Review

Treatment decisions for chronic tic disorders

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Practice Points

- Tics are sudden, repetitive movements or vocalizations, ranging from simple to highly complex, that tend to wax and wane.
- Tics require a careful differential diagnosis between psychiatric, neurologic, substance-induced and movement disorders.
- Screening for tics should be performed for youth presenting with neuropsychiatric complaints. If tics are reported, clinicians should be aware of common co-occurring disorders including: attention-deficit hyperactivity disorder, obsessive–compulsive disorder, anxiety/mood disorders and learning disabilities.
- Pharmacotherapy and behavioral treatments are available for tic disorders.
- Pharmacotherapy includes α-2 agonists and antipsychotics. Risks and side-effect profiles, especially in the latter, should be carefully evaluated and monitored. For mild-to-moderate tics, the Comprehensive Behavioral Intervention for Tics (utilizing habit-reversal therapy) has performed well in randomized trials of both adults and youth.
- Evaluating both severity of tics and functional impairment due to tics is important prior to choosing treatment. Providing patient education about tics is a key responsibility of healthcare providers.

SUMMARY: Chronic tic disorders (CTDs) are a category of movement disorders, including Tourette's syndrome, that typically onset in youth and can be associated with a wide range of topography, complexity, severity and co-occurring conditions. We present an overview of evidence-based recommendations on the assessment and management of CTD for healthcare

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professionals. In particular, the following article focuses on the assessment and differential diagnosis of CTDs from other movement or psychiatric conditions, pharmacological and behavioral treatments of CTDs, as well as considerations and recommendations for treatment decisions for CTDs.

Overview of chronic tic disorders

Chronic tic disorders (CTDs) are characterized by sudden, intermittent and repetitive body movements or vocalizations (i.e., tics) [1,2]. Although most individuals with CTDs present with multiple tic locations, the complexity of tics varies considerably, ranging from simple to highly complex or orchestrated **(Table 1)**. Tic severity tends to wax and wane over time. The categories of CTD include persistent (chronic) motor or vocal tic disorder, and Tourette's syndrome (TS; a combination of multiple motor tics and at least one vocal tic). According to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 [1], tics must be present for at least 1 year to be considered a CTD. If not present for at least 1 year, a diagnosis of provisional tic disorder is given. Diagnoses of 'other specified tic disorder' applies when symptoms characteristic of a tic disorder result in significant distress and/or impairment, but do not meet full criteria for a tic disorder, or the clinician chooses to communicate the reason why criteria are not met. 'Unspecified tic disorder' is similar to other specified tic disorders, but the clinician does not document the reason, diagnostic criteria are not met or there is insufficient information to assign a specific diagnosis [1]. Impairment is not required for diagnosis of a tic disorder [1].

Onset of tics typically occurs in early childhood (i.e., between 5 and 8 years of age), although tic-onset in infants can also occur [3,4]. On average, preadolescence (i.e., 10–12 years of age) is the peak point of severity and prevalence for tics, with symptoms declining during adolescence [3]. While the reported prevalence of CTD has varied considerably across studies, probably due to method and sampling variances [5,6], meta-analysis has estimated mean prevalence in youth as approximately 0.77% for TS (95% CI: 0.39–1.51%); 0.69% for chronic vocal tics (95% CI: 0.49–0.95%); and 1.65% for chronic motor tics (95% CI: 0.64–4.28%) [7]. However, these estimates may be low as a large portion of individuals' tics go undiagnosed [8]. Gender differences indicate that tic disorders occur in approximately two- to four-times more males than females [5,7]. By adulthood, two-thirds of youth will have experienced a considerable reduction in tic severity, including approximately 10–30% of youth who will be completely tic-free, while only a fifth of youth will have tics of moderate or severe presentation continuing into adulthood [3,9]. Adult prevalence estimates appear to reflect the phenomenology of CTDs, with most estimates falling between 0.05 and 0.20% [7]. Older prevalence estimates may be lower given that prior editions of the DSM required tic-related impairment in order to meet criteria for a CTD [10].

Co-occurrence of psychopathology is the norm, with estimates suggesting that the majority of youth with CTDs present with at least one additional diagnosis [11]. The exact frequency of co-occurring conditions is dependent on specific diagnosis of CTD (e.g., co-occurring conditions are more frequent in youths with TS than CTD) as well as the nature of the sample (e.g., lower in population-based, rather than clinical, samples) [12]. In particular, attention-deficit hyperactivity disorder (ADHD) and obsessive–compulsive disorder (OCD) are common, although youths with CTDs are also more likely to present with non-OCD anxiety disorders, mood disorders, learning disabilities and autism spectrum disorders than youths without CTDs **(Table 2)**. Co-occurring disorders contribute significantly to morbidity in youths with CTDs. For example, some studies have found that when compared with CTD-only youths, youths with CTDs and OCD demonstrate greater tic severity, as well as increased likelihood and severity of additional conditions [13,14], while youths with CTDs and ADHD demonstrate poorer global functioning and increased stress [13]. Additionally, social deficits have been demonstrated to mediate the relationship between tic severity and social problems, as well as quality of life [15]. Notably, other studies did not support greater severity in a cohort with co-occurring conditions [16]. Often, with the exception of particularly severe cases of tics, in most youths with CTD tics are not the

Table 1. Common tics†.

Type of tic	Motor tic	Vocal tic
Simple	Eye movements: ▪ Blinking, squinting, rolling ▪ Opening eyes wide Facial movements: ▪ Nose twitching, grimacing ▪ Biting/chewing/licking the lip ▪ Teeth baring/grinding Head jerks/movements: ▪ Touching the shoulder with the chin, throwing the head back Shoulder jerks/movements: ▪ Jerking, shrugging Arm or hand movements: ▪ Flexing/extending arms Leg, foot or toe movements: ▪ Knee-bending, flexing/extension of the ankles Other: ▪ Tensing the abdomen/buttocks	Breathing: ▪ Sniffing, blowing Sounds: ▪ Coughing, throat clearing ▪ Whistling, animal/bird noises
Complex	Eye movements: ▪ Looking surprised, looking to one side for a brief period of time Facial movements: ▪ Flaring nostrils, holding funny expressions, sticking out the tongue Arm or hand movements: ▪ Nail-biting, popping knuckles, touching objects or others, writing tics Leg, foot or toe movements: ▪ Kicking, skipping, stomping, taking one step forward and two steps backward, squatting Other: ▪ Smelling odors/fingers, obscene gestures (corpropraxia), unusual postures, rotating/spinning, copying others (echopraxia)	Words: ▪ Simple words, phrases, statements, rude words or phrases (corprolalia) Repeating: ▪ Others (echolalia) ▪ Oneself (palilalia) Speech problems: ▪ Changes in volume/pitch

†List is not inclusive of all tics.
Data taken from [34].

primary psychiatric concern, with functional impairment (i.e., "inability to perform routine and age-appropriate tasks in the domains of school, home and social activities" [17]) from co-occurring disorders (e.g., OCD, ADHD and disruptive behavior disorders) outranking tic-specific impairment [17,18]. Nevertheless, as a group, youths with CTD often present with some form of functional impairment, with 37% reporting tic-related impairment in two or more domains [17].

Co-occurring psychiatric disorders are also common in adults with CTD, with approximately 49–75% meeting diagnostic criteria for at least one other psychiatric diagnosis [19,20]. Similar to youths, ADHD, OCD, non-OCD anxiety disorders and depression are particularly common (Table 2). In addition, a study of 460 adults with CTDs suggested that adult women are twice as likely to present with additional psychopathology when compared with men [21]. In particular, women may be at increased risk for OCD (1.61-times), non-OCD anxiety disorders (2.75-times), mood disorders (1.83-times), and eating disorders (11.25-times) [21]. Moderator analysis has also suggested that severity of depressive and anxious symptoms significantly moderates the relationship between tic severity and functional impairment in adults, suggesting that tic severity may more significantly impact individuals who are also more anxious or more depressed [22].

Table 2. Estimates of common co-occurring disorders in individuals with chronic tic disorders.

Disorder	Youths (%)	Adults (%)
ADHD	35–80 [11,42,125,126]	23–50 [19,20,127]
OCD	20–60 [11,42,128]	22–35 [19,20]
Anxiety disorders	18–40 [5,11,42]	23–68 [19,127,129]
Mood disorders	15–36 [5,11,42]	13–28 [19,20,127,129,130]
Learning disabilities	11–42 [42,131,132]	–
Autism spectrum disorders	5–6 [11,42,133]	–
Behavior problems (conduct and oppositional)	7–43 [5,11,42]	3–29 [20,21]

ADHD: Attention-deficit hyperactivity disorder; OCD: Obsessive–compulsive disorder.

Assessment of CTDs

While diagnostic criteria for CTDs are relatively straightforward, tics are frequently misidentified and/or misdiagnosed and can require a complex differential from idiopathic, neurological/movement and psychiatric disorders. In many cases, tics may not be identified by families. Simple tics, such as blinking and sniffing, are often attributed to factors such as asthma or allergies – in fact, aside from the pediatrician, otolaryngologists, allergy/immunologists and ophthalmologists (not psychiatrists or neurologists) are often the first practitioners seen for symptoms eventually determined to be tics [23–25]. In addition, in young children, stereotypies may be misidentified as tics [4]. Even when it is determined that tics are present, a careful history is needed to assign the appropriate tic disorder diagnosis and to rule out other movement/psychiatric disorders. When a clear diagnosis of CTD cannot be made or significant co-occurring conditions are present, assessment of tics may require a multidisciplinary approach of more than one type of professional. No biological markers for tics exist, so this differential can be a multistep process that should include any necessary medical workup to rule out alternative diagnoses, a comprehensive assessment of the locations and chronicity of tics, as well as the presence and impact of co-occurring neuropsychiatric disorders.

■ Screening & differential diagnosis

Including screening for tics is recommended in the initial evaluation of any youth presenting with psychiatric concerns, in order to alert practitioners to potential tic-related impairment (e.g., embarrassment, low self-esteem and physical harm) and/or as an indicator to probe for associated co-occurring conditions. Initial screening should probe youths and parents on any unusual movements, sounds or behaviors, which may also include stereotypies, compulsions or other movement disorders, as well as obtain a record of family history. Use of broad-based parent- or teacher-rated screening measures that also include statements on tic-like behavior (e.g., 'nervous movements or twitching'; 'often makes noises [e.g., humming or odd sounds]'; 'has motor or verbal tics [sudden, rapid, recurrent, nonrhythmic motor or verbal activity']), such as these items on the Child Behavior Checklist [26], Conners' Parent Rating Scale [27] or the Swanson, Nolan and Pelham is recommended [28].

If unusual or repetitive movements are identified, clinicians must attempt to distinguish symptoms in order to obtain differential diagnosis of CTD versus other repetitive behaviors that may have alternative neurological, substance-induced or psychiatric origins. To begin, identification of a family history, as well as the nature and triggers, of repetitive movements can provide valuable information on potential diagnosis. For example, premonitory urge (i.e., uncomfortable sensation experienced prior to completion of a movement) and urge-relief following completion of a movement are hallmarks of CTD and therefore, if present, may help distinguish CTD from alternative movement disorders such as dystonia, chorea and myoclonus that do not feature premonitory urge or relief [2]. In addition, premonitory urge may help distinguish tics from stereotypies, frequently present in autism spectrum disorders that tend to occur as responses to excitement or as self-stimulation [2]. Limited variation of the repetitive behavior over time, as well as movements that primarily involve the whole-body and/or hands/fingers, may suggest stereotypies rather than tics [2,29]. As compared with tics, obsessive–compulsive behaviors are typically distinguishable by the presence of anxious thoughts and behaviors that are intended to alleviate them. However, in some cases youths with OCD may report urge-driven (i.e., 'just-right' feeling) compulsions that appear tic-like (touching/tapping/rubbing compulsions), while youths with CTDs may demonstrate complex, seemingly purpose-driven tics. In these cases, examination of the youth's clinical profile (e.g., other anxious symptomatology, history of simple tics) may help make a clarification between the presence of OCD versus CTD.

While helpful, this information may be insubstantial in ruling out alternative diagnoses. For example, a lack of reported premonitory urge should not be used as the exclusive decision in differential diagnosis as many individuals, particularly youths <10 years, lack insight into premonitory urges [30]. When further differentiation is needed, medical tests can also aid in differentiating CTDs from tics as a result of other causes (e.g., substance-induced or head trauma), as well as other movement disorders (e.g., chorea, dystonia and seizure) [31]. A brief guide to differential diagnoses is available in the DSM-5 [1]; more detailed information can be found in Scahill *et al.* [31] and the American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters [32].

■ Evidence-based assessment measures

In the case that screening identifies the presence of a CTD as probable, use of multi-informant, empirically supported assessment measures is recommended to obtain a full clinical picture of the youth's tics [33]. While the obtainment and/or use of measures can occasionally be burdensome, thorough assessment will provide clinicians with tangible and valuable information regarding symptom location, chronicity, severity and impairment of tics and can be used to track symptom change over time (or with intervention). The Yale Global Tic Severity Scale is a clinician-rated semi-structured interview that evaluates for the number, frequency, intensity, complexity and interference of tics, as well as tic-related impairment [34]. With longstanding use, excellent psychometric properties and treatment sensitivity, it is a well-established clinician-rated measure of tics for both children and adults [34–36].

No single parent- or self-report measure has been established as the gold standard; however, a number of measures have garnered either well-established or promising empirical support [33]. Recommended parent-report measures include the Tourette Disorder Scale – Parent Report [37], Parent Tic Questionnaire [38] and Child Tourette Syndrome Impairment Scale – Parent Report [17]. When age-appropriate, empirically supported self-report measures for youths include the Child Tourette Syndrome Impairment Scale – Self-Report [17] and the Motor Tic, Obsessions and Compulsions, Vocal Tic Evaluation Survey [39], which is also suitable for adults. In addition, the Premonitory Urge for Tics Scale [30] is an empirically supported self-report measure of premonitory urge that is appropriate for ages 10 years and above. In cases where tics are reported by parents, but have not been active during clinical assessment, use of video recordings or additional reports (e.g., from teachers) may be beneficial in making a diagnosis.

■ Additional considerations

Even after identification and differential diagnosis of tics, further evaluation may be required. For certain youths, particularly those with atypical symptom onset or presentation (e.g., sudden onset and uncommon tics), or abnormalities in mental status (e.g., disorientation) a more thorough medical workup may be indicated. A sudden and dramatic onset of OCD along with tics, handwriting changes or other regressive behavior may suggest the presence of infection- or autoimmune-triggered symptoms and expert evaluation for whether the child meets pediatric acute-onset neuropsychiatric syndrome criteria should be considered [40,41]. Given the high rates of co-occurring psychopathology, youths and adults with CTD should be carefully screened for ADHD, OCD, anxiety and mood disorders [11,21]. In addition, youths should be screened for learning disabilities and autism spectrum disorders [11,42]. If needed, more specific and detailed information on screening, assessment (including of co-occurring conditions) and differential diagnosis can be found in a few previous reviews as well as the upcoming AACAP Practice Parameters [31–33,43].

Treatment of CTD

Both pharmaceutical and behavioral approaches have been identified as efficacious treatments for CTD. This section will outline the empirical evidence currently available for treatments of CTD, with a focus on those with the strongest empirical support.

■ Pharmacotherapy

α-2 (adrenergic receptor) agonists

α-2 (adrenergic receptor) agonists are medications that were initially introduced as antihypertensives; however, in 1979 a study by Cohen and colleagues suggested their treatment potential for CTD [44]. In general, α-2 receptor adrenergic agonists are hypothesized to reduce tics through modulation of noradrenergic signaling

in the locus coeruleus. Whereas clonidine has α-2B and α-2C receptor activity [45], guanfacine acts selectively at postsynaptic α-2A receptors in the prefrontal cortex [46] and therefore has less sedating and hypotensive effects than clonidine.

While both of these α-2 agonists have demonstrated empirical support in youths with CTD, improvement with these medications may be dependent on the presence of co-occurring ADHD. Clonidine has demonstrated beneficial effects in randomized controlled trials for children with CTD co-occurring with ADHD, including an approximate response rate of 52% and a moderate treatment effect (d = 0.62) [47]. Similarly, in a randomized controlled trial, guanfacine was associated with significant improvement in youths with CTDs and ADHD (d = 0.75) [48]. However, for individuals without co-occurring ADHD, reductions in tic severity appear considerably smaller (d = 0.15) [49–51]. Only one pilot study has investigated the efficacy of transdermal clonidine, therefore its comparative efficacy cannot be determined at this time [52].

Although not yet approved by the US FDA for the treatment of CTD (although they are for ADHD), α-2 agonists may be particularly beneficial due to their generally favorable side effect profile and utility for both ADHD and tic symptoms. Common side effects include sedation, dizziness, fatigue, headache, constipation and dry mouth [53,54]. Newer extended-release forms of clonidine and guanfacine have not yet been examined in youths with tics.

Antipsychotics

First-generation (typical) antipsychotics

First-generation (typical) antipsychotics, which include haloperidol, pimozide and fluphenazine, are medications initially developed and supported for schizophrenia and acute psychotic states [55]. Specific to tics, typical psychotics are theorized to reduce symptoms by acting as potent dopamine antagonists, thereby decreasing dopaminergic signaling from the substantia nigra to the basal ganglia as well as ventral tegmental signaling to the frontal cortex [53].

In a number of randomized placebo-controlled clinical trials, haloperidol has demonstrated a good treatment response (response rate: 60%; d = 0.23–0.57) [56,57], maintaining its status as a second- or third-line agent for severe and/or refractory CTD [56–58]. While haloperidol remains an important option, it has the potential to cause more severe side effects (although considered rare at the lower doses used for tics), such as tardive dystonia, other extrapyramidal symptoms and QTc prolongation. Weight gain, sedation or cognitive dulling are the most frequent side effects that limit use. Tardive dyskinesia is also a common side effect of haloperidol and other antipsychotics; however, a large chart review of individuals with TS found a low frequency of tardive dyskinesia resulting from use of any antipsychotic, including haloperidol [59].

Beyond haloperidol, pimozide, with similar response rates and effect sizes [57], also has double-blind, randomized trials in children and adolescents supporting its use [56,60]. Given potential for QTc prolongation, ECG monitoring is recommended. Drug–drug interactions will also need to be considered. In addition, fluphenazine, a member of the trifluoperazine family, has been used for many years to treat CTD; however, as compared with haloperidol relatively few studies have investigated its efficacy [61,62]. While possibly having a better side effect profile compared with haloperidol, the use of this agent has continued to decrease with the rise in popularity of the atypical antipsychotics. To date, haloperidol and pimozide remain the only medications FDA-approved specifically for CTD.

Second- & third-generation (atypical) antipsychotics

Second- and third-generation (atypical) antipsychotics, including risperidone, olanzapine, quetiapine, clozapine, ziprasidone and aripiprazole are thought to act primarily on serotonin 5-HT2A receptors, rather than dopamine D2 receptors as typical antipsychotics do [53]. Although a specific mechanism of tic-reduction has not yet been identified, the relative potency on D2 receptors is hypothesized to explain differences in efficacy among atypicals, although their actions at α-1-adrenergic, D3, D4, and H1-histamine receptors may also be contributory [53]. For CTD, risperidone is the best studied atypical antipsychotic, although the use of aripiprazole, ziprasidone and olanzapine has also been investigated in this population. There is no indication for clozapine for the treatment of CTD.

The efficacy of risperidone has been demonstrated in a number of randomized controlled

trials, having been associated with a high rate of response (54–100%) and large treatment effects (d = 0.8–1.0) [60,63–65]. While the side effect profile is improved from atypical antipsychotics, risperidone is still associated with a significant potential for side effects including cardiometabolic symptoms (i.e., weight gain), increased QTc interval and extrapyramidal side effects. Furthermore, worsening tics with withdrawal of those agents with more potent dopamine D2 receptor inhibitory potential is also an important consideration.

In a small randomized placebo-controlled trial, children and adolescents with TS given ziprasidone demonstrated a reduction in tic severity when compared with those receiving placebo (d = 1.0) [66]. Concerns for increased risk for QTc prolongation has limited its use in this population [67].

Some pilot evidence also supports the use of olanzapine for the treatment of CTD. In particular, a 52-week double-blind cross-over study in adults involving comparison with pimozide [68], as well as open label trials in children, supported its use [69–71]. Perhaps to a greater extent compared with other atypical antipsychotics, this agent has significant potential for weight gain, blood glucose changes and other cardiometabolic effects [72].

Interestingly, several open-label studies and case-series suggest that aripiprazole, a partial dopamine D2 receptor agonist, may be efficacious in children and adolescence with CTD with fewer cardiometabolic side effects compared with risperidone, quetiapine or olanzapine (response rate: 79–91%; d = 1.50–2.25) [73–79]. Randomized controlled trials investigating aripiprazole are underway. Regarding FDA-approval, no typical antipsychotics are approved specifically for CTD; however, risperidone and aripiprazole carry approvals in youths and adults for other psychiatric disorders, while ziprasidone and olanzapine are only approved for use in adults (for non-CTD indications).

Other

Other nonbehavioral approaches for the treatment of CTD, including tetrabenazine [80], benzodiazepines [81], tetrahydrocannabinol [82], pergolide [83], naloxone [84], botulinum toxin [85], nicotine [86], mecamylamine [87], baclofen [88], flutamide [89] and repetitive transcranial magnetic stimulation [90] are not recommended at this time due to limited empirical support (including nonsupportive findings or insufficient study). The anticonvulsant topiramate has demonstrated promising results from one randomized controlled trial [91]; however, further research is needed before it can be recommended as an empirically supported treatment option. For severe, treatment refractory adults, neurosurgical interventions, such as deep brain stimulation, have garnered some initial support [92–94]; however, they are invasive neurological procedures associated with significant risk. Neurosurgical options are not recommended unless:

- Less invasive treatments are exhausted;
- Consultation with a CTD expert with expertise in neurosurgical treatments has been obtained.

Additional information on recommended dosing levels of pharmaceutical treatments can be found in the Canadian guidelines for the evidence-based treatment of tic disorders: pharmacotherapy [95].

Behavioral treatments

Habit-reversal training

Habit-reversal training (HRT) is a behavioral treatment approach initially introduced as a method of eliminating nervous habit disorders (e.g., nail-biting, skin picking and hair pulling) and tics [96]. HRT purports that tics are, in part, maintained by a system of negative reinforcement. Individuals with tics experience a build-up of an unpleasant physical sensation (i.e., premonitory urge) that is then relieved through performance of the tic. The tic–urge relationship is maintained as the tic reduces the tension/sensation, thus increasing the likelihood of the tic continuing via the negative reinforcement paradigm.

Based on this model, the two primary components of HRT are awareness training/self-monitoring and the use of competing responses [97,98]. Awareness training teaches individuals to become aware of their tic behavior, as well as its premonitory urges. Once aware, individuals learn to employ a competing response at the first sign/feeling of an impending tic. Initially, the competing response limits the expression of tics, while over time, it helps break the tic–urge relationship and reduces the frequency and severity of urges via extinction.

As described by Azrin and Nunn, an appropriate competing response has the individual tense tic-related muscles in a tic-antagonist, socially inconspicuous fashion [96]. For example, if an individual has a head-jerk tic, an appropriate competing response would be to tighten the muscles of the neck involved in the tic so that the tic is inhibited by this action and the behavior is minimally noticeable. Over time, the relationship between the urge and tic is attenuated, decreasing the need for the individual to tic (to reduce an urge/sensation) and often decreasing the frequency/intensity of the premonitory urge. HRT has been demonstrated to be an effective intervention for tics [97].

Comprehensive behavioral interventions for tics

Comprehensive behavioral interventions for tics (CBIT) is an HRT-focused intervention that incorporates psychoeducation and additional behavioral strategies and has been the focus of two large randomized controlled trials. While the primary treatment goal remains the reduction of tic severity, the additional components of CBIT provide patients with a few additional coping/tic-management strategies [99]. As a whole, CBIT involves a brief introductory psychoeducation session, a functional analysis and behavior management component, a number of HRT sessions (see HRT section above) and a relaxation component.

Psychoeducation

Psychoeducation is the provision of disorder-related information to the patient and their families and is a common initial component of psychosocial treatment for many psychiatric disorders. While not intended to reduce tics, by providing patients and their families with important information, psychoeducation may help reduce emotional consequences associated with tics [100], and is generally viewed as an important first step after diagnosis for youths with CTD [101]. For CTD, psychoeducation is intended to do the following:

- Increase understanding of the nature of CTDs, as well as reduce misunderstanding and stigma, by providing information on etiology, course, prognosis, common symptom presentations, and symptom waxing and waning;
- Improve youth coping by promoting acceptance of CTD as a component of self-identity, and teach youth how to explain their tics to their peers;
- Assist parents in obtaining classroom accommodations (e.g., permission to leave the room) by providing information on individualized education, or other school-based accommodation plans (e.g., 504 Plan [101]).

Generally, psychoeducation regarding CTD is central to any patient seeking treatment – behaviorally or pharmacologically. Good examples of information can be found in: Treating Tourette Syndrome and Tic Disorders: a Guide for Practitioners [102]; and Tic Disorders, Trichotillomania, and Other Repetitive Behavior Disorders: Behavioral Approaches to Analysis and Treatment [103].

Functional analysis

Functional analysis is a behavioral assessment strategy that involves identification of antecedents, behaviors and consequences maintaining a behavior – in this case, tics. Individuals attempt to identify situational antecedents (e.g., stress, specific locations, people and situations) and consequences (e.g., irritability, escape from demands, attention and criticism from others) that are related to exacerbation/attenuation of tics [104]. Based on this information, an individualized plan is introduced to reduce the influence of these exacerbating situations and maximize the use of ameliorating situations [104]. The individualized plan, based on the functional analysis, often focuses on parent implementation of behavioral strategies, such as differential reinforcement and contingency management. A workbook by Woods and colleagues provide examples for therapists [99].

Relaxation training

Relaxation training is included in CBIT primarily as a method of anxiety management [99]. Typically, relaxation training includes physically focused strategies that help reduce perceived stress and anxiety such as progressive muscle relaxation and diaphragmatic breathing; however, it may also include cognitive strategies (e.g., imagery). Considering the exacerbating effect of anxiety on tics, it is not surprising that relaxation training is associated with temporary (during relaxed state) reductions in tics, but has

not been associated with long-term improvements in tic symptoms [105,106]. Relaxation may not be needed for many individuals with CTD.

Empirical support for CBIT.

Designed to be developed into a disseminable, empirically supported treatment for CTD in youths (9–17-years old) and adults, the efficacy of CBIT was compared with a treatment control (i.e., supportive therapy) in two simultaneous, randomized controlled treatment studies. Supportive therapy consisted of education and therapist contact, but did not include any specific recommendations for tic management [104]. The first study examined the efficacy in a sample of 126 youths, with large effects for CBIT in terms of treatment response (CBIT: 52%; control: 18.5%), improvement in global tic severity (d = 0.68) and overall functioning (d = 0.64) [104]. Similarly, in a sample of 122 adults, CBIT was found to be significantly more effective compared with supportive therapy in terms of treatment response (CBIT: 38.1%; control: 6.8%) and improvement in total tic score (d = 0.57) [107]. In addition, within both studies CBIT was not associated with any adverse events. Taken together, the above results suggest that exposure-focused treatments such as HRT/CBIT are efficacious and safe for CTDs in both youths and adults. Further investigation of CBIT is needed to fully establish its efficacy in a younger child population.

Despite the efficacy of CBIT and lack of adverse events, many professionals are skeptical of the idea to employ extinction-based treatments. Historical conjecture, exacerbated by continued misinformation, has resulted in a commonly held belief among medical professionals that tic suppression, via competing response or contingency management, results in a 'rebound' effect (i.e., tics increase higher than baseline following suppression) [108,109]; however, substantial research has debunked this assumption [110,111]. Direct examination of the hypothesized rebound effect suggests that following successful suppression, tic frequency returns at lower, not higher, than baseline levels [110]. Furthermore, within clinical trials, HRT/CBIT has not been associated with tic worsening or with the emergence of new tics [104,107].

Other

Beyond HRT, a few additional treatments for TS have been investigated. Cognitive therapy [112], relaxation therapy [106], supportive therapy and biofeedback do not appear to be beneficial for reducing tic severity. Individual components included in CBIT, for example, functional analysis, contingency management and differential reinforcement, may be beneficial strategies for improving tics/tic-related impairment, but have only been studied in combination with other methods such as HRT) [113,114]. A randomized controlled trial comparing exposure and response prevention (ERP; i.e., an extinction-based technique) with HRT suggested larger effects for ERP treatment; however, individuals in the ERP group received more than twice the time in therapy compared with those in HRT [115]. Given the similar mechanisms between HRT and ERP, ERP may hold promise as a treatment for tics; however, more balanced comparisons between the treatments are needed to establish its comparability or superiority to HRT.

Treatment decisions

Review of the currently available literature suggests that efficacious pharmaceutical and behavioral treatments exist for individuals with CTD. In particular, extinction-based treatments (i.e., HRT/CBIT) appear to be efficacious in reducing tic severity and tic-related impairment in youths and adults with CTD. With this in mind, presented below are recommendations for making treatment decisions for patients with CTD.

Recommendations are made based on a risk–benefit perspective, with the intent to provide patients with the most effective care, while minimizing the chance of adverse events. To organize recommendations, they are presented first based on the patient's level of severity; however, additional considerations regarding the level of impairment from tics and/or from co-occurring conditions, as well as patient-specific factors (e.g., access to care and preference) are also discussed. In order to determine severity of a patient's CTD, clinicians are recommended to use psychometrically established measures (e.g., Yale Global Tic Severity Scale). However, as a general guide:

- Mild tics would be those that are relatively simple, as well as minimally invasive, noticeable and/or bothersome;
- Moderate tics would be those that are more cumbersome, invasive, orchestrated and/or

time-consuming, and therefore generally associated with a larger degree of distress;

- Severe tics would be those that are highly complex/orchestrated, time consuming, physically injurious, socially inappropriate, and/or cause significant distress.

Mild tics

Intervention for individuals who present with very mild tics is typically not required. The natural course of tics for the majority of youths (i.e., declining symptoms during adolescence) [3] make a 'wait and see' approach (i.e., intervention only occurs if tics significantly worsen) advisable for most patients with mild tics. Despite this, psychoeducation, which may also include aspects of functional analysis, is still recommended at this level.

Moderate tics

The presence of moderate tics in cases with associated distress or impairment may necessitate intervention. As with mild tics, provision of psychoeducation is recommended prior to making treatment decisions. In cases where misinformation or environmental factors (e.g., peer bullying) have led to poor tic outcomes, psychoeducation may be particularly beneficial in improving patient coping.

Beyond psychoeducation, employment of an HRT-focused behavioral treatment (e.g., CBIT) is recommended as it has been associated with comparable treatment effects with pharmacological interventions, with the least adverse risk profile of currently available treatments. Considering the relatively similar treatment effects and considerably larger risk of adverse effects, pharmacological treatment is not necessarily advised as a first-line treatment for moderate tics [32].

Severe tics

For those youths who do present with severe tics, intervention will probably be required. Psychoeducation should still be provided prior to beginning any intervention, particularly so families can be informed regarding potential treatment options/risks/research findings. Based on the evidence, an HRT-focused behavioral intervention is still recommended to be among the first-line treatments; however, youths with particularly severe tics may warrant simultaneous behavioral and pharmaceutical treatment. A combined approach may be particularly beneficial if the presence of co-occurring symptoms can be simultaneously addressed via medication. However, it should be noted that no studies have directly investigated the added benefit of a combined approach.

If the use of psychotropic medications is deemed appropriate, clinicians must attempt to determine what medication is best suited for their patient, balancing evidence for efficacy, severity, risk of adverse events and patient factors. Generally, for mild-to-moderate CTDs with co-occurring ADHD, α-2 agonists, given their efficacy, relative tolerability and safe side effect profile, are recommended prior to atypical antipsychotics. For those with CTDs without ADHD the evidence of efficacy for α-2 agonists in the treatment of CTDs is much weaker at present; however, the risk:benefit ratio may still favor a trial of α-2 agonists depending on secondary patient factors (e.g., obesity or other cardiometabolic risk factors). For those who fail an adequate trial of α-2 agonists, or those with moderate or severe CTD, the atypical antipsychotic risperidone has the strongest empirical support among the atypical antipsychotics and appears to be better tolerated in comparison with typical antipsychotics; although it is still associated with a number of serious side-effects. The atypical antipsychotic aripiprazole may be a promising treatment with comparable efficacy and fewer metabolic side effects compared with risperidone; however, at present, its empirical basis is limited. In the case that tics are severe and refractory to α-2 agonists, atypical antipsychotics and a full course of HRT, pimozide and haloperidol remain powerful third-line options for those with CTDs.

Impairment & co-occurring conditions

Level of tic severity may be a good guideline for judging the need of specific intervention; however, treatment decisions should also account for the degree of functional impairment present. For example, while intervention is generally not required when tics are mild, if tics are associated with moderate-to-severe levels of impairment (e.g., severe bullying and lowered school performance), then initiating treatment may be beneficial for the patient.

Conversely, in many cases functional impairment from tics may be minimal, or at least less significant compared with impairment from co-occurring conditions. Recalling that co-occurring conditions are common in individuals with CTDs, it is recommended that in cases when

impairment due to co-occurring psychopathology supersedes tic-specific impairment, treatment focus on reducing co-occurring symptoms concurrent with or prior to attempting to improve tics. If possible, selecting treatments that have the potential to target tics and co-occurring disorders should be considered; however, ultimately treatment decisions should first address the primary concern. For example, for ADHD, α-2 agonists for tics may also address impulsivity/hyperactivity inherent in ADHD. However, if ADHD is the primary treatment concern, stimulant medications may have a larger benefit for ADHD symptomatology [49]. Although there is the potential for stimulants to exacerbate tics, increases are generally reversible and transient; stimulants are no longer contraindicated for youths with CTDs, but providers should titrate cautiously (small increments with frequent observation) [47,116]. For OCD, anxiety and mood disorders, cognitive–behavioral treatments for co-occurring disorders (e.g., CBT for OCD) may improve tic levels through:

- Teaching the requisite skills need for HRT;
- Improvement of overall coping skills and reductions in daily stress levels.

Treatment availability & preferences

While our recommendations are designed to inform clinician decisions, ideally making treatment decisions should be a joint process between patients, their families and the clinician. Severity and impairment are useful guides to determining if, and what, treatment is appropriate, but other patient-specific factors may limit the generalizability of our recommendations. Primarily, access to appropriate care, particularly behavioral intervention such as CBIT, may be limited by a shortage/lack of trained clinicians. Generally, dissemination and implementation of empirically supported treatments for psychopathology is suboptimal [117], while the relatively recent development of HRT/CBIT may make treatment particularly difficult to obtain. Even if treatment is available, restraints on resources (e.g., money, time, missed work/school and transportation) may present further barriers to care. In these cases, providers should seek out the best possible care considering the circumstances. Finally, incorporation of patient (or family) treatment preferences (e.g., most minimal side effect profile, least time-intensive) into treatment decisions should occur whenever possible. In some cases, parents and children may differ in their perception of the severity/impact of tics [118] and the desire to pursue intervention.

Other reviews & recommendations

This review is designed to provide an overview of CTD – we refer the reader to the European guidelines for treatment [101,119] and the Canadian guidelines for treatment [95,120], as well as a number of other reviews [50,53,121,122] for additional information. Generally, recommendations across the extant reviews and guidelines converge, particularly in support of HRT/CBIT [53,101,120]; however, a few differences may be of note. The first key difference is over whether α-2 agonists or atypical antipsychotics should be considered the first-line pharmaceutical treatment. Weighing the benefit–risk profiles, AACAP and Canadian parameters, along with other expert reviews, suggest α-2 agonists as the first-line choice, particularly for mild-to-moderate tics and when ADHD is present, due to their efficacy and, more importantly, tolerability [50,53,95,121]. However, other reviews are more skeptical of the efficacy of α-2 agonists and recommend risperdone or other atypical antipsychotics [119,122] that although potentially more effective, are associated with a severe side-effect profile. Regarding behavioral treatment, both the European and Canadian guidelines provide stronger support of treatment with ERP than is provided here [101,120]; however, the lack of a strong empirical base for ERP has often left it unmentioned in a number of other reviews [53,121]. Finally, one review provides slightly dampened support for HRT/CBIT in favor of pharmacological treatment; however, reasoning was due to potential lack of availability, rather than poor efficacy or tolerability [121]. Overall, the recommendations contained here are consistent with the field and while provided in a more applied format, mirror those outlined in a draft of the Practice Parameter for the Treatment and Assessment of Children and Adolescents with Tourette Disorder and Chronic Tic Disorders, prepared by the American Academy of Child and Adolescent Psychiatry (workgroup led by TK Murphy) scheduled to be released later this year [32].

Conclusion & future perspective

With proper diagnosis and treatment, currently available evidence suggests that the severity and

associated impairment of CTDs can be successfully managed for a sizable proportion of individuals. While empirical evidence supporting this conclusion has grown considerably in recent years, treatment of CTDs still lacks the comprehensive research base present for many other psychiatric disorders (e.g., OCD and depression). There are a number of promising treatments for CTD that have been associated with modest reductions in tic symptoms; however, limited studies examining combined therapies (e.g., behavioral and pharmacological), as well as severe side effect profiles associated with some treatments, limit enthusiasm.

Unfortunately, to date no study has directly investigated the additive benefit of combined behavioral and pharmaceutical treatments for CTDs. Dual treatment has been associated with slightly improved efficacy over monotherapy for some psychological disorders (e.g., OCD) [123], while not for others (e.g., depression [124]). Overall, empirical work is needed to better support decision-making guidelines for individuals with CTDs. Finally, despite growing empirical support for CBIT, access to trained providers is limited. Additional emphasis on dissemination of evidence-based treatment for CTD is needed as is study of the effectiveness of these attempts.

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