AAN Practice Guideline Summary for **Clinicians**

Practice Guideline: The Treatment of Tics in People with Tourette Syndrome and Chronic Tic Disorders

This is a summary of the American Academy of Neurology (AAN) practice guideline, "The Treatment of Tics in People with Tourette Syndrome and Chronic Tic Disorders," which was published in *Neurology*® online on May 6, 2019, and appears in the May 7, 2019, print issue.

Please refer to the full guideline at AAN.com/guidelines for more information, including descriptions of the processes for classifying evidence, deriving conclusions, and making recommendations.

Counseling Recommendations: Natural History of Tourette Syndrome Recommendation 1

Rationale

Providing information to families about the natural history of a disorder can help inform treatment decisions. Tics begin in childhood and demonstrate a waxing and waning course. Peak tic severity usually occurs between the ages of 10 and 12 years, with many children experiencing an improvement in tics in adolescence.[1] A longitudinal study demonstrated that tic severity declined yearly during adolescence, with 18% of adolescents older than 16 years having no tics and 60% having minimal or mild tics 6 years after initial examination.[2] There is no evidence that treatment is more effective the earlier it is started. As tics may improve with time, watchful waiting is an acceptable approach in individuals who do not experience any functional impairment from their tics. However, even in such cases, the Comprehensive Behavioral Intervention for Tics (CBIT) could be employed if the patient is motivated to attempt treatment. As a result of partial or complete remission during the natural course of the disorder, medication prescribed for tics in childhood may no longer be required over time.

Level	Recommendation
Level A	Clinicians must inform patients and their caregivers about the natural history of tic disorders.
Level A	Clinicians must evaluate functional impairment related to tics from the perspective of the patient and, if applicable, the caregiver.
Level B	Clinicians should inform patients and caregivers that watchful waiting is an acceptable approach in people who do not experience functional impairment from their tics.
Level C	Clinicians may prescribe CBIT, as an initial treatment option relative to watchful waiting, for people with tics who do not experience functional impairment if they are motivated to attempt treatment.
Level A	Physicians prescribing medications for tics must periodically re-evaluate the need for ongoing medical treatment.

Psychoeducation, Teacher and Classroom Recommendation 2

Rationale

Tourette syndrome (TS) is common, affecting approximately 1% of schoolchildren.[3] Psychoeducation about TS with peers can result in more positive attitudes toward a person with TS, while psychoeducation about TS with teachers can improve knowledge about the condition.[4] Improving peers' attitudes about and teachers' knowledge of TS may positively affect people with TS.

Level	Recommendation
Level B	Clinicians should refer people with TS to resources for psychoeducation for teachers and peers, such as the Tourette Association of America.

Assessment and Treatment of ADHD in Children with Tics Recommendation 3

Rationale

Comorbid attention-deficit/hyperactivity disorder (ADHD) is common in people with TS, with prevalence ranging from 30% to 50%.[5,6] Several trials have specifically addressed the medical treatment of both ADHD and tics in children with both disorders. This includes trials of psychostimulants and atomoxetine, in which the aim was to demonstrate efficacy of these treatments for ADHD symptoms without concomitant worsening of tics. In children with tics and ADHD, clonidine, clonidine plus methylphenidate, methylphenidate, and guanfacine are probably more likely than placebo to reduce tic severity and reduce ADHD symptoms. In children with tics and ADHD, atomoxetine does not worsen tics relative to placebo and reduces ADHD symptoms. Comorbid ADHD is strongly associated with functional impairment in children with TS.[7] While ADHD symptoms may improve in adolescence,[2] adults with TS may require ongoing care for this comorbidity.

Level	Recommendation
Level B	Clinicians should ensure an assessment for comorbid ADHD is performed in people with tics.
Level B	Clinicians should evaluate the burden of ADHD symptoms in people with tics.
Level B	In people with tics and functionally impairing ADHD, clinicians should ensure appropriate ADHD treatment is provided.

Assessment and Treatment of OCD in Children with Tics Recommendation 4

Rationale

Obsessive-compulsive behaviors are common in people with TS, with a comorbid diagnosis of obsessive-compulsive disorder (OCD) made in 10% to 50%.[5, 6] Sub-analyses of trials of interventions for OCD in children suggest that individuals with tics may not respond as well as those without tics to selective serotonin reuptake inhibitors but respond equally well to cognitive behavioral therapy (CBT) for OCD symptoms.[8, 9] For this reason, CBT is considered first-line treatment of OCD in individuals with tic disorders.

Level	Recommendation
Level B	Clinicians should ensure an assessment for comorbid OCD is performed in people with tics.
Level B	In people with tics and OCD, clinicians should ensure appropriate OCD treatment is provided.

Other Psychiatric Comorbidities Recommendation 5

Rationale

Population-based and clinic-based studies have shown that people with TS are at high risk of other psychiatric comorbidities, including anxiety disorders, oppositional defiant disorder, and mood disorders.[5, 6] Comorbid mood disorders appear more prevalent in adolescents and adults than children and in those with greater tic severity.[6, 10] A matched case-cohort study using a national registry has shown an increased risk of dying by suicide and attempting suicide in people with TS compared with controls, which persisted after adjusting for psychiatric comorbidity. Persistence of tics beyond young adulthood, previous suicide attempts, and comorbid personality disorders increased the risk of death by suicide.[11]

Level	Recommendation
Level A	Clinicians must ensure appropriate screening for anxiety, mood, and disruptive behavior disorders is performed in people with tics.
Level A	Clinicians must inquire about suicidal thoughts and suicide attempts in people with TS and refer to appropriate resources if present.

Assessment of Tic Severity and Treatment Expectations Recommendation 6

Rationale

There are several rating scales available for measuring tic severity, with the Yale Global Tic Severity Scale the most extensively deployed and validated.[12] Evaluation of the effect of treatment on tic severity in trials is measured using such scales. The use of validated scales to measure tic severity can aid the evaluation of treatment response in the clinical setting. While medications, behavioral therapy, and neurostimulation can result in meaningful reduction in tics, these interventions rarely result in complete cessation of tics.

Level	Recommendation
Level C	Clinicians may measure tic severity using a valid scale to assess treatment effects.
Level A	Clinicians must counsel patients that treatments for tics infrequently result in complete cessation of tics.

Behavioral Treatments Recommendation 7

Rationale

People with tics receiving CBIT are more likely than those receiving psychoeducation and supportive therapy to have reduced tic severity. CBIT is a manualized treatment program consisting of habit-reversal training (HRT), relaxation training, and a functional intervention to address situations that sustain or worsen tics.[13] The child and adult CBIT trials demonstrated the efficacy of an 8-session protocol, though cases complicated by poor tic awareness, treatment motivation, more severe tics, or substantial clinical comorbidity may benefit from a longer course of therapy. Most children (aged 9 years or older) and adults showing an initial positive response to CBIT will maintain their treatment gains for at least 6 months. CBIT can be effective for children younger than 9 years, though there is little evidence to determine efficacy in children of this age group.[14] There is some evidence that the efficacy of CBIT for reducing tics is greater for patients not concurrently taking anti-tic medication.[15] There is insufficient evidence to determine the relative efficacy of HRT compared with exposure and response prevention or educational group treatment in reducing tic severity. There is insufficient evidence to determine the relative efficacy of HRT by video conferencing compared with either face-to-face HRT or wait-list control for reducing tic severity. There is insufficient evidence to determine the efficacy of relaxation training for reducing tic severity. The evidence demonstrates no increased risk of adverse effects for people treated with CBIT compared with those treated with psychoeducation plus supportive therapy. The effect size for CBIT appears similar to effect sizes for medications. In light of clinician responsibility to optimally balance safety and effectiveness in treatment decisions, CBIT should be considered as an initial treatment choice for tics. Given the effort required from patients or their families, along with its benign safety profile, CBIT is an acceptable intervention for people with tics that lead to psychosocial or physical impairment and who are motivated to participate in treatment.

Level	Recommendation
Level B	For people with tics who have access to CBIT, clinicians should prescribe CBIT as an initial treatment option relative to other psychosocial/behavioral interventions.
Level B	For people with tics who have access to CBIT, clinicians should offer CBIT as an initial treatment option relative to medication.
Level C	Clinicians may prescribe CBIT delivered over teleconference or secure voice-over-internet protocol delivery systems if face-to-face options are unavailable in a patient care center. If CBIT is unavailable, other behavioral interventions for tics may be acceptable, such as exposure and response prevention.

Alpha Agonists for the Treatment of Tics
Recommendation 8

Rationale

People with tics receiving clonidine are probably more likely than those receiving placebo to have reduced tic severity, and people with tics receiving guanfacine are possibly more likely than those receiving placebo to have reduced tic severity, with the majority of trials conducted in children. In children with tics and comorbid ADHD, clonidine and guanfacine have demonstrated beneficial effects on both tics and ADHD symptoms. The effect size of clonidine and guanfacine on tics appears larger in children with tics and ADHD compared with individuals with tics without a comorbid diagnosis of ADHD. Relative to placebo, clonidine is probably associated with higher rates of sedation, and guanfacine is probably associated with higher rates of drowsiness. A systematic review of alpha-2 adrenergic agonists for ADHD in children and adolescents demonstrated hypotension, bradycardia, and sedation with both agents, and QTc prolongation with guanfacine extended release.[16] Abrupt withdrawal of alpha-2 adrenergic agonists may cause rebound hypertension.[17]

Level	Recommendation
Level B	Physicians should counsel individuals with tics and comorbid ADHD that alpha-2 adrenergic agonists may provide benefit for both conditions.
Level B	Physicians should prescribe alpha-2 adrenergic agonists for the treatment of tics when the benefits of treatment outweigh the risks.
Level A	Physicians must counsel patients regarding common side effects of alpha-2 adrenergic agonists, including sedation.
Level A	Physicians must monitor heart rate and blood pressure in patients with tics treated with alpha-2 adrenergic agonists.
Level A	Physicians prescribing guanfacine extended release must monitor the QTc interval in patients with a history of cardiac conditions, patients taking other QT-prolonging agents, or patients with a family history of long QT syndrome.
Level A	Physicians discontinuing alpha-2 adrenergic agonists must gradually taper them to avoid rebound hypertension.

Antipsychotic Treatment for Tics
Recommendation 9

Rationale

Haloperidol, risperidone, aripiprazole, and tiapride are probably more likely than placebo to reduce tic severity, and pimozide, ziprasidone, and metoclopramide are possibly more likely than placebo to reduce tic severity. There is insufficient evidence to determine the relative efficacy of these drugs. Relative to placebo, the evidence demonstrates a higher risk of drug-induced movement disorders with haloperidol, pimozide, and risperidone; a higher risk of weight gain with risperidone and aripiprazole; a higher risk of somnolence with risperidone, aripiprazole, and tiapride; a higher risk of QT prolongation with pimozide; and a higher risk of elevated prolactin with haloperidol, pimozide, and metoclopramide. Systematic reviews of trials and cohort studies demonstrate a higher risk of drug-induced movement disorders (including tardive dyskinesia, drug-induced parkinsonism, akathisia, acute dystonia, and tardive dystonia), weight gain, adverse metabolic side effects, prolactin increase, and QT prolongation with both first- and second-generation antipsychotics across psychiatric and neurologic conditions.[18, 19] The long-term use of metoclopramide is associated with tardive dyskinesia, resulting in a black box warning from the US Food and Drug Administration.[20] The relative propensity for these adverse effects varies by agent and is often dose dependent. Physicians have a duty to monitor the effectiveness and safety of prescribed medications, and evidence-based monitoring protocols are available.[21] Abrupt discontinuation of antipsychotic medications can cause withdrawal dyskinesias.[22, 23]

Level	Recommendation
Level C	Physicians may prescribe antipsychotics for the treatment of tics when the benefits of treatment outweigh the risks.
Level A	Physicians must counsel patients on the relative propensity of antipsychotics for extrapyramidal, hormonal, and metabolic adverse effects to inform decision making on which antipsychotic should be prescribed.
Level A	Physicians prescribing antipsychotics for tics must prescribe the lowest effective dose to decrease the risk of adverse effects.
Level B	Physicians prescribing antipsychotics for tics should monitor for drug-induced movement disorders and for metabolic and hormonal adverse effects of antipsychotics, using evidence-based monitoring protocols.
Level A	Physicians prescribing antipsychotics for tics must perform electrocardiography and measure the QTc interval before and after starting pimozide or ziprasidone, or if antipsychotics are coadministered with other drugs that can prolong the QT interval.
Level B	When attempting to discontinue antipsychotics for tics, physicians should gradually taper medications over weeks to months to avoid withdrawal dyskinesias.

Botulinum Toxin Injections for Tics
Recommendation 10

Rationale

Botulinum toxin injections with onabotulinum toxin A are probably more likely than placebo to reduce tic severity in adolescents and adults. Premonitory urges may also be improved by botulinum toxin injections.[24] Relative to placebo, onabotulinum toxin A is associated with higher rates of weakness. Hypophonia is a common side effect of botulinum toxin injections in the laryngeal muscles for vocal tics.[25] The effect of botulinum toxin injections last 12 to 16 weeks, after which treatment needs to be repeated.

Level	Recommendation
Level C	Physicians may prescribe botulinum toxin injections for the treatment of adolescents and adults with localized and bothersome simple motor tics when the benefits of treatment outweigh the risks.
Level C	Physicians may prescribe botulinum toxin injections for the treatment of older adolescents and adults with severely disabling or aggressive vocal tics when the benefits of treatment outweigh the risks.
Level A	Physicians must counsel individuals with tics that botulinum toxin injections may cause weakness and hypophonia, and that all effects are temporary.

Topiramate for the Treatment of Tics
Recommendation 11

Rationale

Topiramate is possibly more likely than placebo to reduce tic severity. In patients with mild but troublesome tics who are not obtaining a satisfactory response or experience adverse effects from other treatments, topiramate may be a useful alternative. While generally well tolerated at low doses (25 to 150 mg/d), it may cause adverse effects, including cognitive and language problems, somnolence, and weight loss, and may increase the risk of renal stones.[26-28]

Level	Recommendation
Level B	Physicians should prescribe topiramate for the treatment of tics when the benefits of treatment outweigh the risks.
Level A	Physicians must counsel patients regarding common adverse effects of topiramate, including cognitive and language problems, somnolence, weight loss, and an increased risk of renal stones.

Cannabis-based Medications for the Treatment of Patients with TS
Recommendation 12

Rationale

Some patients with TS use cannabis as a self-medication for tics and comorbidities.[29] There is limited evidence that delta-9-tetrahydrocannabinol (THC), dronabinol, is possibly more likely than placebo to reduce tic severity in adults with TS. There is insufficient evidence to determine whether the efficacy of nabiximols, nabilone, and cannabidiol (CBD) as well as different strains of medicinal cannabis—standardized for different levels of THC and CBD—is similar to THC. Compared with placebo, cannabis-based medications are associated with increased risk of short-term adverse events, most commonly dizziness, dry mouth, and fatigue.[30] There is no evidence that controlled treatment with cannabis-based medication may induce addiction to cannabinoids. Acute withdrawal of cannabinoids is generally safe and well tolerated without significant adverse events.[30, 31] Cannabis-based medications should be avoided in children and adolescents, not only due to a paucity of evidence but due to the association between cannabis exposure in adolescence and potentially harmful cognitive and affective outcomes in adulthood.[32] Cannabis-based medication should not be used in women who are pregnant or breastfeeding or in patients suffering from psychosis. Prescription of and access to medical marijuana varies by region; practitioners must abide by regional legislation on the use of medical marijuana.

Level	Recommendation
Level A	Due to the risks associated with cannabis use and widespread self-medication with cannabis for tics, where regional legislation and resources allow, physicians must offer to direct patients to appropriate medical supervision when cannabis is used as self-medication for tics. (Appropriate medical supervision would entail education and monitoring for efficacy and adverse effects.)
Level C	Where regional legislation allows, physicians may consider treatment with cannabis-based medication in otherwise treatment-resistant adults suffering from clinically relevant tics.
Level C	Where regional legislation allows, physicians may consider treatment with cannabis-based medication in adults with TS who already use cannabis efficiently as a self-medication in order to better control and improve quality of treatment.
Level A	Where regional legislation allows, physicians prescribing cannabis-based medication must prescribe the lowest effective dose to decrease the risk of adverse effects.
Level A	Physicians prescribing cannabis-based medication must inform patients that medication may impair driving ability.
Level A	Physicians prescribing cannabis-based medication to patients with TS must periodically re-evaluate the need for ongoing treatment.

Deep Brain Stimulation for Tics in the Setting of TS
Recommendation 13

Rationale

Patients with severe TS, resistant to medical and behavioral therapy, may benefit from the application of deep brain stimulation (DBS). An important challenge and limitation in the evaluation of the evidence around DBS in TS is that, even in expert DBS centers, few operations per year are performed. Furthermore, there is limited information from randomized clinical trials for analysis and interpretation. There is no consensus on the optimal brain target for the treatment of tics, but the following regions have been stimulated in patients with TS: the centromedian thalamus, the globus pallidus internus (ventral and dorsal), the globus pallidus externus, the subthalamic nucleus, and the ventral striatum/ventral capsular nucleus accumbens region. DBS of the anteromedial globus pallidus is possibly more likely than sham stimulation to reduce tic severity. There is insufficient evidence to determine the efficacy of DBS of the thalamus or the centromedian-parafascicular complex region of the thalamus in reducing tic severity. Complications of treatment, including infection and removal of hardware, appear more common with TS than with other neurologic conditions.

Recommendations from the Movement Disorders Society suggest that, when DBS is used in TS, best practices used for other DBS applications are followed, including confirmation of diagnosis, use of multidisciplinary screening, and stabilization of psychiatric comorbidities inclusive of active suicidality.[33] Appropriate patient selection is one of the most important predictors of success of DBS treatment, making multidisciplinary evaluation essential.[34] Because of the complexity of the patient population, centers performing DBS have been encouraged to screen candidates preoperatively and to follow them postoperatively. There has been concern about high risk of suicide and other negative psychiatric sequelae in patients with TS not screened and monitored for depression, anxiety, and bipolar tendencies. The largest available randomized trials of DBS have revealed benefits on motor and phonic tics for the ventral globus pallidus internus and the centromedian thalamic region target; however, these studies have raised methodologic concerns that need to be addressed in future trials.[35] There is little information on the effects of DBS on psychiatric comorbidities and on the efficacy of DBS in children with TS.

Level	Recommendation
Level A	Physicians must use a multidisciplinary evaluation (psychiatrist or neurologist, neurosurgeon, and neuropsychologist) to establish when the benefits of treatment outweigh the risks for prescribing DBS for medication-resistant motor and phonic tics.
Level B	Physicians should confirm the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (*DSM-5*) diagnosis of TS and exclude secondary and functional tic-like movements when considering DBS for medication-resistant tics.
Level A	A mental health professional must screen patients preoperatively and follow patients postoperatively for psychiatric disorders that may impede the long-term success of the therapy.
Level A	Physicians must confirm that multiple classes of medication (antipsychotics, dopamine depleters, alpha-1 agonists) and behavioral therapy have been administered (or are contraindicated) before prescribing DBS for tics.
Level C	Physicians may consider DBS for severe, self-injurious tics, such as severe cervical tics that result in spinal injury.

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This practice guideline was endorsed by the Child Neurology Society and the European Academy of Neurology.

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