Practice Parameter for the Assessment and Treatment of Children and Adolescents With Tic Disorders

Tanya K. Murphy, M.D., Adam B. Lewin, Ph.D., Eric A. Storch, Ph.D., Saundra Stock, M.D., and the American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI)

Tic disorders, including Tourette's disorder, present with a wide range of symptom severity and associated comorbidity. This Practice Parameter reviews the evidence from research and clinical experience in the evaluation and treatment of pediatric tic disorders. Recommendations are provided for a comprehensive evaluation to include common comorbid disorders and for a hierarchical approach to multimodal interventions. J. Am. Acad. Child Adolesc. Psychiatry, 2013;52(12):1341–1359. **Key Words:** tic disorders, Tourette's disorder, treatment, Practice Parameter

This Parameter is intended to guide the practice of medical and mental health professionals that assess and treat youth with tic disorders including Tourette's disorder. Child and adolescent psychiatrists are often not the first point of contact for the assessment and treatment of tic disorders, but more often are involved when comorbid conditions arise or when tics develop while treating another neurodevelopmental disorder. Given the increased complexity in assessing the medical and psychiatric well-being of children presenting with these tic disorders and related comorbid conditions, as well as recent developments in evidence-based pharmacologic and behavioral treatments, a comprehensive and developmentally sensitive Practice Parameter is needed. The recommendations in this Parameter are applicable to children, adolescents, and young adults.

METHODOLOGY

Information and treatment recommendations used in this Parameter were obtained by using the terms *Tourette's Disorder*, *Tourette syndrome*, or *Tic Disorder*, *English Language*, and *Human Studies* to search *Medline, PubMed, PsycINFO,* and *Cochrane Library* databases and by iterative bibliographic exploration of articles and reviews. Beginning with more inclusive and sensitive searches using the search terms noted above, multiple free text and relevant medical subject headings (MeSH terms), and the time period from January 1, 1965 to March 29, 2013, yielded 3,764 citations in Medline, 3,172 in PsycINFO, and 3 reviews in the Cochrane Library. The search was narrowed to the following designations: *Meta-Analysis* (11 all, 2 child), *Practice Guideline* (5 all), *Review* (811 all, 296 child). The original search was also narrowed to the following designations: *Treatment and 0-18* (1206), and *Treatment and 0-18 and RCT* (87). We selected 149 publications and 25 RCTs that enrolled pediatric subjects with an effective N $\geq$ 20 for careful examination based on their weight in the hierarchy of evidence, the quality of individual studies, and their relevance to clinical practice. This Practice Parameter has been reviewed by acknowledged experts in the field, and their comments and suggestions are included.

CME This article can be used to obtain continuing medical education (CME) at www.jaacap.org

CLINICAL PRESENTATION AND COURSE

A tic is a sudden, rapid, recurrent, nonrhythmic movement or vocalization. Tics can be simple (rapid, meaningless) or complex (more purposeful, elaborate, or orchestrated), and transient or chronic. Chronic tic disorders (CTD), including Tourette's disorder (TD) and persistent motor or

vocal tic disorder, are long-lasting neuropsychiatric disorders, typically of childhood onset (<18 years). They are characterized by multiple motor and/or vocal/phonic tics that wax and wane in severity and are often accompanied by an array of behavioral problems, including symptoms of attention-deficit/hyperactivity disorder (ADHD) and obsessive compulsive disorder (OCD). *Persistent motor or vocal tic disorder* has tics limited to each of those domains whereas TD has both motor and vocal tics at some point in the illness.[1] For either diagnosis, however, tics need to be present for at least one year. For tics present for less than 1 year, *provisional tic disorder* (formerly transient tic disorder) is used. *Other specified tic disorder or unspecified tic disorder* diagnoses are used for tic disorders that do not meet full criteria for TD, persistent tic disorder, or provisional tic disorder. In the case of the other specified tic disorder, clinicians specify the reason the full criteria were not met (e.g., atypical clinical presentation or age of onset).[1]

The clinical manifestations of CTD[2] may involve varying combinations of fluctuating tics. Simple motor tics are fast, brief movements involving 1 or a few muscle groups, such as eye blinking, shoulder shrugs, head jerks, or facial grimaces. Complex motor tics are sequentially and/or simultaneously produced relatively coordinated movements that can seem purposeful, such as tapping the bottom of the foot. Simple vocal/phonic tics are solitary, meaningless sounds and noises such as grunting, sniffing, snorting, throat clearing, humming, coughing, barking, or screaming. Complex vocal/phonic tics are linguistically meaningful utterances and verbalizations such as partial words (syllables), words out of context (Oh boy!), repeated sentences, coprolalia, palilalia, or echolalia. Sensory phenomena that precede and trigger the urge to tic have been described and are referred to as *premonitory urges*.[2] Patients with CTD can volitionally suppress tics for varying periods of time, particularly when external demands (e.g., social pressure) exert their influence or when deeply engaged in a focused task or activity. For this reason, teachers and family often perceive that when the child is not suppressing his/her tics that they are "choosing" to tic, that tics are intentional or are habits that can be easily stopped. Although parents may describe a rebound effect of increased frequency of tics at the end of the school day,

TABLE 1 Repetitive Movements of Childhood

	Description	Typical Disorders Where Present
Tics	Sudden rapid, recurrent, nonrhythmic vocalization or motor movement	Transient tics, TD, CTD
Dystonia	Involuntary, sustained, or intermittent muscle contractions that cause twisting and repetitive movements, abnormal postures, or both	DYT1 gene, Wilson's, myoclonic dystonia, extrapyramidal symptoms due to dopamine blocking agents,
Chorea	Involuntary, random, quick, jerking movements, most often of the proximal extremities, that flow from joint to joint. Movements are abrupt, nonrepetitive, and arrhythmic and have variable frequency and intensity	Sydenham's chorea, Huntington's chorea
Stereotypies	Stereotyped, rhythmic, repetitive movements or patterns of speech, with lack of variation over time	Autism, stereotypic movement disorder, intellectual disability
Compulsions	A repetitive, excessive, meaningless activity or mental exercise that a person performs in an attempt to avoid distress or worry	OCD, anorexia, body dysmorphic disorder, hoarding disorder, trichotillomania, excoriation disorder
Myoclonus	Shock-like involuntary muscle jerk that may affect a single body region, 1 side of the body, or the entire body; may occur as a single jerk or repetitive jerks	Hiccups, hypnic jerks, Lennox-Gastaut syndrome, juvenile myoclonic epilepsy, mitochondrial encephalopathies, metabolic disorders
Habits	Action or pattern of behavior that is repeated often	Onchophagia
Akathisia	Unpleasant sensations of "inner" restlessness, often prompting movements in an effort to reduce the sensations	Extrapyramidal adverse effects from dopamine blocking agents; anxiety
Volitional behaviors	Behavior that may be impulsive or due to boredom like tapping peers, making sounds (animal noises)	ADHD, ODD, sensory integration disorders

Note: ADHD = attention-deficit/hyperactivity disorder; CTD = chronic tic disorders; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder; TD = Tourette's disorder.

research has not supported volitional suppressing of tics leading to tic rebound.[3-5]

Average age of onset of CTD is 7 years, with onset as early as a few months of age.[6] The prevalence and severity of tic disorders has a peak around age 9 to 12 years,[7] followed by a decrease in prevalence with age,[7,8] with remission or marked attenuation of tic severity in most individuals (65%) by age 18 to 20 years.[2] The early presentation of CTD may be indistinguishable from bouts of transient tics, but then progresses to a more typical chronic waxing and waning course.[8-10] Children with only OCD or tics may develop additional symptoms months or years later.[10] Although some patients will have complete or partial remissions of their illness in early adulthood, others may continue to have a chronic and disabling illness for many years.[11,12]

Many youth with CTD experience impairment in daily functioning[2,13] Youth with TD have been shown to experience greater psychosocial stress relative to healthy controls.[14] Socially, many youth with tics experience peer difficulties that may further contribute to distress.[13] With regard to home life, there is an increased risk for marital difficulties, substance abuse in parents, family conflict, poorer quality of parent–child interactions, and higher levels of parenting frustration in families with a child with CTD, especially when associated with comorbid conditions.[15] Many people with CTD seek mental health services to assist them in coping with CTD and related problems, such as stigma, anxiety, and depression.[16] Not only has stress been linked to symptom exacerbations, but it has also been associated with increased depressive symptoms among youth with tics.[14]

EPIDEMIOLOGY

The prevalence of CTD has been estimated as 0.5% to 3%,[17] with approximately 7% of school age children having had tics in the previous year.[18,19] It is estimated that the prevalence of transient tics is approximately 5%. This figure may be an underestimate, given that most cases of tics are mild and may be misdiagnosed or unrecognized by medical professionals.[2] Prevalence rates for all tics (chronic or transient) range from 5.9% to 18% for boys and from 2.9% to 11% for girls.[18] In general, CTD have a male preponderance, with a gender ratio of at least 2:1 or higher.[11,20] Tic disorders have been reported in numerous Asian, Middle Eastern, and European samples. Although ethnic differences in prevalence are understudied, the Great Smoky Mountains Youth Study and the CDC study found higher rates in white compared to African American youth.[20,21]

ETIOLOGY

Although the pathophysiology of CTD is not entirely understood, there is evidence that motor programs at both a cortical and subcortical level are not properly modulated. Tics are proposed to be the result of dysfunctional cortico-striatal-thalamo-cortical circuits, prominently those subserving motor function. Magnetic resonance imaging (MRI) morphometric studies have demonstrated a loss of the normal asymmetry of the caudate nucleus and, in some studies, other regions as well.[22,23] Functional neuroimaging studies have revealed a pattern of decreased activity in the basal ganglia, often with asymmetries that are not consistent from 1 study to the next (although a left-sided preponderance is often noted).[23] Greater activity in sensorimotor regions (e.g., primary motor cortex, putamen) and reduced activity in the anterior cingulate and caudate during spontaneous tics have suggested deficient engagement of circuits that inhibit either tic behaviors or the sensorimotor urges.[24]

Other studies have revealed that during the performance of a motor task, a larger area of cortex was recruited in subjects with TD than in controls.[25] Transcranial magnetic stimulation revealed that the cortical silent period was shortened and intracortical inhibition reduced; abnormalities that were particularly prominent when tics were present.[26] Motor threshold and peripheral motor excitability, however, did not differ from that of controls.[26] During tic suppression, there were significant changes in signal intensity in the basal ganglia and thalamus and interconnected cortical regions. These changes in signal intensity were inversely correlated with the severity of tic symptoms.[27,28] Male predominance in CTD and childhood OCD may be due to influences of sex hormones on the neurodevelopment of these cortico-striatal-thalamo-cortical circuits, as reflected by a study of anti-androgens in the treatment of TD.[29]

Relatives of those with TD have repeatedly been shown to be at an increased risk for developing tic disorders. Family studies suggest a 10- to 100 fold increase in the risk of CTD among first-degree relatives compared to rates in the general population.[30] Twin studies also support a

genetic link of CTD, with 77% to 94% of monozygotic twins showing concordance for CTD and 23% concordance for dizygotic twins.[31,32] Candidate-gene association and nonparametric linkage studies have not yielded definitive susceptibility genes for TD; results of a large-scale, recent genome-wide association study revealed that no markers reached a genome wide threshold of significance.[30,33] Identified rare variants via cytogenetic assays and analysis of copy number variations have shown overlap with other neuropsychiatric disorders, and affect a small percentage of those with TD.[34] A parametric linkage study has ignited interest in histidine decarboxylase that has implications for histaminergic and dopaminergic signaling in the striatum.[34,35]

Tics appear to be sensitive to an array of environmental stimuli such as temperature changes,[36] stress,[37] illness,[38] and fatigue that can exacerbate tics. Some cases of tic disorders have been proposed to result from an infection-triggered autoimmune process similar to that of Sydenham chorea (SC).[39] Swedo coined the term PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcus) to describe cases of childhood-onset OCD and/or tics that resemble SC characterized by an acute onset following a streptococcal infection, accompanying neurological signs, and an episodic course. More recently, PANS (pediatric acute-onset neuropsychiatric syndrome) has been used to describe a subtype of sudden-onset OCD (tics are not a required feature) in children, as a link to prior streptococcal infections is not always evident.[40] In addition to a diagnosis of OCD and/or tics, children with PANS/PANDAS were frequently observed to have symptoms of separation anxiety, nightmares, personality change, oppositional behaviors, and deterioration in mathematics skills and handwriting. Increasingly, studies suggest that, in some cases, a prior history of infections may increase risk for developing tic disorder, although this remains controversial.[41]

DIFFERENTIAL DIAGNOSIS

Other repetitive movements may mimic tics, such as those in stereotypies, myoclonus, dystonia, and chorea (Table 1).[42,43] Perhaps the most common difficulty for pediatric providers is differentiating repetitive behaviors that are more stereotypic than is typical of tics. Although stereotypies may closely resemble tics, stereotypies are typically rhythmic movements and do not demonstrate the change in body location or movement type over time that is typical of tics. Stereotypies are observed in autism spectrum disorders and in stereotypic movement disorders. They can co-occur with tic disorders. The context, onset, type, and course of the movements should help to differentiate the movement typology. In addition, stereotypy lacks a premonitory urge (i.e., many children say that they are "thinking," or parents report that the stereotypy occurs when the child is excited).

Compulsions may be difficult to differentiate from tics motivated by "just right" feelings, as many patients describe a sensory component that the compulsion alleviates. Similarly, compulsive tics with strong premonitory urges will overlap in presentation with compulsions, making it difficult to distinguish a tic from a compulsion in those patients who clearly have OCD and tics.[44] Age may confound a child's ability to introspectively describe symptoms.

Tics may be idiopathic or may result from a variety of medications or general medical conditions. Some of the substances reported to potentially worsen tics include stimulants, selective serotonin reuptake inhibitors (SSRIs), lamotrigine, and cocaine.[45] If tics develop in close temporal relationship to the initiation or dosage increase of a substance and then remit within a few weeks of stopping the substance, a causal relationship is possible. The possibility that stimulants may trigger tics in a child without a prior history of tics has been a long-time concern of many clinicians and families (see the ADHD Practice Parameter[46] for a brief review). However, there is no scientific evidence in controlled studies that stimulants increase tics.[47]

Tics should be differentiated from a variety of developmental and benign movement disorders (e.g., benign paroxysmal torticollis, Sandifer's syndrome, benign jitteriness of newborns, or shuddering attacks).[48] Furthermore, tics may present in various neurological diseases.[48] Patients with tics that occur in the context of declining motor or cognitive function should be referred for further neurological assessment. Examples of possible general medical conditions include CNS insult that may occur with a tumor, trauma, anoxia, or neurological disease (e.g., Wilson's disease, neurocanthocytosis, Huntington's syndrome, pantothenate kinase–associated neurodegeneration, and a variety of frontal–subcortical brain lesions).[49] However, it is rare for tics to be the only manifestation in those diseases.

COMORBID PSYCHIATRIC DISORDERS

In clinical samples of CTD, co-occurring psychiatric disorders are common.[44] Frequently, patients with CTD will meet criteria for 2 or more conditions that are often viewed by the patient and family as more problematic than the tics per se.[50]

Obsessive-Compulsive Disorder

The association between CTD (especially TD) and obsessive-compulsive disorder (OCD) appears to be bidirectional, with 20% to 60% of TD patients meeting criteria for OCD, and 20% to 38% of youth with OCD reporting comorbid tics.[51] However, youth with comorbid CTD and OCD may not have tic or OCD severity scores as high as do youth with a CTD or OCD alone.[52] Delineating OCD symptoms from tic symptoms can sometimes be a challenge, especially when the child presents with evening up, "just right," or tapping tics.

Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) co-occurs in as many as 50% of all childhood CTD cases[53]; however, estimates in clinically referred patients suggest that rates of ADHD among individuals with TD may be as high as 60% to 80%.[54] Even in mild cases of CTD, the incidence of ADHD is 7 to 8 times greater than in the general population.[55] The co-occurrence of CTD and ADHD is often accompanied by disruptive behaviors, including low frustration tolerance, outbursts, noncompliance, and aggression as well as learning disorders and academic difficulties.[56] Together, these disorders may worsen social adjustment and academic achievement[57] beyond the effects of CTD alone. In a study of 138 youth with CTD (age range, 5–18 years), 46% demonstrated school-related problems, with those having comorbid ADHD symptoms at a nearly 4-fold increased risk for academic difficulty.[58] Notably, co-occurrence may be inflated because of referral bias—youth with comorbidities may be more likely to seek treatment.

Learning Disabilities

Studies of children with TD demonstrate high rates of school-related problems,[59] particularly in those with ADHD symptoms.[58] Erenberg *et al.* revealed that 36% of 200 pediatric TD cases had some degree of academic difficulties.[60] Although most patients with tics possess average intelligence,[61] learning disabilities (LD) are common in youth with chronic tics (approximately 23%),[59,62] especially among those with comorbid ADHD.[63] Male gender and a history of perinatal problems also increase the risk of LD in youth with tics.[59] The impact on learning and academics because of poor sleep quality that is frequently reported in youth with TD has not been fully explored.[64] Neuropsychological impairment in youth with CTD may be attributed to comorbid ADHD[65] rather than to the presence of a tic disorder. However, there is some evidence that even after controlling for ADHD, youth with CTD may have increased problems on tasks of executive functioning, attention/concentration, and visual-motor decoding (in contrast to healthy controls and youth with OCD).[66] Fine motor deficits have been implicated to predict adult tic severity in a small study.[12]

Autism Spectrum Disorders (ASD). Some patients with tic disorders will display symptoms found on the autism spectrum.[67] Careful assessment to determine symptom onset, course, language development, and social ability is needed to differentiate first whether the child has primary TD, primary ASD, or ASD with co-occurring tics. Burd *et al.* found that 4.6% of youth with TD had a comorbid ASD and that youth with TD and ASD were more likely to be male and had an increased number of other comorbidities.[68]

EVIDENCE BASE FOR PRACTICE PARAMETERS

In this Parameter, recommendations for best assessment and treatment practices are stated in accordance with the strength of the underlying empirical and/or clinical support, as follows:

- Clinical Standard [CS] is applied to recommendations that are based on rigorous empirical evidence (e.g., meta-analyses, systematic reviews, individual randomized controlled trials) and/or overwhelming clinical consensus
- Clinical Guideline [CG] is applied to recommendations that are based on strong empirical evidence (e.g., non-randomized controlled trials, cohort studies, case-control studies) and/or strong clinical consensus
- Clinical Option [OP] is applied to recommendations that are based on emerging empirical evidence (e.g., uncontrolled trials or case series/reports) or clinical opinion, but lack strong empirical evidence and/or strong clinical consensus

- Not Endorsed [NE] is applied to practices that are known to be ineffective or contraindicated

The strength of the empirical evidence is rated in descending order as follows:

- [rct] Randomized, controlled trial is applied to studies in which subjects are randomly assigned to 2 or more treatment conditions
- [ct] Controlled trial is applied to studies in which subjects are non-randomly assigned to 2 or more treatment conditions
- [ut] Uncontrolled trial is applied to studies in which subjects are assigned to 1 treatment condition
- [cs] Case series/report is applied to a case series or a case report

RECOMMENDATIONS

Assessment

Recommendation 1. The psychiatric assessment should involve routine screening for unusual movements, stereotypies, tics, and family history of tic disorders. [CS]

Parents and youth should be asked about unusual movements or vocalizations during the initial assessment. Screening for abnormal movements before initiation of any psychotropic medications and assessing previous psychotropic medication exposure/dosage changes is important when evaluating for abnormal movements in children. Many families are unaware that frequent sniffing, coughing, or blinking may be indicative of tics, attributing these behaviors to allergies or visual problems. Careful assessment of the timing, triggers, and characteristics may help differentiate tics from another medical problem. If the clinician is unsure, referral to a pediatric specialist (allergist, pulmonologist, and ophthalmologist) is warranted. Commonly used parent-rated behavioral screening tools such as the *Child Behavior Checklist (CBCL)*[69] and the 90-item version of the *Swanson, Nolan, and Pelham (SNAP)*[70] include tic-specific questions.

Recommendation 2. If screening is positive, a more thorough assessment for tic disorders should be conducted. [CS]

If the clinician's screening receives endorsement of the possibility of tics or the clinician observes tics during the evaluation, a more systematic assessment for tics will be needed, including the age of onset, types of tics, tic frequency, alleviating and aggravating factors, and a family history of tics. Rating scales specific for tics may be used. Parent report rating scales for type, severity and impairment of tics include the *Motor tic, Obsessions and compulsions, Vocal tic Evaluation Survey* (MOVES),[71] *Tic Self-Report Scale,*[72] *Tourette's Disorder Scale,*[73] *Parent Tic Questionnaire* (PTQ)[74] (*freely available at*: http://www.uab.edu/ot/practice/tourette-syndrome-clinic/parent-tic-questionnaire) and *Child Tourette's Disorder Impairment Scale–Parent Version.*[75] For clinician-rated tic severity, the most commonly used is the *Yale Global Tic Severity Scale* (YGTSS),[76] which assesses the nature of motor and phonic tics over the previous week. This scale has excellent clinicometric properties and treatment sensitivity has been documented.[76-78] The *Tourette Syndrome Severity Scale* (TSSS)[79] contains 5 ordinal scales with differing ranges and item weights that focus on TD-related social impairment. The *Tourette Syndrome Global Scale* (TSGS)[80] assesses the frequency and impairment of simple and complex tics, as well as common comorbid problems (e.g., behavioral problems, functional impairment). Short, structured videotape protocols have been used to count tics,[81] although issues have been raised with their scoring structures, feasibility, and ease of implementation.

Recommendation 3. The assessment for tic disorders should involve a careful examination for general medical condition or substance etiologies. [CS]

A medical workup should be considered for new-onset tics or tic-like movements. Certain clinical features such as the sudden onset of severe tics, atypical tics, or mental status abnormalities suggestive of an organic process (i.e., disorientation, inability to copy figures or to draw a clock) should prompt further medical investigation.

Basic laboratory measures such as a hemogram, renal/hepatic function panel, thyroid panel, and ferritin, along with urine drug screen for adolescents, are reasonable. For new sudden (overnight)–onset or severe symptom exacerbation, the provider may assess for co-occurring infection with diagnostic tests that indicate acute illness (e.g., culture, rapid viral tests).[41]

EEG and brain imaging are not routinely recommended and are reserved for cases with other neurological findings. In cases with unusual or complex presentations, additional specialty consultation (e.g., pediatric neurology, genetics) may be helpful.

TABLE 2 Controlled Trials in Pediatric Tourette's Disorder (TD) with N > 20

Refererence	N	Age, y, Range (Mean)	Study Design	Tic Outcome Measure	Medication[a]	Dose Range, mg[a] (Mean)	Baseline Score	Post Score	Effect Size	NNT	Average Weight Change (lb)	Observations
96	57	8–46 (21.1)	Parallel and crossover	TSSS	Haloperidol Pimozide Placebo	0.5–10 (4.5) 1.0–20 (10.6) ___	4.1±2.0	1.2±1.2 2.5±3.0 2.9±2.5	0.57	___	___ ___ ___	Haloperidol and Pimozide compared with placebo are effective in TS treatment. Haloperidol is slightly more effective than pimozide.
97	47	7–48 (15.6)	Parallel	TSGS	Clonidine Placebo	0.05–0.25 (0.0044 mg/kg/d)	36.4±8.9 35.4±8.9	27.0±11.1 31.5±9.6	0.40	___	___	Clonidine was significantly more efficacious than placebo (26% vs. 11%).
98	24	7–16 (12)	Crossover	YGTSS[c]	Deprenyl Placebo	5 b.i.d.	40.8±16.1 48.2±18.8	31.5 ___	___[a] ___[a]	___	___	Deprenyl showed substantial beneficial effect on ADHD symptoms and tic reduction in the first period.
99	22	7–16 (10.2)	Crossover	TSGS	Pimozide Haloperidol Placebo	(3.4) (3.5) ___	28.5±14.5	17.1±14.1 20.7±17.3 26.8±15.9	0.23	2.4	___ ___ ___	64% Treatment response to either active medication. Pimozide significantly reduced tic symptoms when compared to placebo and haloperidol.
100	24	7–17	Crossover	YGTSS[c]	Peroglide Placebo	0.025–0.3 (0.2)	48.0±13.3	23.5±18.7 42.0±20.4	0.95	3.2	___ ___	35% mean change in scores from patients on peroglide vs. 6% change on placebo
101	28	7–17 (11.6)	Parallel	YGTSS	Ziprasidone Placebo	5–40 (28.2)	24.7±6.8 24.6±9.6	16.1±7.4 22.9±10.8	1.0	3.5	1.5 1.8	38.4% change in tic reduction on Ziprasidone compared to 6.9% reduction on placebo

TABLE 2 Continued

Refererence	N	Age, y, Range (Mean)	Study Design	Tic Outcome Measure	Medication[a]	Dose Range, mg[a] (Mean)	Baseline Score	Post Score	Effect Size	NNT	Average Weight Change (lb)	Observations
102	50	10–65 (21.5)	Parallel	TSSS	Risperidone Pimozide	0.5–6 (3.8) 1–6 (2.9)	4.3 4.3	1.9 2.0	___[b] ___[b]	6.1	8.6 6.5	Risperidone shown to be as efficacious as pimozide in treatment of TD.
103	34	7–15 (10.4)	Parallel	YGTSS	Guanfacine Placebo	1.5–3.0 (2.5)	15.2±6.6 15.4±7.0	10.7±7.0 15.4±5.5	0.67	3.0	___ ___	31–37% decrease in ADHD and tic symptoms on guanfacine compared to 0–8% on placebo
104	61	8–17 (11.3)	Parallel	TODS-CR	Mecamylamine Placebo	2.5–7.5	76.8 65.9	65.6	___[b]	___	___	Mecamylamine does not appear to be effective as a monotherapy
105	48	14–49 (32)	Parallel	TSSS	Risperidone Placebo	1–6 (2.5)	5.24±1.30 5.37± 1.35	3.39±2.18 4.59±2.17	0.80	2.9	___ ___	60.8% improved in tic severity on risperidone; 26.1% on placebo
77	21	7–17 (11.3)	Parallel	YGTSS[c]	Risperidone Clonidine	1–1.5 (1.5) 0.083–0.175 (0.175)	51.8±13.8 52.3±17.0	40.9±11.7 38.5±16.9	0.17	18	4.6 0.2	21% improvement on risperidone, 26% improvement on clonidine. Risperidone demonstrated as efficacious as clonidine
106	41	5–17 (10.6)	Parallel	YGTSS[c]	Desipramine Placebo	154±63 mg/kg 150±48 mg/kg	63±18 65±15	43±23 61±15	0.93	1.9	___	Desipramine significantly reduced tic and ADHD symptoms
107	136	7–14 (10)	Parallel	YGTSS	Methlyphenidate Clonidine Clon + MPH Placebo	1–60 (25.7) 0.1–0.6 (0.25) 26.1 ___	19.0±4.45 20.3±4.9 21.9±4.5 20.3±4.9	___ ___ ___ ___	0.64 0.75 0.75 ___[b]	___ ___ ___	___ ___ ___ ___	Clonidine significantly reduced tic severity and was beneficial for ADHD compared to placebo group. Methylphenidate did not exacerbate tics.

TABLE 2 Continued

Refererence	N	Age, y, Range (Mean)	Study Design	Tic Outcome Measure	Medication[a]	Dose Range, mg[a] (Mean)	Baseline Score	Post Score	Effect Size	NNT	Average Weight Change (lb)	Observations
108	57	7–17 (11)	Parallel	YGTSS[c]	Pergolide Placebo	0.15–0.45 (0.43)	50.6±13.1 45.0±13.0	36.4±16.5 39.6±19.4	0.18	___	___	Pergolide reduced tic severity by approximately 25 % with significant ADHD symptom reduction and is associated with few side effects
78	34	6–62 (19.7)	Parallel	YGTSS	Risperidone Placebo	1.5–3.5 (2.5)	26.0±5.07 27.4±8.51	17.6±4.75 25.4±8.75	1.0	3.9	6.2 0	32% tic reduction in risperidone group while 7% reduction in tic severity in placebo
109	43	7–55 (20.6)	Parallel	YGTSS	Exposure Response Prevention Habit Reversal Therapy	___	26.2±7.6 24.1±7.2	17.6±7.6 19.7±9.3	1.42	3.3	___	ERP and HRT are effective interventions in reducing tic symptoms. ERP was marginally confirmed to be more beneficial.
110	166	7–17 (11.2)	Parallel	YGTSS	Atomoxetine Placebo	0.5–1.5 mg/kg/d (1.33)	21.7±7.8 22.2±8.3	16.2±6.9 19.2±8.7	0.3	6.2	– 2 3.5	Atomoxetine resulted in 50% tic reduction and is shown to be effective in treating ADHD symptoms. 33.8% tic reduction with placebo.
111	27	7–18 (11.9)	Parallel	YGTSS	Metoclopramide Placebo	5–40 (32.9)	22.6±5.3 22.2±6.8	13.9±3.7 19.4±5.8	0.95	5	2.2 1.1	Metoclopramide resulted in 39% tic reduction and is shown to be an effective treatment for tics. Placebo resulted in 13% tic reduction.
112	30	12–46 (21.7 ± 9.14 y)	Parallel	TSGS YGTSS TSGS YGTSS	Ondansetron Placebo	8–24 titrated over 3 wk	29.6±20.3 24.0±9.4 47.1±17.6 31.8±7.2	20.6±12.8 17.5±9.5 40.8±23.7 27.3±12.1	1.06	3.1	____	54% of patients in the ondansetron group and 21% in the placebo group were considered improved

TABLE 2 Continued

Refererence	N	Age, y, Range (Mean)	Study Design	Tic Outcome Measure	Medication[a]	Dose Range, mg[a] (Mean)	Baseline Score	Post Score	Effect Size	NNT	Average Weight Change (lb)	Observations
113	22	8–16 (12.2)	Crossover	YGTSS	Levetiracetam Placebo	750–3,000 (1,563)	18.95±7.35 20.4±5.32	16.8±6.25 18.95±7.28	0.32	___	___	Levetiracetam did not demonstrate a significant benefit to suppressing tics compared with placebo.
114	437	6–18 (10.0)	Parallel	YGTSS	Clonidine adhesive patch Placebo	1.0–2.0 (1.5)	21.35±8.67 22.56±8.79	9.83±7.77 11.84±8.01	0.25	4.6	___	A response rate of 68.8% compared to placebo response rate of 46.85%
115	12	8–27 (14.9)	Crossover	YGTSS	Clonidine Levitiracetam	0.15–0.3 (0.20) 250–1,750 (1,150)	25.2±4.3 22.7±5.7	21.8±4.4 23.6±10.6	0.57	___	___ ___	Clonidine resulted in a small improvement in tic reduction. Levitracetan exhibited no improvement in tic symptoms
116	29	7–65 (16.5)	Parallel	YGTSS	Topiramate Placebo	25–200 (118)	26.64±8.78 28.77±7.53	12.36±12.04 23.10±8.99	1.0	___	−4.6 4.2	Topiramate showed significant tic severity reduction compared to placebo
92	126	9–17 (11.7)	Parallel	YGTSS	Habit Reversal Training Supportive therapy	8 Sessions of HRT or supportive therapy	24.7±7.2 24.6±6.0	17.1 21.1	0.68	3	___	Comprehensive behavioral intervention resulted in greater improvement in symptoms severity compared to supportive therapy.
117	62	6–17	Parallel	YGTSS	Placebo Pramipexole	0.0625–0.5 (0.4302 mg)		−7.17 −7.16	.003	27	___	No evidence that pramipexole has efficacy in suppressing tics. It may decrease symptoms of associated ADHD.

Note: ADHD = attention-deficit/hyperactivity disorder; ERP = exposure and response prevention; HRT = habit reversal training; NNT = number needed to treat; TSGS = Tourette Syndrome Global Scale; TSSS = Tourette Syndrome Severity Scale; YGTSS = Yale Global Tic Severity Scale.

[a]*Dose given in mg/d.*

[b]*Standard deviations not reported.*

[c]*Global severity score.*

TABLE 3 Tic Disorder Medications, Doses, Uses, and Comments

Medication	Starting Dose (mg)	Usual dose range (mg/d)	Comments
Haloperidol	0.25–0.5	1–4	FDA approval for TD, EPS concerns; reports of anxiety flares
Pimozide	0.5–1.0	2–8	FDA approval for TD, ECG monitoring, 2D6 pharmacogenomic testing recommended
Fluphenazine	0.5–1.0	1.5–10	EPS < haloperidol
Risperidone	0.125–0.5	0.75–3.0	Metabolic effects, prolactin elevation
Ziprasidone	5–10	10–40	Current available doses above those used in RCT
Olanzapine	2.5–5.0	2.5–12.5	Metabolic effects are a major concern
Quetiapine	25	25–200	Metabolic effects
Aripiprazole	1.0–2.5	2.5–15	No prolactin elevations, reports of improvement in OCD
Sulpiride	50–100 (2 mg/kg)	100–500	Not approved in USA; larger open-label pediatric study (N = 189)
Tiapride	50–100 (2 mg/kg)	100–500	Not approved in USA
Tetrabenazine	25	37.5–150	Sedation, weight gain, depression, 2D6 pharmacogenomic testing recommended
Clonidine	0.025–0.05	0.1–0.4	Sedation, short acting, most helpful for those with initial insomnia, ADHD
Clonidine ER	0.1	0.1–0.4	FDA approved for ADHD
Guanfacine	0.5–1.0	1.0–4.0	Support especially for tics +ADHD
Guanfacine ER	1.0	1–4	FDA approved for ADHD
Clonazepam	0.25	0.25–3	Sedation, dependence, behavioral side effects

Note: ADHD = attention-deficit/hyperactivity disorder; FDA = Food and Drug Administration; ECG = electrocardiogram; EPS = extrapyramidal side effects; ER = extended release; OCD = obsessive-compulsive disorder; RCT = randomized controlled trial; TD = Tourette's disorder.

Recommendation 4. The assessment for tic disorders should involve a careful examination for comorbid psychiatric conditions. [CS]

Any assessment of a child or adolescent that reveals the presence of tics should prompt assessment for common externalizing and internalizing psychiatric disorders, and current social functioning along with any developmental delays. Given the frequent comorbidity of CTD with other psychiatric conditions,[82] incorporating measures for comorbid conditions into the assessment of youth is frequently warranted, depending on the clinical presentation. Although those individuals with uncomplicated CTD are less likely to present with neurocognitive deficits, those with comorbid conditions (especially ADHD) have significant risk of educational struggles and in most cases should be considered for educational testing.[66,83] A complete discussion of these comorbid conditions is outside the scope of this paper; thus the reader is referred to the AACAP Practice Parameters[84] for each disorder.

TREATMENT

Recommendation 5. Education regarding CTD should be provided regarding expectations for course and prognosis, and treatment planning should consider classroom-based accommodations. [CS]

Psychoeducation should be provided to the youth and family regarding tics including common symptom presentations, risks related to co-occurring conditions, the typical course across the lifetime, prognosis (25% with tics into adulthood), and treatment options.[9,10] The youth's typical exacerbating (e.g., illness, stress, heat) and alleviating factors (e.g., rest, listening to music) should be reviewed. Families (and clinicians) can find an abundance of information related to CTD that is especially produced for clinicians, parents, youth, or educators (including information on school-based accommodations and local advocacy groups) on the Tourette Syndrome Association website (www.tsa-usa.org) or on the Tourette Syndrome "Plus" website (www.tourettesyndrome.net/).

Classroom accommodations are often necessary to help the child best access his or her curricula, and an Individualized Education Plan (IEP) or 504 plan may be necessary. Parents should be guided to information on tic disorders designed for teachers and school personnel. Approximately 72% of children with tic disorders receive some form of accommodation from their teachers, with the most common being ignoring

of the tics and permission to leave the room as needed.[85]

Recommendation 6. Treatment for CTD should address the levels of impairment and distress caused by the tics as well as any comorbid conditions. [CS]

The decision to treat tics is a sensitive one, made in conjunction with the child and family based on the level of impairment and distress caused by the tics. If the tics are mild in severity, there may be no need for intervention after psychoeducation is provided. Often children and families cope well with tics of mild to moderate severity until the child enters the pre-teen age group or middle school, at which time teasing from peers may prompt the child and family to request intervention. Potential adverse events associated with treatment interventions should be carefully weighed.

When establishing the treatment hierarchy, one should begin with the most impairing condition. In many circumstances, it is the comorbid condition, and not the tic disorder, that causes the most impairment in functioning or has the most impact on quality of life. Frequently the initial interventions address target symptoms from a comorbid condition, with only ongoing monitoring of tics.

Recommendation 7. Behavioral interventions for CTD should be considered when tics cause impairment, are moderate in severity, or if behavioral-responsive psychiatric comorbidities are present. [CG]

Behavioral intervention offers a nonpharmacological alternative to tic treatment. The majority of those with tics experience them as somewhat voluntary.[86] In addition, many individuals with tics describe a distinct aversive sensation or a buildup of tension that is relieved by tic expression.[87,88] Termed a premonitory urge,[86,88] this pattern of tension buildup and release is similar to the relationship between obsessions and compulsions in OCD, but with a sensory trigger rather than a cognitive one.[89] In a similar manner, tic expression eliminates the aversive premonitory sensation just as completing the compulsion eliminates the obsession, suggesting that tics are maintained, in part, by negative reinforcement (i.e., removal of an unpleasant stimulus).[87]

The behavioral intervention with the strongest empirical support relies on this formulation and is called habit reversal training (HRT). Typical components of HRT include awareness training, building a competing response and social support. HRT has been shown to have efficacy in youth with moderate or greater tic severity compared to those not receiving HRT.[90[rct]] In that randomized trial comparing HRT to an attention control in 25 youth with tic disorders, HRT was associated with a 50% response rate, 30% reduction in tic severity, and approximately 50% reduction in tic-related impairment.[90[rct]] In the HRT group, 46% were classified as treatment responders versus only 25% of those in the attention control arm. A therapist guide and parent workbooks for HRT are available.[91]

The multisite, randomized controlled Comprehensive Behavioral Intervention for Tics (C-BIT), co-sponsored by the Tourette Syndrome Association (TSA) and National Institutes of Health, evaluated an HRT-based protocol versus a psychosocial control.[92[rct]] In the C-BIT trial, 126 youth with TD were randomized to an 8-session, 10-week HRT-based intervention or an equivalently dosed psychoeducational control. In the HRT condition, 52.5% responded compared to 18.5% in the control condition; the percent reduction in tic symptom severity was 51% and 30% for HRT and control respectively (between-groups effect size = 0.64). In addition to HRT, the C-BIT intervention included sessions focused on the functional assessment of tics. These sessions aimed to help parents to identify factors that sustained or exacerbated tics. The biological etiology of tics was emphasized; however, the role of environmental operant factors such as escape and attention were highlighted as well. The functional analysis involved identification of antecedents and consequences influencing tics, followed by the implementation of behavioral strategies to mitigate tic severity/frequency.[91] The C-BIT intervention also included relaxation training components.[93] In this study, 87% of those receiving HRT were also taking medications. A pilot trial suggests C-BIT delivered by telemedicine can be effective.[94[rct]]

Behavioral treatment may also address less adaptive coping strategies (e.g., avoidance, withdrawal) that develop secondary to tics and contribute to heightened impairment. In some youth, self-concept can become overly centered on having tics rather than focusing on their areas of strength and resilience. The unfortunate consequence of this adaptation to illness (e.g., lingering dependence on parents) can compound

the sense of marginalization. Skill-based therapies that target distorted cognitions and avoidance should be beneficial in improving quality of life and reducing sustained reliance on problematic coping mechanisms. There is preliminary support for structured parent training to address disruptive behavior problems in youth with chronic tics.[95[rct]] This study enrolled 24 youth with tics and at least moderate disruptive behavior symptoms. Seven of the 11 youth receiving 10 sessions of structured behavioral parent training were considered responders, compared to 2 of 12 controls.

There are no systematic studies to date comparing HRT to medication or combined therapies in youth. HRT is nonetheless an excellent example of a therapy that offers the advantage of having lower risks compared to metabolic adverse effects of medications. Severe tics or tics whose character interferes with the child's ability to function in school may require medication intervention at an earlier time or combined medication and HRT. In all cases, the treating clinician must balance tic severity and treatment efficacy with the adverse effect profile.

Recommendation 8. Medications for CTD should be considered for moderate to severe tics causing severe impairment in quality of life or when medication responsive psychiatric comorbidities are present that target both tic symptoms and comorbid conditions. [CG]

Large, multi-site, randomized, placebo-controlled trials for the treatment of tic disorders are few in number, especially in pediatric populations (Table 2).[77,78,92,96-117] Most medication treatment studies target moderate to severe tic severity, resulting in symptom reduction but not remission. Despite the limited number of studies, however, medical treatments for tics should have evidence-based support whenever feasible.[7] The only 2 Food and Drug Administration (FDA)–approved medications to treat TD are haloperidol and pimozide; however, most clinicians use atypical antipsychotics before these agents (Table 3). Recent reviews provide overviews of pharmacological approaches and suggested dosing.[118,119] A clinician survey found that the most common medications used to treat tics are risperidone followed by clonidine then by aripiprazole,[120] and another survey found aripiprazole to be most commonly used, followed by clonidine followed by risperidone.[121]

α-2 Agonists

α-Adrenergic medications have demonstrated an effect size of 0.5 for the amelioration of tics.[103[rct],107[rct]] Some prescribers prefer α-2 agonists as first-line agents over antipsychotic medications because of the adverse effect profile, which is perceived as less serious than with antipsychotic medications. A recent meta-analysis found that trials that enrolled subjects with tics and ADHD demonstrated a medium-to-large effect in reducing tic severity (0.68), whereas trials that excluded subjects with ADHD demonstrated only a small, nonsignificant benefit (0.15).[120,122] Clonidine activates the presynaptic auto-receptors in the locus ceruleus, thereby reducing norepinephrine release that may diminish tics. The starting dose is 0.05 mg per day with gradual increases up to 0.3 mg per day to control tics often administered in divided doses 3 to 4 times per day. The main adverse effect limiting its use is sedation.[123] A transdermal patch of clonidine is available, as is a sustained release oral formulation that was recently approved for the treatment of ADHD,[124] but has not been studied for use in children and adolescents with CTD.

Compared to clonidine, guanfacine appears to bind more selectively to postsynaptic prefrontal α (2A)–receptors to enhance functioning of prefrontal cortex.[125] A double-blind, placebo-controlled trial showed efficacy for tic severity.[103[rct]] A sustained release formulation has been approved for ADHD[126] and trials for CTD are underway.

Antipsychotic Medications

Several conventional antipsychotic medications have been shown to be effective for decreasing tic severity, although these studies enrolled primarily adults. Haloperidol has been shown to be effective in several randomized controlled trials (RCTs); however, up to 84% of patients have experienced adverse events with roughly one-third having extrapyramidal side effects.[99] A haloperidol and pimozide placebo-controlled crossover trial found pimozide to be more effective at reducing total number of tics and to be better tolerated as compared with haloperidol.[99[rct]] Although much lower doses are needed when using typical or atypical antipsychotics for CTD than for bipolar or psychotic disorders, a careful risk/benefit assessment and adverse effect monitoring are recommended.

Concerns about adverse effects have led to studies with the atypical antipsychotics for the

treatment of TD. The best studied atypical antipsychotic to date is risperidone with 4 randomized controlled trials[78[rct],102[rct],105[rct]]; however only 1 of the trials was conducted exclusively with children and adolescents, showing risperidone to be an effective treatment.[77[rct]] Active comparator trials (clonidine and pimozide versus risperidone) found risperidone at least as effective. In pediatric subjects, common adverse effects were weight gain and mild to moderate sedation. No clinically signficant extrapyramidal symptoms in pediatric patients were observed.[77,78] Effective doses for patients with TD ranged from 1.0 to 3.5 mg per day.[78]

In an RCT of ziprasidone, a 39% decrease on the YGTSS scale compared to 16% for placebo was observed.[101[rct]] No differences were found in vital signs or ECG measures. Despite those results, concerns about ECG changes persist. A prospective study evaluating ECG changes in pediatric patients taking ziprasidone for TD, OCD, or a pervasive developmental disorder reported a mean increase in the QTc interval from baseline to peak of 28 $\pm$ 26 milliseconds, leading to a recommendation of obtaining screening ECGs read by experienced cardiologists if considering ziprasidone treatment.[127]

Several open-label or pilot trials of olanzapine have been published[128[ut],129[ut],130[ut],131[ct]] and 1 double-blind crossover with olanzapine and pimozide.[132[rct]] Only 2 of these studies were with pediatric patients.[129[ut],131[ct]] In these trials, although olanzapine resulted in a decrease in both tics and aggression, there was a mean increase in weight of 9 to 12 pounds.[129,131] Thus, despite potential reduction of tics and co-occurring symptoms, the risk of weight gain and metabolic effects suggests that olanzapine should not be the first line medication for CTD.

A recent open-label trial with aripiprazole found a 52% reduction in the Korean version of the YGTSS with 79% of patients reported to be "much improved" or "very much improved" on the CGI-I.[133[ut]] The mean dose in this study was 9.8 mg per day; the most common adverse effects were hypersomnia (37.5%), nausea (20.8%), and headache (16.6%). In open trials of youth with CTD, tic improvement was observed at lower doses with mean weight gain of 2 to 5 pounds.[134[ut],135[ut]] Further double-blind controlled trials are underway.

Treatment in Context of Comorbidity

Comorbid OCD. The efficacy of pharmacotherapy for OCD in pediatric populations has been demonstrated in several controlled trials with clomipramine and SSRIs (see *AACAP Practice Parameter for the Assessment and Treatment of Obsessive Compulsive Disorder*[136]).

Some studies suggest that the presence of tics may yield a less robust response to SSRIs. In a response rate analysis from a large pediatric paroxetine trial, the response rate for patients with a diagnosis of OCD only (75%) was significantly greater than patients with comorbid psychopathology, for example, ADHD (56%), tic disorder (53%), and ODD (39%).[137[rct]] Similarly, individuals with comorbid tics in the Pediatric OCD Treatment Study (POTS) did not respond as well to sertraline as did those without tics.[138] The use of an antipsychotic with SSRI therapy may result in additional benefit for those with OCD and tics. A meta-analysis of the adult literature examining the use of antipsychotic augmentation in the treatment of OCD showed that the NNT for OCD and tics was 2.3 compared to 5.9 for those with OCD alone.[139] One open-label study reported improvement in OCD severity when aripiprazole was used to treat tic disorders.[134[ut]]

Comorbid ADHD. Treatment of ADHD in the context of tic disorders can, at times, be challenging because of concerns of worsening tic severity.[140] For children with ADHD, recent studies have demonstrated that tics are not universally increased by stimulant medication[47,140]; however the FDA package insert for stimulants does list tics as a contraindication. No differences were observed in worsening of tics in children with comorbid ADHD and a CTD taking methylphenidate, clonidine, or placebo, with about 20% in each group showing an exacerbation.[107[rct]] The presence of tics did appear to limit the maximum dose achieved. Other options are the use of atomoxetine with reported benefits on tic symptoms as well as ADHD[110]; however, occasional reports of tics worsening exist.[141,142] Guanfacine has been shown to have a clinically relevant effect size for both ADHD and tic symptoms.[103[rct]] TCAs have shown benefit for ADHD with comorbid tics,[106[rct],143[rct]] but cardiovascular risks likely outweigh the benefit of this option. Please refer to the Cochrane Database review for a detailed overview.[140]

Comorbid Mood/Anxiety (Non-OCD). This area is understudied, but clearly many youth with TD have co-occurring mood and non-OCD anxiety disorders.[51] Currently, the best approach is to use evidence based treatment for the co-occurring mood or anxiety disorder.

Explosive/Rage Symptoms. Anger and rage outbursts are not uncommon among patients with tics, with a survey of clinicians estimating 37% of their tic patients present with anger control problems.[144] In some cases, OCD symptoms or sensory issues (too hot, too noisy) may serve as triggers, and other times anger is due to poor frustration tolerance. Behavioral therapies that address antecedents and anger management may be useful. In clinic-referred tic samples, up to 80% of youth are estimated to have co-occurring disruptive behavior disorders.[54,143] There are no controlled pharmacological studies in youth with tic disorders and aggressive/anger outbursts. Although there are preliminary data for olanzapine,[129[ut],131[ct]] aripiprazole[145[cs]] and risperidone,[146[cs]] in reducing disruptive behavior disorder symptoms, these findings should be interpreted cautiously given significant design limitations, small samples, relatively weak effects, and risks associated with these medications. Similarly, a reduction in rage attacks was observed after an 8-week open trial of paroxetine,[147[ut]] but the age range was markedly variable (n = 45, aged 6–55 years) and self-report was used to assess rage.

Recommendation 9. Deep brain stimulation, repetitive magnetic stimulation, special diets, and dietary supplements lack empirical support for the treatment of CTD/TD and are not recommended. [NE]

Deep brain stimulation (DBS) is a surgical treatment approach that may hold benefit for a few treatment-refractory adults; however, few cases have been reported of youth receiving DBS for severe, treatment-resistant tics. At this time, DBS guidelines have advised that this procedure should not be conducted in individuals less than 25 years of age outside of a research setting, because the severity of TD often diminishes in late teen/early adulthood.[148[ut]]

An open-label study examining repetitive transcranial magnetic stimulation (rTMS) in youth with TD has been conducted with no reported adverse outcomes.[149] Small studies examining rTMS in the treatment of adults with TD have shown negative results.[150[ct],151[ct]] Very few youth have received rTMS and this treatment option should be considered preliminary until larger blinded studies have resolved issues regarding the safety, ethics, and long term impact on development.[152] Notably, neurosurgery and neurostimulation should be considered only in refractory cases, and clinicians should carefully weigh the risks and benefits for these experimental procedures before recommending them for use in pediatric patients.

Many parents have found purported therapies (e.g., special diets, supplements, brushing) via the Internet or support groups. Although many patients with tic disorders do use complementary and alternative medical therapies,[153] support for this practice is not currently at the evidence based level.[118,154,155] Some therapies, such as high-dose vitamin B6 or St. John's wort, have the potential for adverse outcomes or interactions with psychoactive medications and are not recommended until studied appropriately in children.[156]

PARAMETER LIMITATIONS

AACAP Practice Parameters are developed to assist clinicians in psychiatric decision making. These Parameters are not intended to define the sole standard of care. As such, the Parameters should not be deemed inclusive of all proper methods of care nor 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 other available resources. &

This Parameter was developed by Tanya K. Murphy, M.D., Adam B. Lewin, Ph.D., Eric A. Storch, Ph.D., Saundra Stock, M.D., and the American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI): Oscar G. Bukstein, M.D., M.P.H. and Heather J. Walter, M.D., M.P.H., Co-Chairs, and Christopher Bellonci, M.D., R. Scott Benson, M.D., Regina Bussing, M.D., Allan Chrisman, M.D., Tiffany R. Farchione, M.D., John Hamilton, M.D., Munya Hayek, M.D., Helene Keable, M.D., Joan Kinlan, M.D., Nicole Quiterio, M.D., Carol Rockhill, M.D., Ulrich Schoettle, M.D., Matthew Siegel, M.D., and Saundra Stock, M.D.

AACAP Practice Parameters are developed by the AACAP CQI in accordance with American Medical Association policy. Parameter development is an iterative process between the primary author(s), the CQI, topic experts, and representatives from multiple constituent groups, including AACAP membership, relevant AACAP Committees, the AACAP Assembly of Regional Organizations, and the AACAP Council. Details of the Parameter development process can be accessed on the AACAP website. Responsibility for Parameter content and review rests with the author(s), the CQI, the CQI 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 assessment and treatment practices. Recommendations are based on the critical appraisal of 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 clinical consensus. This Parameter is a patient-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.

The authors acknowledge the following experts for their contributions to this Parameter Barbara Coffey, M.D., M.S., Carol Mathews, M.D., Cathy Budman, M.D., James Leckman, M.D., Michael Bloch, M.D. and Jonathan W. Mink, M.D., Ph.D.

Kristin Kroeger Ptakowski and Jennifer Medicus served as the AACAP staff liaisons for the CQI.

This Parameter was reviewed at the Member Forum at the AACAP Annual Meeting in October 2011.

From December 2012 to January 2013, this Parameter was reviewed by a Consensus Group convened by the CQI. Consensus Group members and their constituent groups were as follows: Oscar Bukstein, M.D., M.P.H., Saundra Stock, M.D., Regina Bussing, M.D., and Allan Chrisman, M.D. (CQI); Barbara Coffey, M.D., James Leckman, M.D., (Topic Experts); Melissa DelBello, M.D. (AACAP Committee on Research); Debra Koss, M.D., Felissa Goldstein, M.D. (AACAP Assembly of Regional Organizations); and David DeMaso, M.D., Jenna Saul, M.D. (AACAP Council).

This Practice Parameter was approved by the AACAP Council on July 29, 2013.

This Practice Parameter is available on the internet (www.aacap.org).

Correspondence to the AACAP Communications Department, 3615 Wisconsin Ave., NW, Washington, D.C. 20016.

Disclosures: Tanya K. Murphy, M.D. receives research funding from NIH/NIMH, CDC, Otsuka Pharmaceuticals, NARSAD, IOCDF, Ortho-McNeil Janssen Pharmaceuticals, Shire Pharmaceuticals, Pfizer, Inc. and Indevus Pharmaceuticals. She has received travel support from the Tourette Syndrome Association and honorarium from grand rounds lectures. Adam B. Lewin, Ph.D. serves as a consultant for Otsuka America Pharmaceutical and ProPhase, Inc. He receives grant support from International Obsessive Compulsive Disorder Foundation; National Alliance for Research on Schizophrenia and Depression; University of South Florida Research Foundation, Inc. He has received travel support from University of South Florida Research Foundation, Inc. Eric A. Storch, Ph.D., serves on the advisory board for the International Obsessive Compulsive Disorder Foundation. He serves as a consultant for Otsuka America Pharmaceutical, Inc. and ProPhase Inc. He receives grant support from Centers for Disease Control; National Institutes of Health; Ortho-McNeil Neurologics; Transportation Security Administration. He has intellectual property with Springer and Taylor and Francis. He serves on the speakers bureau for International Obsessive Compulsive Disorder Foundation. Saundra Stock, M.D. has received research funding from Glaxo-SmithKline and served as a sub-investigator n studies funding by Forest Research Institute, Merck/Schering-Plough, Supernus, Bristol-Myers Squibb, AstraZeneca and Boehringer-Ingelheim. She also has served on the expert panel consulting to the Florida Medicaid Drug Therapy Management Program for Behavioral Health. Oscar Bukstein, M.D., M.P.H., co-chair, has served as a consultant with PRIME CME and EZRA Inovations, and has intellectual property with Routledge Press. Heather Walter, M.D., M.P.H., co-chair, has no financial relationships to disclose. Disclosures of potential conflicts of interest for all other individuals named above are provided on the AACAP website on the Practice Information page.

http://dx.doi.org/10.1016/j.jaac.2013.09.015

REFERENCES

1. American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Publishing; 2013.
2. Leckman JF, Bloch MH, King RA, Scahill L. Phenomenology of tics and natural history of tic disorders. Adv Neurol. 2006; 99:1-16.
3. Kepley H, Connors S. Management of learning and school difficulties in children with Tourette syndrome. In: Woods D, Piacentini J, Walkup J, eds. Treating Tourette Syndrome and Tic Disorders: a Guide for Practitioners. New York: Guilford Press; 2007:242-264.
4. Meidinger AL, Miltenberger RG, Himle M, Omvig M, Trainor C, Crosby R. An investigation of tic suppression and the rebound effect in Tourette's disorder. Behav Mod. 2005;29:716-745.
5. Verdellen CW, Hoogduin CA, Keijsers GP. Tic suppression in the treatment of Tourette's syndrome with exposure therapy: the rebound phenomenon reconsidered. Mov Disord. 2007;22: 1601-1606.
6. Zinner S. Tourette syndrome in infacy and early childhood. Infants Young Child. 2006;19:353-370.
7. Scahill L, Erenberg G, Berlin CM Jr, *et al*. Contemporary assessment and pharmacotherapy of Tourette syndrome. NeuroRx. 2006;3:192-206.
8. Leckman JF, Zhang H, Vitale A, *et al*. Course of tic severity in Tourette syndrome: the first two decades. Pediatrics. 1998; 102:14-19.
9. Bloch MH, Leckman JF. Clinical course of Tourette syndrome. J Psychosom Res. 2009;67:497-501.
10. Leonard HL, Lenane MC, Swedo SE, Rettew DC, Gershon ES, Rapoport JL. Tics and Tourette's disorder: a 2- to 7-year follow-up of 54 obsessive-compulsive children. Am J Psychiatry. 1992; 149:1244-1251.
11. Bloch MH, Peterson BS, Scahill L, *et al*. Adulthood outcome of tic and obsessive-compulsive symptom severity in children with Tourette syndrome. Arch Pediatr Adolesc Med. 2006; 160:65-69.
12. Coffey BJ, Biederman J, Geller D, *et al*. Reexamining tic persistence and tic-associated impairment in Tourette's disorder: findings from a naturalistic follow-up study. J Nerv Ment Dis. 2004;192:776-780.
13. Storch EA, Merlo LJ, Lack C, *et al*. Quality of life in youth with Tourette's syndrome and chronic tic disorder. J Clin Child Adolesc Psychol. 2007;36:217-227.
14. Lin H, Katsovich L, Ghebremichael M, *et al*. Psychosocial stress predicts future symptom severities in children and adolescents with Tourette syndrome and/or obsessive-compulsive disorder. J Child Psychol Psychiatry. 2007;48:157-166.
15. Elstner K, Selai CE, Trimble MR, Robertson MM. Quality of life (QOL) of patients with Gilles de la Tourette's syndrome. Acta Psychiatr Scand. 2001;103:52-59.
16. Robertson MM. Mood disorders and Gilles de la Tourette's syndrome: an update on prevalence, etiology, comorbidity, clinical associations, and implications. J Psychosom Res. 2006;61: 349-358.
17. Tabori-Kraft J, Dalsgaard S, Obel C, Thomsen PH, Henriksen TB, Scahill L. Prevalence and clinical correlates of tic disorders in a community sample of school-age children. Eur Child Adolesc Psychiatry. 2012;21:5-13.
18. Robertson MM. The prevalence and epidemiology of Gilles de la Tourette syndrome. Part 1: the epidemiological and prevalence studies. J Psychosom Res. 2008;65:461-472.
19. Khalifa N, von Knorring AL. Prevalence of tic disorders and Tourette syndrome in a Swedish school population. Dev Med Child Neurol. 2003;45:315-319.
20. Scahill L, Bitsko RH, Visser SN, Blumberg SJ. Prevalence of diagnosed Tourette syndrome in persons Aged 6–17 Years—United States, 2007. Morbid Mortal Wkly Rep. 2009;58: 581-585.
21. Costello EJ, Angold A, Burns BJ, *et al*. The Great Smoky Mountains Study of Youth. Goals, design, methods, and the prevalence of DSM-III-R disorders. Arch Gen Psychiatry. 1996;53: 1129-1136.

22. Leckman J, Bloch MH, Smith ME, Larabi D, Hampson M. Neurobiological substrates of Tourette's disorder. J Child Adolesc Psychopharmacol. 2010;20:237-247.
23. Rickards H. Functional neuroimaging in Tourette syndrome. J Psychosom Res. 2009;67:575-584.
24. Wang Z, Maia TV, Marsh R, Colibazzi T, Gerber A, Peterson BS. The neural circuits that generate tics in Tourette's syndrome. Am J Psychiatry. 2011;168:1326-1337.
25. Biswal B, Ulmer JL, Krippendorf RL, *et al*. Abnormal cerebral activation associated with a motor task in Tourette syndrome. AJNR Am J Neuroradiol. 1998;19:1509-1512.
26. Ziemann U, Paulus W, Rothenberger A. Decreased motor inhibition in Tourette's disorder: evidence from transcranial magnetic stimulation. Am J Psychiatry. 1997;154:1277-1284.
27. Peterson BS, Skudlarski P, Anderson AW, *et al*. A functional magnetic resonance imaging study of tic suppression in Tourette syndrome. Arch Gen Psychiatry. 1998;55:326-333.
28. Plessen KJ, Royal JM, Peterson BS. Neuroimaging of tic disorders with co-existing attention-deficit/hyperactivity disorder. Eur Child adolescent Psychiatry. 2007;16 (Suppl 1):60-70.
29. Peterson BS, Leckman JF, Scahill L, *et al*. Steroid hormones and CNS sexual dimorphisms modulate symptom expression in Tourette's syndrome. Psychoneuroendocrinology. 1992;17:553-563.
30. Grados MA. The genetics of obsessive-compulsive disorder and Tourette syndrome: an epidemiological and pathway-based approach for gene discovery. J Am Acad Child Adolesc Psychiatry. 2010;49:810-819.
31. Hyde TM, Aaronson BA, Randolph C, Rickler KC, Weinberger DR. Relationship of birth weight to the phenotypic expression of Gilles de la Tourette's syndrome in monozygotic twins. Neurology. 1992;42:652-658.
32. Price RA, Kidd KK, Cohen DJ, Pauls DL, Leckman JF. A twin study of Tourette syndrome. Arch Gen Psychiatry. 1985;42:815-820.
33. Scharf J, Yu D, Mathews C, *et al*. Genome-wide association study of Tourette's syndrome. Mol Psychiatry. 2012;18:721-728.
34. State MW. The genetics of Tourette disorder. Curr Opin Genet Dev. 2011;21:302-309.
35. Ercan-Sencicek AG, Stillman AA, Ghosh AK, *et al*. L-histidine decarboxylase and Tourette's syndrome. N Engl J Med. 2010;362:1901-1908.
36. Kessler AR. Effects of medications on regulation of body temperature of patients with Tourette syndrome. J Child Neurol. 2004;19:220-224.
37. Leckman JF. Phenomenology of tics and natural history of tic disorders. Brain Dev. 2003;25(Suppl 1):S24-S28.
38. Hoekstra PJ, Anderson GM, Limburg PC, Korf J, Kallenberg CG, Minderaa RB. Neurobiology and neuroimmunology of Tourette's syndrome: an update. Cell Mol Life Sci. 2004;61:886-898.
39. Swedo SE, Leonard HL, Garvey M, *et al*. Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections: clinical description of the first 50 cases. Am J Psychiatry. 1998;155:264-271.
40. Swedo S, Leckman J, Rose N. From research subgroup to clinical syndrome: modifying the PANDAS criteria to describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome). Pediatr Therapeut. 2012;2:113. http://dx.doi.org/10.4172/2161-0665.1000113.
41. Murphy TK, Kurlan R, Leckman J. The immunobiology of Tourette's disorder, pediatric autoimmune neuropsychiatric disorders associated with streptococcus, and related disorders: a way forward. J Child Adolesc Psychopharmacol. 2010;20:317-331.
42. Zinner SH, Mink JW. Movement disorders I: tics and stereotypies. Pediatr Rev. 2010;31:223-233.
43. Sanger TD. Neuro-mechanical control using differential stochastic operators. Conf Proc IEEE Eng Med Biol Soc. 2010;2010:4494-4497. http://dx.doi.org/10.1109/IEMBS.2010.5626029.
44. Tourette Syndrome Association. Medical and Allied Professional Resources. Available at: http://www.tsa-usa.org/aMedical/medical_main.html. Accessed.
45. Brust JC. Substance abuse and movement disorders. Mov Disord. 2010;25:2010-2020.
46. Pliszka S. 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.
47. Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF. Meta-analysis: treatment of attention-deficit/hyperactivity disorder in children with comorbid tic disorders. J Am Acad Child Adolesc Psychiatry. 2009;48:884-893.
48. Bonnet C, Roubertie A, Doummar D, Bahi-Buisson N, Cochen de Cock V, Roze E. Developmental and benign movement disorders in childhood. Mov Disord. 2010;25:1317-1334.
49. McAbee GN, Wark JE, Manning A. Tourette syndrome associated with unilateral cystic changes in the gyrus rectus. Pediatr Neurol. 1999;20:322-324.
50. Scahill L, Sukhodolsky DG, Williams SK, Leckman JF. Public health significance of tic disorders in children and adolescents. Advanc Neurol. 2005;96:240-248.
51. Coffey BJ, Biederman J, Smoller JW, *et al*. Anxiety disorders and tic severity in juveniles with Tourette's disorder. J Am Acad Child Adolesc Psychiatry. 2000;39:562-568.
52. Lewin AB, Chang S, McCracken J, McQueen M, Piacentini J. Comparison of clinical features among youth with tic disorders, obsessive-compulsive disorder (OCD), and both conditions. Psychiatry Res. 2010;178:317-322.
53. Spencer TJ, Sallee FR, Gilbert DL, *et al*. Atomoxetine treatment of ADHD in children with comorbid Tourette syndrome. J Atten Disord. 2008;11:470-481.
54. Coffey BJ, Biederman J, Geller DA, *et al*. The course of Tourette's disorder: a literature review. Harv Rev Psychiatry. 2000;8:192-198.
55. Walkup JT, LaBuda MC, Singer HS, Brown J, Riddle MA, Hurko O. Family study and segregation analysis of Tourette syndrome: evidence for a mixed model of inheritance. Am J Hum Genet. 1996;59:684-693.
56. Swain JE, Scahill L, Lombroso PJ, King RA, Leckman JF. Tourette syndrome and tic disorders: a decade of progress. J Am Acad Child Adolesc Psychiatry. 2007;46:947-968.
57. Dykens E, Leckman J, Riddle M, Hardin M, Schwartz S, Cohen D. Intellectual, academic, and adaptive functioning of Tourette syndrome children with and without attention deficit disorder. J Abnorm Child Psychol. 1990;18:607-615.
58. Abwender DA, Como PG, Kurlan R, *et al*. School problems in Tourette's syndrome. Arch Neurol. 1996;53:509-511.
59. Burd L, Freeman RD, Klug MG, Kerbeshian J. Tourette syndrome and learning disabilities. BMC Pediatrics. 2005;5:34.
60. Erenberg G, Cruse RP, Rothner AD. Tourette syndrome: an analysis of 200 pediatric and adolescent cases. Clevel Clinic Q. 1986;53:127-131.
61. Chappell PB, Riddle MA, Scahill L, *et al*. Guanfacine treatment of comorbid attention-deficit hyperactivity disorder and Tourette's syndrome: preliminary clinical experience. J Am Acad Child Adolesc Psychiatry. 1995;34:1140-1146.
62. Gorman DA, Thompson N, Plessen KJ, Robertson MM, Leckman JF, Peterson BS. Psychosocial outcome and psychiatric comorbidity in older adolescents with Tourette syndrome: controlled study. Br J Psychiatry. 2010;197:36-44.
63. Khalifa N, von Knorring AL. Psychopathology in a Swedish population of school children with tic disorders. J Am Acad Child Adolesc Psychiatry. 2006;45:1346-1353.
64. Kostanecka-Endress T, Banaschewski T, Kinkelbur J, *et al*. Disturbed sleep in children with Tourette syndrome: a polysomnographic study. J Psychosom Res. 2003;55:23-29.
65. Denckla MB. Attention deficit hyperactivity disorder: the childhood co-morbidity that most influences the disability burden in Tourette syndrome. Adv Neurol. 2006;99:17-21.
66. Piacentini JC, Chang SW. Behavioral treatments for tic suppression: habit reversal training. Adv Neurol. 2006;99:227-233.
67. Jankovic J, Mejia NI. Tics associated with other disorders. Adv Neurology. 2006;99:61-68.
68. Burd L, Li Q, Kerbeshian J, Klug MG, Freeman RD. Tourette syndrome and comorbid pervasive developmental disorders. J Child Neurol. 2009;24:170-175.
69. Achenbach TM, Ruffle TM. The Child Behavior Checklist and related forms for assessing behavioral/emotional problems and competencies. Pediatr Rev. 2000;21:265-271.
70. Swanson JM. School-Based Assessments and Interventions for ADD Students. Irvine, CA: K C Publishing; 1992.
71. Gaffney G, Sieg K, Hellings J. The MOVES: a self-rating scale for Tourette's syndrome. J Child Adolesc Psychopharmacol. 1994;4:269-280.

72. Cohen DJ, Leckman JF, Shaywitz BA. The Tourette's syndrome and other tics. In: Shaffer D, Ehrhardt AA, Greenhill L, eds. Diagnosis and Treatment in Pediatric Psychiatry. New York: Macmillan Free Press; 1984.
73. Shytle RD, Silver AA, Sheehan KH, *et al*. The Tourette's Disorder Scale (TODS): development, reliability, and validity. Assessment. 2003;10:273-287.
74. Chang S, Himle M, Tucker B, Woods D, Piacentini J. Initial development and psychometric properties of the Parent Tic Questionnaire (PTQ) to assess tic severity in children with chronic tic disorders. Child Fam Behav Ther. 2009;31:181-191.
75. Storch EA, Lack CW, Simons LE, Goodman WK, Murphy TK, Geffken GR. A Measure of functional impairment in youth with Tourette's syndrome. J Pediatr Psychol. 2007;32:950-959.
76. Leckman JF, Riddle MA, Hardin MT, *et al*. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry. 1989;28: 566-573.
77. Gaffney GR, Perry PJ, Lund BC, Bever-Stille KA, Arndt S, Kuperman S. Risperidone versus clonidine in the treatment of children and adolescents with Tourette's syndrome. J Am Acad Child Adolesc Psychiatry. 2002;41:330-336.
78. Scahill L, Leckman JF, Schultz RT, Katsovich L, Peterson BS. A placebo-controlled trial of risperidone in Tourette syndrome. Neurology. 2003;60:1130-1135.
79. Shapiro AK, Shapiro E. Controlled study of pimozide vs. placebo in Tourette's syndrome. J Am Acad Child Psychiatry. 1984;23: 161-173.
80. Harcherik DF, Leckman JF, Detlor J, Cohen DJ. A new instrument for clinical studies of Tourette's syndrome. J Am Acad Child Psychiatry. 1984;23:153-160.
81. Chappell PB, McSwiggan-Hardin MT, Scahill L, *et al*. Videotape tic counts in the assessment of Tourette's syndrome: stability, reliability, and validity. J Am Acad Child Adolesc Psychiatry. 1994;33:386-393.
82. Connolly SD, Bernstein GA. Practice parameter for the assessment and treatment of children and adolescents with anxiety disorders. J Am Acad Child Adolesc Psychiatry. 2007;46: 267-283.
83. Channon S, Gunning A, Frankl J, Robertson MM. Tourette's syndrome (TS): cognitive performance in adults with uncomplicated TS. Neuropsychology. 2006;20:58-65.
84. Practice parameters for the assessment and treatment of children and adolescents with language and learning disorders. AACAP. J Am Acad Child Adolesc Psychiatry. 1998;37 (10 Suppl):46S-62S.
85. Packer LE. Tic-related school problems: impact on functioning, accommodations, and interventions. Behav Modification. 2005; 29:876-899.
86. Leckman JF, Walker DE, Cohen DJ. Premonitory urges in Tourette's syndrome. Am J Psychiatry. 1993;150:98-102.
87. Scahill LD, Leckman JF, Marek KL. Sensory phenomena in Tourette's syndrome. Adv Neurol. 1995;65:273-280.
88. Woods DW, Piacentini J, Himle MB, Chang S. Premonitory Urge for Tics Scale (PUTS): initial psychometric results and examination of the premonitory urge phenomenon in youths with tic disorders. J Dev Behav Pediatr. 2005;26:397-403.
89. Shapiro AK, Shapiro E. Evaluation of the reported association of obsessive-compulsive symptoms or disorder with Tourette's disorder. Comprehens Psychiatry. 1992;33:152-165.
90. Piacentini J, Chang S. Habit reversal training for tic disorders in children and adolescents. Behav Modif. 2005;29:803-822.
91. Woods D, Piacentini J, Chang S, *et al*. Managing Tourette Syndrome: a Behavioral Intervention for Children and Adults. New York: Oxford University Press; 2008.
92. Piacentini J, Woods DW, Scahill L, *et al*. Behavior therapy for children with Tourette disorder: a randomized controlled trial. JAMA. 2010;303:1929-1937.
93. Tourette Syndrome Association. Tourette Syndrome Comprehensive Behavioral Intervention for Tics (CBIT)—Skills Development Workshop Video. 2011. Available at: http://www.tsa-usa.org/news/CBIT_intro.html.
94. Himle MB, Freitag M, Walther M, Franklin S, Ely L, Woods DW. A randomized pilot trial comparing videoconference versus face-to-face delivery of behavior therapy for childhood tic disorders. Behav Res Ther. 2012.
95. Scahill L, Sukhodolsky DG, Bearss K, *et al*. Randomized trial of parent management training in children with tic disorders and disruptive behavior. J Child Neurol. 2006;21:650-656.
96. Shapiro E, Shapiro AK, Fulop G, *et al*. Controlled study of haloperidol, pimozide and placebo for the treatment of Gilles de la Tourette's syndrome. Arch Gen Psychiatry. 1989;46: 722-730.
97. Leckman JF, Hardin MT, Riddle MA, Stevenson J, Ort SI, Cohen DJ. Clonidine treatment of Gilles de la Tourette's syndrome. Arch Gen Psychiatry. 1991;48:324-328.
98. Feigin A, Kurlan R, McDermott MP, *et al*. A controlled trial of deprenyl in children with Tourette's syndrome and attention deficit hyperactivity disorder. Neurology. 1996;46:965-968.
99. Sallee FR, Nesbitt L, Jackson C, Sine L, Sethuraman G. Relative efficacy of haloperidol and pimozide in children and adolescents with Tourette's disorder. Am J Psychiatry. 1997;154: 1057-1062.
100. Gilbert DL, Sethuraman G, Sine L, Peters S, Sallee FR. Tourette's syndrome improvement with pergolide in a randomized, double-blind, crossover trial. Neurology. 2000;54:1310-1315.
101. Sallee FR, Kurlan R, Goetz CG, *et al*. Ziprasidone treatment of children and adolescents with Tourette's syndrome: a pilot study. J Am Acad Child Adolesc Psychiatry. 2000;39:292-299.
102. Bruggeman R, van der Linden C, Buitelaar JK, Gericke GS, Hawkridge SM, Temlett JA. Risperidone versus pimozide in Tourette's disorder: a comparative double-blind parallel-group study. J Clin Psychiatry. 2001;62:50-56.
103. Scahill L, Chappell PB, Kim YS, *et al*. A placebo-controlled study of guanfacine in the treatment of children with tic disorders and attention deficit hyperactivity disorder. Am J Psychiatry. 2001; 158:1067-1074.
104. Silver AA, Shytle RD, Sheehan KH, Sheehan DV, Ramos A, Sanberg PR. Multicenter, double-blind, placebo-controlled study of mecamylamine monotherapy for Tourette's disorder. J Am Acad Child Adolesc Psychiatry. 2001;40:1103-1110.
105. Dion Y, Annable L, Sandor P, Chouinard G. Risperidone in the treatment of tourette syndrome: a double-blind, placebo-controlled trial.PG-31-9. J Clin Psychopharmacol. 2002;22:31-39.
106. Spencer T, Biederman J, Coffey B, *et al*. A double-blind comparison of desipramine and placebo in children and adolescents with chronic tic disorder and comorbid attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 2002;59:649-656.
107. Tourette Syndrome Study Group. Treatment of ADHD in children with tics: a randomized control trial. Neurology. 2002;58: 526-536.
108. Gilbert DL, Dure L, Sethuraman G, Raab D, Lane J, Sallee FR. Tic reduction with pergolide in a randomized controlled trial in children. Neurology. 2003;60:606-611.
109. Verdellen CW, Keijsers GP, Cath DC, Hoogduin CA. Exposure with response prevention versus habit reversal in Tourettes's syndrome: a controlled study. Behav Res Ther. 2004;42:501-511.
110. Allen AJ, Kurlan RM, Gilbert DL, *et al*. Atomoxetine treatment in children and adolescents with ADHD and comorbid tic disorders. Neurology. 2005;65:1941-1949.
111. Nicolson R, Craven-Thuss B, Smith J, McKinlay BD, Castellanos FX. A randomized, double-blind, placebo-controlled trial of metoclopramide for the treatment of Tourette's disorder. J Am Acad Child Adolesc Psychiatry. 2005;44:640-646.
112. Toren P, Weizman A, Ratner S, Cohen D, Laor N. Ondansetron treatment in Tourette's disorder: a 3-week, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2005;66: 499-503.
113. Smith-Hicks CL, Bridges DD, Paynter NP, Singer HS. A double blind randomized placebo control trial of levetiracetam in Tourette syndrome. Mov Disord. 2007;22:1764-1770.
114. Du YS, Li HF, Vance A, *et al*. Randomized double-blind multicentre placebo-controlled clinical trial of the clonidine adhesive patch for the treatment of tic disorders. Aust N Z J Psychiatry. 2008;42:807-813.
115. Hedderick EF, Morris CM, Singer HS. Double-blind, crossover study of clonidine and levetiracetam in Tourette syndrome. Pediatr Neurol. 2009;40:420-425.
116. Jankovic J, Jimenez-Shahed J, Brown LW. A randomised, double-blind, placebo-controlled study of topiramate in the treatment of Tourette syndrome. J Neurol Neurosurg Psychiatry. 2009; 81:70-73.

117. Kurlan R, Crespi G, Coffey B, Mueller-Vahl K, Koval S, Wunderlich G. A multicenter randomized placebo-controlled clinical trial of pramipexole for Tourette's syndrome. Move Disord. 2012;27:775-778.
118. McNaught KSP, Mink JW. Advances in understanding and treatment of Tourette syndrome. Nature Rev Neurol. 2011;7: 667-676.
119. Chadehumbe MA, Greydanus DE, Feucht C, Patel DR. Psychopharmacology of tic disorders in children and adolescents. Pediatr Clin North Am. 2011;58:259-272, xiii.
120. Roessner V, Plessen KJ, Rothenberger A, *et al*. European Clinical Guidelines for Tourette Syndrome and Other Tic Disorders. Part II: Pharmacological Treatment. Eur Child Adolesc Psychiatry. 2011;20:173-196.
121. Robertson MM. Gilles de la Tourette syndrome: the complexities of phenotype and treatment. Br J Hosp Med (Lond). 2011;72: 100-107.
122. Weisman H, Qureshi IA, Leckman JF, Scahill L, Bloch MH. Systematic review: Pharmacological treatment of tic disorders—efficacy of antipsychotic and alpha-2 adrenergic agonist agents. Neurosci Biobehav Rev. 2013;37:1162-1171.
123. Goetz CG. Clonidine and clonazepam in Tourette syndrome. Adv Neurol. 1992;58:245-251.
124. Kollins SH, Jain R, Brams M, *et al*. Clonidine extended-release tablets as add-on therapy to psychostimulants in children and adolescents with ADHD. Pediatrics. 2011;127:e1406-e1413.
125. Scahill L. Alpha-2 adrenergic agonists in children with inattention, hyperactivity and impulsiveness. CNS Drugs. 2009;23 (Suppl 1):43-49.
126. Sallee FR, McGough J, Wigal T, Donahue J, Lyne A, Biederman J. Guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder: a placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2009;48:155-165.
127. Blair J, Scahill L, State M, Martin A. Electrocardiographic changes in children and adolescents treated with ziprasidone: a prospective study. J Am Acad Child Adolesc Psychiatry. 2005; 44:73-79.
128. Budman CL, Gayer A, Lesser M, Shi Q, Bruun RD. An open-label study of the treatment efficacy of olanzapine for Tourette's disorder. J Clin Psychiatry. 2001;62:290-294.
129. McCracken JT, Suddath R, Chang S, Thakur S, Piacentini J. Effectiveness and tolerability of open label olanzapine in children and adolescents with Tourette syndrome. J Child Adolesc Psychopharmacol. 2008;18:501-508.
130. Stamenkovic M, Schindler SD, Aschauer HN, *et al*. Effective open-label treatment of tourette's disorder with olanzapine. Int Clin Psychopharmacol. 2000;15:23-28.
131. Stephens RJ, Bassel C, Sandor P. Olanzapine in the treatment of aggression and tics in children with Tourette's syndrome—a pilot study. J Child Adolesc Psychopharmacol. 2004;14:255-266.
132. Onofrj M, Paci C, D'Andreamatteo G, Toma L. Olanzapine in severe Gilles de la Tourette syndrome: a 52-week double-blind cross-over study vs. low-dose pimozide. J Neurol. 2000;247:443-446.
133. Yoo HK, Choi SH, Park S, Wang HR, Hong JP, Kim CY. An open-label study of the efficacy and tolerability of aripiprazole for children and adolescents with tic disorders. J Clin Psychiatry. 2007;68:1088-1093.
134. Murphy TK, Mutch PJ, Reid JM, *et al*. Open label aripiprazole in the treatment of youth with tic disorders. J Child Adolesc Psychopharmacol. 2009;19:441-447.
135. Lyon GJ, Samar S, Jummani R, *et al*. Aripiprazole in children and adolescents with Tourette's disorder: an open-label safety and tolerability study. J Child Adolesc Psychopharmacol. 2009;19: 623-633.
136. Geller DA, March J. Parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2012;51:98-113.
137. Geller DA, Biederman J, Stewart SE, *et al*. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. Am J Psychiatry. 2003;160:1919-1928.
138. March JS, Franklin ME, Leonard H, *et al*. Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in pediatric obsessive-compulsive disorder. Biol Psychiatry. 2007; 61:344-347.
139. Bloch MH, Landeros-Weisenberger A, Kelmendi B, Coric V, Bracken MB, Leckman JF. A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. Mol Psychiatry. 2006;11:622-632.
140. Pringsheim T, Steeves T. Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders. Cochrane Database Syst Rev. 2011; (4): CD007990.
141. Parraga HC, Parraga MI, Harris DK. Tic exacerbation and precipitation during atomoxetine treatment in two children with attention-deficit hyperactivity disorder. Int J Psychiatry Med. 2007;37:415-424.
142. Sears J, Patel NC. Development of tics in a thirteen-year-old male following atomoxetine use. CNS Spectr. 2008;13:301-303.
143. Singer HS, Brown J, Quaskey S, Rosenberg LA, Mellits ED, Denckla MB. The treatment of attention-deficit hyperactivity disorder in Tourette's syndrome: a double-blind placebo-controlled study with clonidine and desipramine. Pediatrics. 1995;95:74-81.
144. Freeman RD, Fast DK, Burd L, Kerbeshian J, Robertson MM, Sandor P. An international perspective on Tourette syndrome: selected findings from 3,500 individuals in 22 countries. Dev Med Child Neurol. 2000;42:436-447.
145. Budman C, Coffey BJ, Shechter R, *et al*. Aripiprazole in children and adolescents with Tourette disorder with and without explosive outbursts. J Child Adolesc Psychopharmacol. 2008;18: 509-515.
146. Sandor P, Stephens RJ. Risperidone treatment of aggressive behavior in children with Tourette syndrome. J Clin Psychopharmacol. 2000;20:710-712.
147. Bruun RD, Budman CL. Paroxetine treatment of episodic rages associated with Tourette's disorder. J Clin Psychiatry. 1998;59: 581-584.
148. Mink JW, Walkup J, Frey KA, *et al*. Patient selection and assessment recommendations for deep brain stimulation in Tourette syndrome. Mov Disord. 2006;21:1831-1838.
149. Kwon HJ, Lim WS, Lim MH, *et al*. 1-Hz low frequency repetitive transcranial magnetic stimulation in children with Tourette's syndrome. Neurosci Lett. 2011;492:1-4.
150. Orth M, Kirby R, Richardson MP, *et al*. Subthreshold rTMS over pre-motor cortex has no effect on tics in patients with Gilles de la Tourette syndrome. Clin Neurophysiol. 2005;116: 764-768.
151. Snijders AH, Bloem BR, Orth M, *et al*. Video assessment of rTMS for Tourette syndrome. J Neurol Neurosurg Psychiatry. 2005;76: 1743-1744.
152. Quintana H. Transcranial magnetic stimulation in persons younger than the age of 18. J ECT. 2005;21:88-95.
153. Kompoliti K, Fan W, Leurgans S. Complementary and alternative medicine use in Gilles de la Tourette syndrome. Mov Disord. 2009;24:2015-2019.
154. Singer HS. Treatment of tics and Tourette syndrome. Curr Treat Options Neurol. 2010;12:539-561.
155. Gabbay V, Babb JS, Klein RG, *et al*. A double-blind, placebo-controlled trial of omega-3 fatty acids in Tourette's disorder. Pediatrics. 2012;129:e1493-e1500.
156. Mantel BJ, Meyers A, Tran QY, Rogers S, Jacobson JS. Nutritional supplements and complementary/alternative medicine in Tourette syndrome. J Child Adolesc Psychopharmacol. 2004;14: 582-589.