliberate? For example, in a child with excellent coping and mild to moderate depression, it may be advisable to attempt a trial of psychotherapy first⁶³ or to allow the family and patient more time to consider pharmacological treatment. On the other hand, it may not be appropriate for parents to delay pharmacological treatment of a depressed and suicidal teenager because of concerns regarding the risk for readily managed side effects. Emphasizing the benefits and minimizing the risks of pharmacological treatment to enhance the chance that the family and patient will agree to a medication trial is not consistent with good clinical care. The prescriber–patient relationship may be harmed, if the discussion of side effects is not detailed enough and significant adverse effects occur.

Prescribers are encouraged to have a similar discussion before adding additional medications and before the transition to maintenance and discontinuation phases.

Implementation of Treatment

Principle 10. Implement Medication Trials Using an Adequate Dose and for an Adequate Duration of Treatment. For most medications, there is a dose level of the medication (measured by milligrams per day, milligrams per kilogram per day, or blood level) and duration of the treatment trial (based on pace of upward adjustment and time frame for observing a response) that will qualify a medication trial as adequate. For example, stimulants can be dosed empirically or on milligrams per kilogram per dose or milligrams per kilogram per day basis. An older child may require larger doses and more upward dose adjustments than a younger and smaller child; therefore, the trial may take longer for older and larger children. Antidepressants do not work as quickly as stimulants and may require upward of 8 weeks of treatment on an optimal dose to identify a response (Child Medication Algorithm Project—MDD Tactics, <http://www.dshs.state.tx.us/mhprograms/mddpage.shtm>). Completing a trial of adequate dose and duration gives the child the best chance to be able to benefit from a single medication. The outcomes of medication trials that are not adequate in either dose or duration are difficult to interpret. Inadequate medication trials may increase the risk that children will not have the opportunity to benefit or put children at risk for multiple medication switches or medication combinations. For example, a child given too low a dose because of unrealistic concerns about side effects may fail to respond. Yet because the child was exposed to medication, the patient, family, and prescriber may consider the child a “nonresponder” and then treat the child with second-line medications or multiple medications.

Principle 11. The Prescriber Reassesses the Patient if the Child Does Not Respond to the Initial Medication Trial as Expected. A variety of factors can be involved in an unexpected lack of response to a medication trial: the original assessment was not accurate (e.g., comorbid disorders or psychosocial factors were unaccounted for or not addressed adequately), the family was not ready to implement and participate in the trial, the trial did not include an adequate dose or duration of medication treatment, or there was poor adherence. If the acute phase trial was adequate in dose, duration, and adherence, then a reassessment of the patient is appropriate. The reassessment can include a review of the original assessment and treatment plan, an actual psychiatric reassessment of the patient, or outside consultation.

Prescribers need to be particularly alert to mistaking behavioral and emotional reactions to psychosocial stressors as symptoms of an underlying biological illness. Such misattribution can occur not only during the initial evaluation but also during treatment. For example, children recovering from a major depressive disorder may have persistent academic and social disability and may become irritable when

facing academic or social challenges. If the irritability is part of the mood disorder, then medication treatments may be appropriate. If, however, the irritability is related to the challenge of getting back to the previous level of functioning after a significant depressive episode, then psychosocial interventions may be more useful. The problem of using medications to address “all” of a patient’s symptoms is not isolated to prescribers. Other stakeholders in the child’s life (e.g., parents, teachers) may also believe that fluctuations in “symptoms” need to be addressed by medication changes or additions. The prescriber who does not appreciate the need for combined psychosocial and psychopharmacological treatment for children with concomitant psychosocial problems (e.g., ADHD with oppositional defiant disorder⁵⁸) may unnecessarily expose the child to increasingly complex pharmacological treatment strategies.

Principle 12. The Prescriber Needs a Clear Rationale for Using Medication Combinations. Before the use of medication combinations, the prescriber needs to develop a treatment and monitoring plan, educate the patient and family, obtain assent/consent, and then implement the treatment trial as described under the principles above.

Commonly used psychotropic medication combinations include the following: medication combinations used to treat multiple disorders in the same patient (e.g., a stimulant and an SSRI for ADHD and anxiety⁴¹ or an antipsychotic and an SSRI for tics and OCD⁴³), medication combinations that offer unique treatment advantages for a single disorder (e.g., the addition of lithium to ongoing antidepressant treatment⁴⁴), and medication combinations to address side effects of an effective agent (e.g., benztropine for extrapyramidal symptoms secondary to an antipsychotic).

Although it is possible that combining medications from the same class may have empirical support in the future, there is limited support for such approaches at this time. For example, there is limited evidence in children and adolescents for the use of two antidepressants or two antipsychotics as an initial treatment approach or as a specific endpoint for treatment. However, it is not uncommon for patients to be taking two antidepressants or two antipsychotics at the same time when transitioning from one medication to another. For bipolar disorder in adults, data do support the use of two mood stabilizers,⁶⁴ and there is preliminary support for the use of similar strategies in children with bipolar disorder.⁶⁵ In addition, two stimulant formulations (i.e., short and long acting) may be used to “sculpt” dosing for coverage of extended periods of time.¹³

Evidence supporting medication combinations based on a matching medication mechanism of action with a hypothesized underlying central nervous system abnormality is rudimentary at best. For example, there is limited data to support

the use of two antidepressants to cover two neurotransmitter systems (i.e., using a serotonergic and a noradrenergic antidepressant for a certain profile of depressive symptoms). Basing treatment decisions on theories about central nervous system functioning or clinical correlates of hypothesized neurotransmitter abnormalities (e.g., specific symptom profiles, EEG, single-photon emission computed tomography testing) may put patients at risk for unnecessary medication combinations “to cover the neurotransmitter bases” or “to treat the EEG or single-photon emission computed tomography results.”

Principle 13. Discontinuing Medication in Children Requires a Specific Plan. More is known about starting children on medication than about how long to treat and how best to discontinue one or more medications in children. Discontinuing medications can occur for a variety of reasons: the patient seems to have recovered and may no longer need medication, the patient has developed side effects to the medication that make it untenable for the patient to continue to take the medication (e.g., weight gain, concerns about growth or the development of involuntary movements), or the patient may be taking a medication that the current prescriber does not feel is warranted or is considered to be no longer effective. A thoughtful and safe plan for medication discontinuation is as important as a thoughtful and safe plan for starting medications.

Before discontinuing any medication, prescribers are encouraged to obtain the history of previous psychiatric symptoms and response to medication. The history gathering can start with the patient and family; however, a review of medical records and discussion with the previous prescribers may also be useful. Although many patients can describe the symptoms of the disorder for which medication was given, not all patients and families are able to do so, and collateral history may be critical to making a decision to implement a discontinuation trial. Reviewing the history is especially important for the prescriber who believes that the current medication is not warranted or is no longer effective. Reviewing the history ensures that the patient will not be exposed to medication discontinuation that may result in a needless and unexpected return of symptoms.

Developing a monitoring plan for a discontinuation trial is also critical. Although it may take only hours to days to identify a return of hyperactivity symptoms in a child with ADHD off stimulants, a more extended period of monitoring may be required to determine whether patients with the inattentive subtype of ADHD are having a return of symptoms. Similarly, patients with mood and anxiety disorders may be able to have their medication tapered only to have a return of symptoms weeks to months after their last dose. Medication discontinuation in inpatient or partial hospital settings with short lengths of stay may be particularly problematic.

Discontinuation of effective medications in such settings may result in an unexpected and unmonitored return of symptoms after discharge.

Although some medications may not actually require gradual tapering, prescribers are generally encouraged to taper medication slowly to avoid withdrawal symptoms (e.g., benzodiazepines or SSRIs) or rebound worsening of symptoms (e.g., antipsychotics for tics or lithium for mania). Gradual tapering may also be prudent if it is unclear whether the current medication is having a beneficial effect.

At this time, there are little or no data to suggest which medication to remove first in children who are taking multiple medications. Given the lack of data, the examples follow general clinical reasoning. If a child is taking two medications that target the same disorder, the first medication to be removed would likely be the medication that was used adjunctively or as an augmenter. For example, in children with OCD treated first with clomipramine and later with a benzodiazepine or antipsychotic to further reduce anxiety, it would be reasonable to reduce and eliminate the benzodiazepine or antipsychotic first. Similarly, in a child with depression who had a partial response to antidepressants and then achieved remission with lithium augmentation, removing the lithium may be the most appropriate first step. A corollary to this approach is to keep the medication with the most prophylactic efficacy or the one with the least long-term side effect potential. For example, a teenager with bipolar disorder may have derived equivalent benefit from an antipsychotic and lithium. Given the relative long-term safety profile and prophylactic effects of these medications, the antipsychotic might be tapered first.

If a child is on two medications, one for the underlying disorder and the second to manage side effects of the first, it is likely that the first to be removed is the one used to manage side effects. For example, if an anticholinergic medication is added to an antipsychotic to reduce the risk for extrapyramidal symptoms during initial treatment, it may be possible to discontinue anticholinergic medication after the child is stabilized on the antipsychotic. However, if the child requires anticholinergic medication for the ongoing management of extrapyramidal symptoms, it would be prudent to maintain the anticholinergic medication well after the antipsychotic is discontinued to prevent the delayed emergence of extrapyramidal symptoms.

If a child is on two medications for two disorders, the first medication to be removed is for the disorder that is more likely to go into remission or which is less severe or impairing. For example, for a child taking stimulants and antidepressants for ADHD and depression who has been stable without depressive symptoms for an extended period, it would be reasonable to consider tapering the antidepressant first, or if the ADHD was mild and never impairing until the child

became depressed, it might be more appropriate to discontinue the stimulant first.

In all of the above cases, the role of the underlying and most severe condition and the sequence and rationale for which medications were combined contribute to the plan for discontinuation of multiple medications in children.

PARAMETER LIMITATIONS

The AACAP practice parameters are developed to assist clinicians in psychiatric decision making. These parameters are not intended to define the standard of care, nor should they be deemed inclusive of all proper methods of care or exclusive of other methods of care directed at obtaining the desired results. The ultimate judgment regarding the care of a particular patient must be made by the clinician in light of all of the circumstances presented by the patient and his or her family, the diagnostic and treatment options available, and available resources.

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REFERENCES

References with an asterisk () are particularly recommended.*

1. Weisz JR, Doss AJ, Hawley KM. Youth psychotherapy outcome research: a review and critique of the evidence base. *Annu Rev Psychol.* 2005;56:337-363.
2. Satcher D. Office of the Surgeon General. Report of the Surgeon General's conference on children's mental health: a national action agenda. <http://www.hhs.gov/surgeongeneral/topics/cmb/childreport.htm>. Published 2000. Accessed March 4, 2008.
3. Olsson M, Marcus SC, Weissman MM, Jensen PS. National trends in the use of psychotropic medications by children. *J Am Acad Child Adolesc Psychiatry.* 2002;41:514-521.
4. Zito JM, Safer DJ, dosReis S et al. Psychotropic practice patterns for youth: a 10-year perspective. *Arch Pediatr Adolesc Med.* 2003;157:17-25.
5. Rosack J. New data show declines in antidepressant prescribing. *Psychiatr News.* 2005;40:1.
6. Hamilton BE, Minino AM, Martin JA, Kochanek KD, Strobino DM, Guyer B. Annual summary of vital statistics: 2005. *Pediatrics.* 2007;119:345-360.
7. American Academy of Child and Adolescent Psychiatry. Practice parameters for the psychiatric assessment of children and adolescents. *J Am Acad Child Adolesc Psychiatry.* 1997;36(10 suppl):69S.
8. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder. *J Am Acad Child Adolesc Psychiatry.* 2007;46:107-125.

9. American Academy of Child and Adolescent Psychiatry. Practice parameters for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry*. 1998;37:(10 suppl)27S–45S.
10. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2007;46:267–283.
11. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. *J Am Acad Child Adolesc Psychiatry*. 2007;46:1503–1523.
12. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. *J Am Acad Child Adolesc Psychiatry*. 2001;40(7 suppl):4S–23S.
13. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46:894–921.
14. Guevara J, Lozano P, Wickizer T, Mell L, Gephart H. Psychotropic medication use in a population of children who have attention-deficit/hyperactivity disorder. *Pediatrics*. 2002;109:733–739.
15. Martin A, Van Hoof T, Stubbe D, Sherwin T, Scahill L. Multiple psychotropic pharmacotherapy among children and adolescent enrollees in Connecticut Medicaid managed care. *Psychiatr Serv*. 2003;54:72–77.
- *16. Jensen PS, Hinshaw SP, Swanson JM et al. Findings from the NIMH Multimodal Treatment Study of ADHD (MTA): implications and applications for primary care providers. *J Dev Behav Pediatr*. 2001;22:60–73.
17. Emslie GJ, Rush AJ, Weinberg WA et al. A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. *Arch Gen Psychiatry*. 1997;54:1031–1037.
18. TADS. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA*. 2004;292:807–820.
19. Wagner KD, Ambrosini P, Rynn M et al. Efficacy of sertraline in the treatment of children and adolescents with major depressive disorder: two randomized controlled trials. *JAMA*. 2003;290:1033–1041.
20. Wagner KD, Robb AS, Findling RL, Jin J, Gutierrez MM, Heydorn WE. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. *Am J Psychiatry*. 2004;161:1079–1083.
21. DeVaugh-Geiss J, Moroz G, Biederman J et al. Clomipramine hydrochloride in childhood and adolescent obsessive-compulsive disorder—a multicenter trial. *J Am Acad Child Adolesc Psychiatry*. 1992;31:45–49.
22. Geller DA, Hoog SL, Heiligenstein JH et al. Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: a placebo-controlled clinical trial. *J Am Acad Child Adolesc Psychiatry*. 2001;40:773–779.
23. Geller DA, Wagner KD, Emslie G et al. Paroxetine treatment in children and adolescents with obsessive-compulsive disorder: a randomized, multicenter, double-blind, placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2004;43:1387–1396.
24. March JS, Biederman J, Wolkow R et al. Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. *JAMA*. 1998;280:1752–1756.
25. Riddle MA, Reeve EA, Yaryura-Tobias JA et al. Fluvoxamine for children and adolescents with obsessive-compulsive disorder: a randomized, controlled, multicenter trial. *J Am Acad Child Adolesc Psychiatry*. 2001;40:222–229.
26. Birmaher B, Axelson DA, Monk K et al. Fluoxetine for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2003;42:415–423.
27. RUPP. Fluvoxamine for the treatment of anxiety disorders in children and adolescents. The Research Unit on Pediatric Psychopharmacology Anxiety Study Group. *N Engl J Med*. 2001;344:1279–1285.
28. Rynn MA, Siqueland L, Rickels K. Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. *Am J Psychiatry*. 2001;158:2008–2014.
29. Rynn MA, Riddle MA, Yeung PP, Kunz NR. Efficacy and safety of extended-release venlafaxine in the treatment of generalized anxiety disorder in children and adolescents: two placebo-controlled trials. *Am J Psychiatry*. 2007;164:290–300.
30. Wagner KD, Berard R, Stein MB et al. A multicenter, randomized, double-blind, placebo-controlled trial of paroxetine in children and adolescents with social anxiety disorder. *Arch Gen Psychiatry*. 2004;61:1153–1162.
31. March JS, Entusah AR, Rynn M, Albano AM, Tourian KA. A randomized controlled trial of venlafaxine ER versus placebo in pediatric social anxiety disorder. *Biol Psychiatry*. 2007;62:1149–1154.
32. Walkup JT, Albano AM, Piacentini J et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *N Engl J Med*. 2008;359:2753–2766.
33. Scahill L, Leckman JF, Schultz RT, Katsovic L, Peterson BS. A placebo-controlled trial of risperidone in Tourette syndrome. *Neurology*. 2003;60:1130–1135.
34. Pappadopulos E, MacIntyre JC II, Crismon ML et al. Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAAY). Part II. *J Am Acad Child Adolesc Psychiatry*. 2003;42:145–161.
35. Schur SB, Sikich L, Findling RL et al. Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAAY). Part I: a review. *J Am Acad Child Adolesc Psychiatry*. 2003;42:132–144.
36. McCracken JT, McGough J, Shah B et al. Risperidone in children with autism and serious behavioral problems. *N Engl J Med*. 2002;347:314–321.
37. MTA. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics*. 2004;113:762–769.
38. Cook EH, Wagner KD, March JS et al. Long-term sertraline treatment of children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry*. 2001;40:1175–1181.
39. Rynn M, Wagner KD, Donnelly C et al. Long-term sertraline treatment of children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol*. 2006;16:103–116.
- *40. McClellan JM, Werry JS. Evidence-based treatments in child and adolescent psychiatry: an inventory. *J Am Acad Child Adolesc Psychiatry*. 2003;42:1388–1400.
41. Abikoff H, McGough J, Vitiello B et al. Sequential pharmacotherapy for children with comorbid attention-deficit/hyperactivity and anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2005;44:418–427.
42. TSSG. Tourette Syndrome Study Group Treatment of ADHD in children with tics: a randomized controlled trial. *Neurology*. 2002;58:527–536.
43. McDougle CJ, Epperson CN, Pelton GH, Wasyluk S, Price LH. A double-blind, placebo-controlled study of risperidone addition in serotonin reuptake inhibitor-refractory obsessive-compulsive disorder. *Arch Gen Psychiatry*. 2000;57:794–801.
- *44. Brent DA, Birmaher B. Treatment-resistant depression in adolescents: recognition and management. *Child Adolesc Psychiatr Clin N Am*. 2006;15:1015–1034.
45. Wilens TE, Spencer T, Biederman J, Wozniak J, Connor D. Combined pharmacotherapy: an emerging trend in pediatric psychopharmacology. *J Am Acad Child Adolesc Psychiatry*. 1995;34:110–112.
46. POTS. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA*. 2004;292:1969–1976.
- *47. Murphy SA, Oslin DW, Rush AJ, Zhu J. Methodological challenges in constructing effective treatment sequences for chronic psychiatric disorders. *Neuropsychopharmacology*. 2007;32:257–262.
48. Goodwin R, Gould MS, Blanco C, Olfson M. Prescription of psychotropic medications to youths in office-based practice. *Psychiatr Serv*. 2001;52:1081–1087.
49. Olfson M, Gameroff MJ, Marcus SC, Waslick BD. Outpatient treatment of child and adolescent depression in the United States. *Arch Gen Psychiatry*. 2003;60:1236–1242.

50. Baird P. Getting it right: industry sponsorship and medical research. *CMAJ*. 2003;168:1267–1269.
51. Perlis RH, Perlis CS, Wu Y, Hwang C, Joseph M, Nierenberg AA. Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry. *Am J Psychiatry*. 2005;162:1957–1960.
52. Brodkey AC. The role of the pharmaceutical industry in teaching psychopharmacology: a growing problem. *Acad Psychiatry*. 2005;29:222–229.
53. Kravitz RL, Epstein RM, Feldman MD et al. Influence of patients' requests for direct-to-consumer advertised antidepressants: a randomized controlled trial. *JAMA*. 2005;293:1995–2002.
- *54. Klein DF. Comments on psychiatric education. *Acad Psychiatry*. 2005;29:128–133.
55. FDA. Guidance for industry. Draft guidance. <http://www.fda.gov/cder/guidance/6019dft.pdf>. Published January 2004. Accessed March 4, 2008.
56. Bryden KE, Carrey NJ, Kutcher SP. Update and recommendations for the use of antipsychotics in early-onset psychoses. *J Child Adolesc Psychopharmacol*. 2001;11:113–130.
- *57. Rush AJ, Kraemer HC, Sackeim HA et al. Report by the ACNP Task Force on response and remission in major depressive disorder. *Neuropsychopharmacology*. 2006;31:1841–1853.
58. Swanson JM, Kraemer HC, Hinshaw SP et al. Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J Am Acad Child Adolesc Psychiatry*. 2001;40:168–179.
59. Pine DS. Treating children and adolescents with selective serotonin reuptake inhibitors: how long is appropriate? *J Child Adolesc Psychopharmacol*. 2002;12:189–203.
60. Leckman JF. Phenomenology of tics and natural history of tic disorders. *Brain Dev*. 2003;25(suppl 1):S24–S28.
- *61. Pruet KD, Martin A. Thinking about prescribing: the psychology of psychopharmacology. In: Martin A, Scahill L, Charney D, Leckman JF, eds. *Textbook of Child and Adolescent Psychopharmacology*. New York: Oxford University Press; 2002:417–442.
62. Prochaska JO, DiClemente CC, Norcross JC. In search of how people change. Applications to addictive behaviors. *Am Psychol*. 1992;47:1102–1114.
63. Curry J, Rohde P, Simons A et al. Predictors and moderators of acute outcome in the Treatment for Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006;45:1427–1439.
64. Zarate CA Jr, Quiroz JA. Combination treatment in bipolar disorder: a review of controlled trials. *Bipolar Disord*. 2003;5:217–225.
65. Findling RL, McNamara NK, Gracious BL et al. Combination lithium and divalproex sodium in pediatric bipolarity. *J Am Acad Child Adolesc Psychiatry*. 2003;42:895–901.