Treating Tourette Together: An Agenda for Patient-Centered Research Focused on Comprehensive Behavior Therapy for Tics

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Treating Tourette Together: Executive Summary

Background

As people living with TDs, family members or providers who care for people with TDs, and researchers studying TDs, we know Tic Disorders and Tourette's Syndrome (TDs) are complex conditions. Effective treatment must be thoughtful, individualized, and comprehensive.

In the last 20 years, the TDs community has come together to develop, test, and spread the word about Comprehensive Behavioral Intervention for Tics (CBIT). CBIT is an eight-session, skills-based treatment in which a patient works with a therapist to learn skills that can help reduce the severity of that person's tics, and to reduce tic-related challenges they are experiencing in their lives.

Large research studies have shown CBIT to be safe and effective for reducing tics in both children and adults (read more about CBIT [here](#)). Given CBIT's effectiveness, the American Academy of Neurology's recent Treatment Guidelines named CBIT as the recommended first-line treatment for TDs. These experts recommend that most people with TDs who want treatment for their tics should start with CBIT, rather than with medication (read more [here](#)).

We know that CBIT is not the only tool in the toolkit for living with TDs. We are aware that there are other important issues for researchers and providers to address (for example, improving the accuracy and speed of diagnosis, continuing to study the genetics and/or biology of TDs, and managing other "comorbid" conditions that can come along with tics), but the purpose of this effort was to focus on improving CBIT.

Now that CBIT has been proven effective, researchers and providers want to conduct the "next generation" of research to improve CBIT and increase its availability. Conducting research is critical for several reasons. It helps ensure that patients receive proven and effective treatments and that clinicians select and offer the best interventions. Research can also reduce health care costs by increasing the impact of services. It can help us to know the most effective methods for sharing effective treatment with others who need it and allow us to improve equality in healthcare access and health outcomes.

Treating Tourette Together Summit

We believe that input from all members of the TDs community is vital for guiding the future of CBIT research. This approach is sometimes called "patient-centered outcomes research" (read more [here](#)). In order to create a plan, we held a two-day Treating Tourette Together (TTT) Summit in Minneapolis, Minnesota in August 2019 for patients, families and caregivers, health care providers, and researchers. First, we got the word out to hundreds of people in the TDs community and collected opinions on CBIT from over 700 respondents in a survey.

Over 100 of these individuals applied to attend the TTT Summit. While we wish we could have invited all applicants to attend, we had to select a smaller group to ensure that we could build community and work flexibly at the Summit.

Ultimately, we brought together a group of 45 individuals for the Summit, with representation from youth and adults with TDs, parents of children with TDs, healthcare providers (including providers from neurology, psychiatry, psychology, pediatrics, occupational therapy, and primary care) and educators who work with people with TDs, TDs researchers, and other stakeholders.

We spent two days getting to know each other, learning from each other's experiences, and sharing thoughts about what is needed to improve the lives of people with TDs. In the second half of this two-day Summit, we worked together to identify key research questions for this next generation of CBIT research. Our aim was to develop focused research questions that:

- 1) have not yet been studied,
- 2) have the potential for high impact,
- 3) are relevant to multiple stakeholders (e.g., patients, families, clinicians, payors), and
- 4) are possible to test scientifically (e.g., the question would lead to an ethical and feasible study with a testable hypothesis and measurable outcomes).

Key Research Areas

After the Summit, we organized this input into 4 Key Research Areas that described the general types of research that attendees felt passionately about.

Here, we list these domains, as well as specific Research Questions within each domain. Even though we number these below, each is considered equally important (for example, #3 isn't a lower priority than #1).

Key Research Domains and Sample Questions

Domain 1: Increasing Access to CBIT

Representative research questions include:

1. Children spend a lot of time in school. Can we train school-based providers (e.g., guidance counselors, school OTs) to provide CBIT effectively in school settings?
2. Currently, there are not enough CBIT providers for all of the people with TDs who want CBIT. What are the most effective ways to train more providers in CBIT?
3. Many people with TDs have to see more than one doctor, or wait a long time to get diagnosed and connected to quality care. What is the best way to train general doctors

(such as pediatricians and family doctors) to recognize TDs and provide appropriate education, resources, treatment recommendations, and referrals?

Domain 2: Increasing CBIT's Effectiveness

Representative research questions include:

1. CBIT in its current form does not work for everyone. Can we improve CBIT outcomes by figuring out what makes it work more, or less, well for some people? This would include looking at numerical information from studies, and also talking with people who have received CBIT about ways to improve it.
2. CBIT involves a number of different parts. Can we make CBIT more efficient by identifying its most “active ingredients”?
3. Many people with TDs do not feel that CBIT is a good fit for them. Can we create a “CBIT Readiness Interview” to explain what CBIT is, discuss concerns, and possibly increase patients’ desire to do CBIT?

Domain 3: Optimizing How CBIT Fits into Individuals’ Broader Care for TDs

Representative research questions include:

1. People with TDs are likely to use multiple kinds of treatments, such as medications and CBIT. What are the best sequences of treatment for TDs (for example, CBIT followed by medication, or vice versa)? *And*, can we identify who will benefit from one treatment sequence instead of another?
2. Many patients who want CBIT have to wait a long time on waitlists to get it. Can we help people with TDs find relief more quickly by having them start with an online, self-help version of CBIT, and then move on to CBIT with a therapist if self-help is not effective for them?
3. Many patients live too far from CBIT providers for weekly visits. Can we evaluate whether other CBIT formats work just as well, such as doing CBIT over videochat or doing a short, intensive “CBIT Bootcamp” (called “intensive outpatient treatment” by healthcare providers)?
4. Many people with TDs take tic-reducing medications but wish they did not have to. Can CBIT be used as a tool to get off of these medications?
5. How well does CBIT work compared to medication alone, *and* the combination of CBIT and medication used simultaneously?

Domain 4: Investigating CBIT's Impact on Outcomes that Matter to People Living with TDs

Representative research questions include:

- 1) TDs impact many aspects of a person's life. Can we evaluate CBIT's effects on the things that patients care about *other* than tic severity and general "tic-related problems"? These could include self-esteem, confidence, perceived control over tics, time spent in class, ability to drive, etc.

Full Research Agenda: Treating Tourette Together

Abstract: Tourette Syndrome and other persistent tic disorders (TDs¹) involve chronic, repetitive, unwanted movements and/or sounds (i.e., tics) that can cause substantial distress and disruption in everyday activities (American Psychiatric Association, 2013). Effective medications for treating TD exist, but, in many cases, they cause significant side effects that limit their usability. Comprehensive Behavioral Intervention for Tics (CBIT) is a therapy that teaches tic-management skills to reduce tic frequency and interference. Large, controlled research studies have shown that CBIT reduces tics in children and adults about as much as medications, but without significant side effects. However, at present, patient demand for CBIT exceeds availability, and many patients do not have access to a local CBIT provider. Also, a smaller percentage of patients perceive CBIT to be a poor fit for their specific situation.

Researchers have been exploring options to make CBIT more available and to tailor it to different settings, but patient, family, and other stakeholder input is essential to understand how to do this most effectively. We established the “Treating Tourette Together” project to bring together patients, clinicians, researchers, and other stakeholders to develop an agenda for a new generation of patient-centered CBIT research.

In this report, we describe the Treating Tourette Together project specifically, but more information about Tourette Syndrome and Tic Disorders and resources for individuals impacted by them can be found through the Tourette Association of America (tourette.org).

CBIT Has Revolutionized Treatment of TDs

The past 20 years have brought vast changes in scientific knowledge about the treatment of Tourette Syndrome (TS) and other TDs. Historically, antidopaminergic medications such as risperidone (Risperdal), haloperidol (Haldol), and pimozide (Orap), were the sole mode of TDs treatment (Pringsheim et al., 2019). Although effective in controlling tics, these medications also often cause significant side effects that make them impractical for long-term use in many, if not most, patients. Effective behavioral treatment of TDs had been described in the research literature since 1973 (Azrin & Nunn, 1973), but research on behavioral treatments occurred outside of the medical mainstream. As a result, adoption of these interventions in clinical settings was minimal (Woods et al., 2010).

In the early 2000s, the Tourette Association of America (TAA) convened a group of scientist-practitioners versed in behavioral treatment of TDs to build and test a comprehensive protocol for the non-medical treatment of tics (i.e., Comprehensive Behavioral Intervention for Tics;

¹ In this report, we use the term “tic disorders” (TDs) to refer collectively to Tourette Syndrome, Persistent Motor Tic Disorder, and Persistent Vocal Tic Disorder. We note that our use of TDs here does not generally include transient tic disorders or adult-onset tic disorders, unless explicitly specified. We also recognize that there is an ongoing discussion about diagnostic labels for tic disorders (Müller-Vahl et al., 2019), including a call for more patient-centered research to identify terms most preferred by impacted individuals (Conelea et al., 2019).

CBIT; (Woods et al., 2008)). CBIT involves eight 60-to-90 minute treatment sessions delivered across 10 weeks by a specialized behavioral health clinician (e.g., a psychologist). Randomized controlled trials have demonstrated CBIT's feasibility, acceptability, safety, and efficacy among children ages 5 and older (Bennett et al., 2019; Piacentini et al., 2010) and adults (Wilhelm et al., 2012). These studies show that CBIT yields symptom reduction comparable to antidopaminergic medications but without notable side effects (Scahill et al., 2013) .

Given this picture, the American Academy of Neurology recently released guidelines recommending CBIT as the first-line treatment for TDs (Pringsheim et al., 2019). This recommendation aligns with prior guidelines from European (Verdellen et al., 2011) and Canadian (Steeves et al., 2012) working groups. These recommendations mark a global paradigm shift in the clinical management of TDs. Although clinical research has clearly signaled the potential of behavioral interventions as a primary TD management approach, it is less clear how to bring a behavior-therapy-first model to scale in clinical care settings. In general, implementation research shows an average delay of 15-20 years for evidence-based practice to be implemented in usual care settings (Sundararaman, 2009). This delay may be even more pronounced for behavioral interventions, according to surveys of mental health service providers (Becker et al., 2004; Cook et al., 2009; Reid et al., 2018; van Minnen et al., 2010; Whiteside et al., 2016; Wolitzky-Taylor et al., 2015).

Efforts to Increase CBIT Access Have Been Somewhat Successful but not Optimal

The TAA and scientist-practitioners have been active in exploring and testing solutions to hasten the dissemination of CBIT in the United States. In 2011, the TAA began partnering with CBIT experts to implement continuing education CBIT programs referred to as "Behavior Therapy Institutes," which have trained over 560 providers to date. Teletherapy studies have shown that CBIT can be effectively delivered via videoconferencing technology to patients in remote clinics (Himle et al., 2012) and directly to patients in their homes (Capriotti, M. R., Wellen, B., Young, B., Himle, M.B., Conelea, C. A., Espil, F. M., & Mathews, C. A., 2019, November; Ricketts, Goetz, et al., 2016). TicHelper, a self-help computerized tool based on CBIT principles that youth and their families can use to effectively, has been developed and demonstrated to be effective in managing tics (Himle, M.B., Wellen, B.A., Woods, D.W., Bauer, C.C., & Mouton-Odum, S., 2018, November).

These multipronged efforts have made progress in increasing access to CBIT. In the TAA's 2018 impact survey of 263 adults with TDs and 623 parents of children with TDs (TAA, 2018), 36% of youth and 25% of adults had tried CBIT (*Impact Survey - Tourette Association of America*, n.d.). This reflects a 5-6 fold increase from a large-scale survey in 2008 (Conelea et al., 2013, 2011), in which 6% of youth and 4% of adults had received CBIT. Still, the 2018 Impact Survey reflects the reality that advances in access have not yet brought CBIT to the majority of people

with TDs. Thirty-three US states have fewer than five CBIT therapists and eight have none. Critically, where CBIT providers are present, many are in settings that are out-of-network with insurance providers, such that accessing care is not financially feasible for many patients.

A Patient-Centered Model to Advance CBIT Research

As seen above, researcher-led efforts to test and develop approaches to increase CBIT access have moved the needle, but not yet brought care to a majority of patients. A variety of approaches show promise, including hosting Behavior Therapy Institutes to train providers, providing teleCBIT remotely, and implementing CBIT in self-help format. However, extant research has not yet identified patients' preferences among these modalities and appraisals of the pros and cons of each. Similarly, little is known about the feasibility of implementing these interventions in different clinical care systems, reimbursability of services, and which care modalities may be preferred by or work best for specific individual patients.

In late 2018, we convened an initiative to bring a patient-centered research (PCR) model to the study of behavioral treatment of TDs. PCR is an alternative to the “traditional” clinical research model. Traditionally, researchers generate novel treatments, test their effectiveness, and then subsequently work to disseminate them to clinical care settings. In PCR, patients, families, community clinicians, and other stakeholders (e.g., educators) are fully partnered in all stages of the research process, including generation of research questions, study design, data collection, interpretation of findings, and dissemination of results (Concannon et al., 2014; Ellis & Kass, 2017; Kirwan et al., 2017; Newhouse et al., 2015). By engaging stakeholders from end-to-end in the process, PCR increases the likelihood that the topic and design of research will answer questions that have the greatest impact on clinical care and patient outcomes.

Treating Tourette Together: Using PCR to Set a Roadmap for CBIT Research

Although CBIT's development and testing was conducted in close consultation with the TAA, we felt that our current effort marked the beginning of efforts to thoroughly apply a PCR model to CBIT research. Given this, we set our first task as convening a summit of stakeholders in order to craft a patient-centered agenda for CBIT research. Our key personnel team began with a network of CBIT and TD researchers who collaborated frequently with each other and with the TAA (Drs. Bennett, Capriotti, Conelea, Himle, & Mathews). The TAA served as the “anchor” of this initiative, represented by VP of Research and Medical Programs, Dr. Shineman. We brought in an additional expert with 20 years' experience in community health engagement and PCR (Hunt). In keeping with PCR's emphasis on patient stakeholders having a true “seat at the table” in all phases of the process, we rounded out our Key Personnel team with Sara Hamilton, a TS advocate and mother of an adolescent with TS.

Together, we applied for funding to support the summit from the Patient Centered Outcomes Research Institute (PCORI), a non-governmental organization that funds and supports PCR to

improve healthcare services and patient outcomes. Our December 2018 application for a PCORI Conference Support award was successful, ensuring financial support for the TTT project. The primary aim and deliverable of this project was to develop and disseminate a patient-centered, stakeholder-driven set of research priorities to inform the next generation of research on behavioral treatment of TS with the ultimate goal of increasing access to care and decreasing disability among TD patients. The TTT summit and related surveys provided the stakeholder input for this research agenda.

The Key Personnel team met biweekly via videoconference beginning in December 2018 to commence planning. We set the Summit for August 17th and 18th, 2019 at the University of Minnesota, which was selected due to its geographic centrality and excellent fit for the meeting's space and support needs.

After core logistics were planned, we established a set of Diversity and Inclusion Principles (Appendix A) to guide our approach to selecting and centering different types of stakeholders. We then launched a “pre-conference survey” to a broad national network of people impacted by TDs and professionals who provide healthcare and educational services to individuals with TDs. The distribution of this survey served to (a) increase the TD community's awareness of TTT, (b) collect broad-reaching data on perceptions on CBIT and key areas for research, and (c) invite individuals to apply to the TTT Summit. We distributed this survey to TAA membership, other patient community organizations, and professional listservs, and information about the survey was shared on social media and “Tourette's Podcast” (Brown, 2020). We received responses from 796 individuals in the TD community within eight weeks, the details of which are described below under “Results and Priorities.”

Following this, we invited full applications from all individuals who had responded to the pre-conference survey, and through other professional and patient networks, including the TAA's member listserv. We received a total of 108 applications. Of these, 25 were from adults with TDs, 49 were from parents and other family members of youth with TDs, 7 were from adolescents with TDs, 29 were from health care professionals working with patients with TDs, and 12 were from clinical researchers who study TDs (note: these numbers sum to greater than 108 because some participants identified themselves as falling in more than one category). The Key Personnel team engaged in a collaborative application review process, using our Diversity and Inclusion Principles as a guiding document (see Appendix A). Our process ultimately led us to assemble a group of 45 individuals who participated in the TTT Summit (see Appendix B). To minimize financial barriers to participation, grant funds were used to cover transportation, lodging, and meals for attendees.

The Big Days: TTT Summit

TTT Summit attendees convened in Minneapolis, MN on August 17th-18th, 2019. Appendix C shows a full agenda detailing activities. After a welcoming reception the previous evening, Day 1

sessions began with icebreakers, welcoming remarks, and introduction activities. These were followed by panel discussions and personal speeches that centered the voices of individuals directly impacted by TS, followed by similar activities that focused on the perspectives of clinicians providing CBIT in the community. Afternoon sessions described existing forms of CBIT and shared individuals' lived experiences with CBIT and TS healthcare services. Day 2 focused on generating and prioritizing research domains and questions via small-group and whole-group activities. We concluded with a reflection on the Summit, feedback, and discussion of next-steps in iterating and disseminating the Research Agenda generated by TTT.

Following the Summit, the Key Personnel continued to meet biweekly to synthesize Summit discussions. This included reviewing research questions, discussing research domains that emerged as common themes of emphasis in the research questions, integrating, and reflecting on Summit attendee feedback. The primary aim of these meetings was to synthesize information from all project activities to create this research agenda document. These post-Summit meetings also involved planning for dissemination and community input regarding this report.

Results and Priorities

Pre-conference Survey

The pre-conference survey was completed by 791 individuals, 625 of whom were individuals impacted by TS and 166 of whom were healthcare providers working with people with TS. Among impacted individuals, 370 were parents of youth with TS, 171 were adults with TS, 44 were parents of adults with TS, 20 were adolescents with TS, and 25 were people impacted by TS in another way (e.g., grandparent of a person with TS). Sixty-seven percent of impacted individuals said they or a family member had tried CBIT. Healthcare professionals included psychologists (40%, n=57), neurologists (11%, n=16), psychiatrists (11%, n=15), social workers, counselors, and psychotherapists (7%, n=11), nurse practitioners (7%, n=10), occupational therapists (7%, n=9), and other kinds of healthcare professionals (13%, n=18), including developmental and behavioral pediatricians, nurses, and others. When asked about the average monthly number of patients with TDs they see in their practice, 66% reported seeing 0-5 patients, 9% (n=13) reported seeing 6-10 patients, 9% (n=13) reported seeing 11-20 patients, and 15% (n=20) said they saw greater than 21 patients.

Impacted individuals rated their interest in in-person CBIT, tele-CBIT, and self-help CBIT on a five-point scale where 1= *not at all interested*, 2= *a little interested*, 3= *moderately interested*, 4= *very interested*, and 5= *extremely interested*. Here, we considered those marking a 4 or 5 for each modality to be “highly interested” in that modality.

Parents expressed high interest in 69% of cases for in-person CBIT, 36% for tele-CBIT, and 32% for self-help CBIT. Among teen respondents, 53% were highly interested in in-person CBIT, 14% in teleCBIT, and 14% in self-help CBIT. Among adults, 40% were highly interested in in-

person CBIT, 33% in self-help CBIT, and 13% in teleCBIT. Patient preferences did not differ according to urbanity (i.e., self-reported living in an urban vs. suburban vs. rural area) or having received CBIT. Respondents with higher self-reported knowledge of CBIT reported greater interest in teleCBIT ($p < .05$), but CBIT knowledge was not related to interest in in-person CBIT or self-help.

Impacted individuals reported interest in receiving CBIT from a variety of types of providers, including psychologists (81%), neurologists, (75%), psychiatrists (63%), occupational therapists (60%), social workers and psychotherapists (59%), primary care providers and pediatricians (53%), school mental health professionals (50%), and nurse practitioners (46%). 35% of respondents indicated they had no preference for a specific provider type (N.B.: These individuals were counted as willing to receive CBIT from any of the above provider types). Interestingly, 90.1% of respondents included at least one mental health professional (i.e., psychologist, psychiatrist, or social worker/psychotherapist) in the set of providers from whom they would be willing to see for CBIT.

Across all impacted individuals, respondents who reported having heard more about CBIT were more likely to endorse high interest in teleCBIT ($p < .05$), but no differences were seen for in-person CBIT or self-help CBIT. Ratings of interest did not differ according to respondents self-described geographic setting (i.e., urban vs. suburban vs. rural) or whether they reported previously receiving CBIT. We were unable to run meaningful (i.e., adequately powered) analyses on differences according to ethnoracial background, as 88% ($n=455$) of participants endorsed White as their background and no greater than 6% ($n=30$) of the sample endorsed any one of the other identities.

Among healthcare providers, 69% perceived high patient interest in in-person CBIT, 44% perceived high interest in teleCBIT, and 29% perceived high interest in self-help CBIT. Perceived patient interest in each modality did not differ according to providers self-reported familiarity with CBIT. Providers who saw more monthly patients with TS perceived a greater interest in teleCBIT ($p < .05$); no such differences were seen for in-person CBIT or self-help. When asked about barriers their patients face in accessing CBIT, respondents highlighted various access related barriers, including lack of local providers 59% ($n=76$), problems with insurance coverage (41%), long waitlists (36%), and high costs of CBIT (30%), higher need for treatment of comorbid conditions rather than tics (28%, $n=36$), and low patient interest in CBIT (11%, $n=14$).

Our team gleaned the following key insights from the survey responses:

- Individuals impacted by TDs generally prefer in-person CBIT to teleCBIT or self-help.
- However, individuals impacted by TDs also show high levels of interest in teleCBIT and self-help, as shown by

- At least 30% of parents expressed high interest in both teleCBIT and self-help CBIT
- 33% of adults expressed high interest in self-help CBIT
- Over 50% of respondents in each group expressing at least “a little interest” in each modality of CBIT (data available on request)
- Patients are comfortable accessing CBIT from a variety of types of healthcare providers, and few patients are opposed to seeing mental health providers for CBIT.
- Providers perceive their patients as largely being interested in CBIT, but as frequently encountering logistical and financial access barriers that prevent them from utilizing CBIT.

These survey data align with other evidence that patient demand for CBIT currently exceeds availability. In a mixed methods study of 295 parents of young people with TS and 42 youths with TD, 76% of parents reported that they wanted CBIT to be available for their child, and roughly one-third of parents and half of young people surveyed reported a lack of knowledgeable providers in their geographic region (Cuenca et al., 2015). Moreover, Tourette.org had close to 60,000 searches for CBIT in the last year (TAA, personal communication, 2018).

We considered these pre-conference survey results as we planned topics and sessions for the TTT Summit. Based on these results, we planned sessions discussing the strengths and weaknesses of each of these 3 CBIT formats in the Summit. We presented results of this pre-conference survey to attendees during Day 1 of the Summit.

Overarching Considerations for the Patient-Centered Research Agenda

The Research Agenda presented here aims to create a roadmap for developing treatment and dissemination solutions that improve access and effectiveness of behavioral treatments for TDs, ultimately reducing the public health impact of this condition. There are several overarching considerations that cross over multiple research domains that are important to address.

Early identification and diagnosis for those living with TDs is an integral first priority to then increasing awareness of treatment modalities such as CBIT. Indeed this was a point of discussion and high priority for many TTT Summit attendees, which relates to the research questions about training “gateway” doctors to recognize, assess, provide referrals and/or initiate CBIT strategies (see Appendix D). Without timely and accurate diagnosis, followed by referral to appropriate resources and providers, an individual with TS is unable to benefit from available care. Although the TTT effort focuses on one such component of care for TDs (CBIT), we recognize that education and research efforts aimed at improving general practitioners’ awareness of TS are critical to improving outcomes for people with TS. Though these issues are not the primary focus on this document, we hope that steps taken to achieve the mission of this Research Agenda will hopefully indirectly increase knowledge about TS, accurate diagnosis, and appropriate referral, by drawing attention to TS and its treatment in general.

While the onset of TS is in childhood, there are many adults living with TS and tic disorders that also need targeted care specific for their needs. Historically, many adults in the TS community have reported feeling underserved by clinical providers and left out of targeted treatment development and awareness-raising programs. Adults may require a different treatment duration or may have unique preferences in terms of the different treatment modalities. It is critical that this viewpoint is recognized throughout our research agenda.

Close to 90% of those with TDs experience co-occurring conditions such as ADHD, OCD, or anxiety. CBIT is highly tic-focused and does not directly treat these co-occurring conditions. On the other hand, research has demonstrated that CBIT does not cause worsening of co-occurring conditions and that those who respond to CBIT may see slight decreases in some co-occurring symptom areas (McGuire et al., 2014; Piacentini et al., 2010; Scahill et al., 2013; Woods et al., 2011), but these co-occurring conditions may influence CBIT's effectiveness. Further strategies for identification and support for these co-occurring conditions should be a consideration when integrating care that includes CBIT. While not specifically addressed in this research agenda, co-occurring conditions are an overarching factor in the TS and Tic Disorder population that must be taken into account.

Finally, there is a lack of diversity and representation of individuals from marginalized backgrounds in TS research and advocacy efforts (e.g., along racial, ethnic, socio-economic, and geographic lines). Part of our effort through developing this research agenda is to engage these diverse communities to ensure we are including the voice of patients from all backgrounds in developing the next phase of research on behavioral therapy for TS and tic disorders.

Research Domains and Questions

Participants at the TTT Summit generated several dozen research questions in small group and whole group activities. Following the Summit, the key personnel team organized these questions into 4 Key Research Domains that described the general types of research that attendees felt passionate about. Appendix D contains a full list of these questions, organized by domain. These four research domains are presented below. Each section describes how the research domain was defined, the extant research to date in this topic area, what is not yet known or requires future research, and sample research questions from the TTT summit that were designated as high-priority by the attendees through voting exercises at the summit. We recognize that all of the research questions generated at the Summit, and those outside of our specific topic area, are of high importance to the TDs community. We have numbered the research domains below, and specific questions within each domain, but these numbers do not reflect prioritization. Each domain is considered equally important (for example, #3 isn't a lower priority than #1).

Domain 1. How to increase access to CBIT

The current state of CBIT access.

Research studies and training initiatives have put forth great effort to make CBIT available to those who need it. Dissemination efforts have included adaptations of CBIT for use in pediatrics and neurology practices (Ricketts, Gilbert, et al., 2016), and for utilization by occupational therapists (Rowe et al., 2013). Brief and intensive forms of CBIT have been developed (Blount et al., 2014, 2018; Kennedy et al., 2016), as well as self-help online (PsycTech Ltd, n.d.) and video adaptations (Specht et al., 2017) to be used at home. Despite efforts to make CBIT more available, a large portion of affected individuals with chronic tic disorders do not have access to CBIT trained providers. Barriers to accessing CBIT include lack of a trained provider in one's geographic area, long waitlists, high fees for services, and/or lack of insurance coverage (Conelea et al., 2013, 2011; *Impact Survey - Tourette Association of America*, n.d.). In addition, early detection of tics by a medical provider and accurate diagnosis of a tic disorder would improve earlier access to the evidence based treatments for the identified condition. Thus, this domain focuses on improving access to assessment and treatment services that have the requisite knowledge and experience to accurately diagnose and effectively treat tic disorders according to the evidence base and consensus expert treatment guidelines (e.g. (Pringsheim et al., 2019)).

The TAA Impact Survey found that of 944 people surveyed, 36% of children and 25% of adults reported having tried CBIT (*Impact Survey - Tourette Association of America*, n.d.). Reasons for not having tried CBIT included lack of awareness, lack of providers, lack of insurance coverage, and disinterest in CBIT or preference for an alternative method of treatment. Moreover, the identification of those in need of treatment for TDs, and the ability to efficiently diagnose and triage individuals with interfering tics to the appropriate treatment, remains an area in need of improvement. The TAA Impact Survey (*Impact Survey - Tourette Association of America*, n.d.) asked respondents how long it took to receive a diagnosis after first noticing tic symptoms. Nearly 50% of adults with TDs said that it took 6 years or more to receive a diagnosis, and a neurologist was the most common type of provider to make the diagnosis. The responses from youth living with TDs reflected some improvement in time to diagnosis with around 1/3 of youth responders receiving a diagnosis less than one year after noticing symptoms, and 40% of youth receiving a diagnosis in 1 to 2 years. However, nearly 20% of youth received a diagnosis three to six years after first noticing symptoms. These data speak to the need for specific education and training for front line providers, such as pediatricians and primary care doctors, who would most quickly be able to identify, assess and diagnose a tic symptom or disorder, and provide treatment recommendations and referrals for evidence based treatment.

Existing efforts to increase CBIT access.

A partnership between the TAA and the Center for Disease Control (CDC) offers educational opportunities for health care providers from a variety of training backgrounds and geographic locations to receive specific training in the assessment and treatment of TDs. The Behavior Therapy Training Institute program mentioned above has increased the number of well-trained providers, but is difficult to bring to scale to meet the demand of providers needed. Research is

underway to produce an online training program which could reach far more providers in the convenience of their own preferred location and training timeline (Himle, Wellen, Woods, Bauer, & Mouton-Odum, 2018). However, questions remain about how to optimize training opportunities to maximize access to care.

CBIT was originally developed by psychologists, and the clinicians in the large-scale CBIT efficacy trials were individuals with masters or doctorate degrees in psychology. Subsequent efforts to expand CBIT access have included training clinicians from other disciplines. Traditional CBIT delivered by occupational therapists has shown similar outcomes to the efficacy trials in one pilot (Rowe et al., 2013) and one feasibility trial (Kim et al., 2015). Another small study modified the traditional CBIT protocol to fit the contexts of neurology and developmental pediatrics clinics (e.g., abbreviated course to 6, 20 minute sessions, variable provider types including nurse practitioners; (Ricketts, Gilbert, et al., 2016)). Outcomes were comparable to the efficacy trials, with about 50% of those completing response showing significant benefit.

These early studies suggest that clinicians from non-psychology disciplines can successfully learn and deliver CBIT, and that CBIT may still be beneficial when modified to fit the practice contexts of other disciplines. However, we do not yet know if these findings hold in larger samples or apply to other disciplines. CBIT training via the TAA's Behavior Therapy Institute is now open to multiple types of licensed healthcare professionals, including psychologists, physicians, nurses, occupational therapists, social workers, and speech pathologists. We are also aware of efforts underway to deliver CBIT in medical clinics via a co-located psychologist specializing in brief primary care interventions. These efforts raise important questions about whether CBIT outcomes are consistent across provider types and settings.

How do we improve CBIT access?

Questions that arose on this topic at the Summit included big picture priorities such as: With limited resources, is it more effective or preferred by more patients to train as many providers as possible and target under-resourced areas, or to invest in technologies that improve access via electronic or online methods? Specific training and implementation questions also arose, including, is there a minimum training requirement for providers that would ensure quality TD care?; and, how should we define and measure "quality"?

Bringing CBIT to the places where youth would have easy, efficient access, like within their pediatrician's office or at school, was an area of interest to stakeholders that has not yet been sufficiently studied. During the Summit, parents in particular expressed interest in knowing whether CBIT could be effectively delivered within a school setting. This generated a number of related questions such as how to entice schools to train a therapist within their system in CBIT, whether or not this would be cost effective, whether the CBIT treatment would need to be

modified in some way (e.g. shorter sessions, group delivery), and whether this would be an effective and preferred model for symptom identification and intervention delivery.

TTT Summit attendees agreed that efforts to increase access should include training providers across disciplines in CBIT delivery. Questions related to provider training included how to incentivize clinicians and clinical systems to get CBIT training, whether there is a type of provider (e.g. occupational therapist vs. psychologist vs. medical doctor) and/or prerequisite level of training required (e.g. Bachelors, Masters, or Doctoral degree) to be able to provide CBIT effectively and with fidelity to the model.

Attendees agreed that future research should address the following questions so that we can best understand how to optimize the reach of CBIT while maintaining optimal benefit for patients:

- Do CBIT outcomes differ depending on the type of provider?
- What level of professional expertise is required to effectively deliver CBIT?
- What are the optimal training requirements to train someone in CBIT to fidelity?
- Does increasing awareness of TDs entice more clinicians to pursue CBIT training?
- Would in person or online methods be most effective for training more clinicians in CBIT?
- Are there optimal ways to tailor CBIT depending on provider type? For example, is there an optimal way to abbreviate CBIT so that it can be delivered by a primary care doctor/pediatrician?
- Is it feasible, acceptable, cost-efficient and effective to provide CBIT in primary care contexts?
- If CBIT is modified for different providers and settings, how will the outcomes compare? For example, would brief instruction in CBIT by a pediatrician work as well as a longer single session with a nurse practitioner or co-located psychologist?
- Does support from a multidisciplinary, co-located treatment team improve outcomes?
- Is it feasible, acceptable, cost-efficient and effective to deliver CBIT in schools via a brief, condensed, or group format?

Domain 2. How to improve CBIT outcomes for individual patients

Research has established that CBIT, when delivered with fidelity (i.e., following the procedures outlined in the published manual; (Woods et al., 2008)), is an effective treatment for reducing tics for many individuals. The most convincing evidence supporting the use of CBIT comes from the aforementioned child and adult randomized controlled trials (i.e., the CBIT studies) showing CBIT to be more effective than general supportive psychotherapy for reducing tics in both children and adults (Piacentini et al., 2010; Wilhelm et al., 2012). While the results of these trials are encouraging, we cannot ignore the fact that many individuals who received CBIT in these studies did not substantially benefit. In fact, among those who received CBIT, 47% of

children and 62% of adults did not achieve “responder status” (defined as much improved or very much improved following treatment). In addition, few (if any) of those who responded to CBIT (i.e., treatment responders) experienced complete symptom remission. Although CBIT was never intended, nor expected, to be a “cure” for tics, these findings confirm that more research is needed to determine how to improve CBIT to make it more effective for more individuals.

A predominant theme of the feedback gathered from the TTT Summit was a need for research efforts to improve CBIT outcomes for individual patients. Doing so will necessitate a multi-pronged research approach to better understand three interrelated questions: (1) what patient factors predict positive outcomes (for *whom* it does and does not work); (2) which CBIT ingredients are necessary, sufficient, and most important for reducing tics; and (3) what is the optimal way to deliver CBIT outside of a research setting.

What patient factors predict positive outcomes in CBIT (for whom does CBIT work)?

A better understanding of who responds to CBIT is important for several reasons. First, CBIT is a time, resource, and effort-intensive intervention. Understanding which patients are more or less likely to respond to treatment (i.e., predicting treatment outcomes) will assist clinicians in treatment planning so that they can better advise patients on the optimal course of clinical care. Doing so has the potential to not only accelerate the time from diagnosis to intervention, but also to increase the likelihood that patients receive individualized treatment plans that are most likely to be beneficial. Second, identifying treatment moderators (i.e., factors associated with differential treatment effects), such as patient characteristics that influence response to CBIT, will inform efforts to effectively tailor CBIT to the individual, thereby increasing the likelihood of positive outcomes.

Currently, relatively little is known about what patient and parent factors predict response to CBIT. Sukhodolsky et al. (Sukhodolsky et al., 2017) recently analyzed the data from the combined child and adult CBIT studies to examine several potential treatment moderators (i.e., factors that influence differential response to CBIT versus supportive therapy) and predictors (factors affecting treatment response regardless of treatment assignment). Those analyses found that age, gender, tic severity, premonitory urge severity, and family functioning did not moderate response to treatment. Likewise, comorbidity status did not moderate treatment outcomes; however, it is important to point out that patients who had one or more comorbid conditions that warranted more immediate treatment were excluded from the studies upon which these analyses were based (Piacentini et al., 2010; Wilhelm et al., 2012). Said differently, these studies suggest that CBIT appears to be comparably effective *regardless* of the above factors. The only significant moderator identified by Sukhodolsky et al. (2017) was medication status. Specifically, they found that the treatment effect (difference between CBIT and supportive therapy) was less pronounced for individuals who entered the study on tic suppressing medications compared to those who were not on tic-suppressing medication at the time treatment

began. Importantly, this finding reflected an increased response (i.e., tic reduction) for individuals who received supportive therapy and who were also on tic suppressing medication (especially alpha-2 agonists), and patients both on and off tic-suppressing medication showed comparable tic reduction following CBIT. In terms of predictors, the study found that greater overall tic severity at the beginning of treatment predicted greater response to treatment (regardless of treatment assignment), and the presence of a comorbid anxiety disorder and more severe pre-tic urges predicted lower tic reduction across both CBIT and supportive therapy.

Discussion of how to improve CBIT outcomes through a better understanding of treatment predictors and moderators of treatment outcome was a major theme raised at the TTT Summit. Key patient-centered questions identified in this domain included:

- How do patients who do not respond well to CBIT differ from responders on variables such as engagement and treatment readiness, patient characteristics, parent support (for children), comorbidity status, and sensory regulation, among others?
- How do we conceptualize, measure, and assess “CBIT readiness,” and does this predict outcome?
- Would individually tailoring CBIT improve outcomes, and how can this be done?
- What other patient-focused research methods can be used to better understand factors related to treatment response (e.g., focus-groups with responders, non-responders, and drop-outs)?
- What is the best way to define treatment response? Is it best to treat to response or remission?
- What parenting factors influence CBIT response in children?
- Does age matter, especially when treating children? Does CBIT work better for pre-pubescent teens? Does it work for younger children? What modifications are necessary or beneficial for different age groups or developmental levels?
- What types and dimensions of tics respond best to CBIT (motor vs. vocal, simple vs. complex, tics associated with urges versus those that are not, frequent vs. infrequent tics, recent onset vs. established tics, etc.)?
- If HRT/CBIT is not done correctly, for example if HRT is only practiced intermittently, can it make tics worse?
- Can we identify subgroups of people who might benefit from augmented treatments (e.g., medications, adjunctive therapeutic techniques such as motivational or other empirically-validated therapy strategies)?
- In the CBIT studies, why was the response rate lower for adults than for children?
- Do sociodemographic and other diversity-related factors (e.g., race, ethnicity, etc.) influence treatment response and access to CBIT?

What CBIT components are necessary and sufficient for positive outcomes, and how should they be delivered?

As noted above, CBIT is a multi-component treatment designed to teach patients a collection of tic management skills (i.e., competing response training, function-based strategies, relaxation techniques). Consistent with common practice in clinical trials, therapists in both CBIT trials delivered treatment according to a highly structured treatment manual in order to ensure that CBIT was delivered with fidelity (Woods et al., 2008). Although manualized delivery allowed therapists to flexibly tailor the intervention to the unique symptoms of individual patients, the overall treatment content remained largely the same for all participants. Such treatment standardization is desired in clinical trials because it allows the investigators to draw conclusions regarding the efficacy of the treatment when it is delivered as intended. It does not, however, afford the opportunity to draw conclusions regarding what treatment components are necessary or sufficient for positive outcomes (HRT vs. function-based techniques). While prior research suggests that HRT is the main “ingredient” for positive outcomes, (Himle et al., 2006; Woods et al., 1996), the stand-alone and additive value of other treatment components remains unknown. Further complicating the issue, it is possible that some components of the intervention might be more beneficial for some individuals than others (Woods et al., 1996) depending upon their individual symptoms or clinical presentation. A better understanding of which CBIT components are necessary, sufficient, and most beneficial for positive outcomes for a particular individual is likely to increase the positive impact of treatment, speed recovery, and make treatment more efficient.

Key patient-centered questions identified in this domain included:

- What treatment components are necessary and sufficient for positive treatment response (competing response training vs. function-based strategies)? What parts of CBIT really cause change? Are there components of CBIT that are less effective, and can these be removed or used “as needed” (e.g., behavioral rewards, social support)? Does treatment fidelity predict positive response (what parts of treatment can be applied flexibly or “as needed”)?
- What parts of treatment do patients find most useful and what parts of treatment do they use or not use?
- Would additional therapy modules or techniques improve outcomes (e.g., including strategies for addressing comorbid symptoms, sensory regulation problems, motivation, etc.)?
- Are there specific CBIT components that can be implemented by parents with minimal child engagement? Would a “parent-only” CBIT protocol be effective?
- Can CBIT be delivered in a condensed format (e.g., single or fewer sessions)? Is a shorter course of treatment sufficient for some individuals? If so, for whom?

- Are there modifications to the CBIT protocol that potentially make tics worse or that are detrimental?
- What constitutes a sufficient / insufficient dose of CBIT?

Domain 3. Understanding CBIT within a broader care model

The trials that established CBIT as a first-line treatment for tics were delivered in a tightly controlled manner, as is typical of efficacy studies. Participants were screened and selected to meet a set of inclusion criteria. All participants received the same manualized intervention, at the same dose, by similar types of providers, in similar outpatient clinical settings. While standardized treatment delivery is desirable within a clinical trial, therapists practicing outside of a research setting often face barriers that limit their ability to adhere to a standardized treatment protocol (e.g., insurance caps on number of sessions, demand of large caseloads limiting training and preparation time, etc.). It is unclear how deviations in treatment delivery (e.g., shorter or fewer sessions, session spacing) might affect outcomes in CBIT. Furthermore, in the broader psychotherapy literature, it is well established that many therapists, for a variety of reasons, do not utilize manuals in their everyday practice (Addis & Krasnow, 2000), and those who do often take considerable liberties in regard to flexibility (Waller & Turner, 2016). Unfortunately, the effectiveness of CBIT delivered in standard practice settings and the extent to which deviations from the CBIT protocol affect patient outcomes both remain largely unknown. While there is ample research demonstrating positive outcomes when evidence-based treatments are implemented flexibly while maintaining fidelity (in fact this can be advantageous, (Kendall & Frank, 2018)), there is currently a dearth of research examining how deviations in treatment delivery affect outcomes, which makes it difficult to advise therapists on how to individually tailor CBIT to meet the needs of the client when practical challenges demand flexibility in administration. In our experience conducting the TAA Behavior Therapy Institutes, such questions are among the most commonly asked by trainees and were a major theme at the TTT Summit.

Are there differences between existing CBIT “makes and models”?

Several variants of the CBIT package have been described in the literature. These variants utilize different modalities or formats to deliver CBIT while sharing the core components of functional intervention, awareness training, and competing response training (see Table 1 for brief descriptions of each variant and pros and cons for each).

Several CBIT variants are delivered in-person by a trained clinician. “Traditional CBIT” refers to the format of CBIT that is described in the published manualized protocol (Woods et al., 2008) that was tested in the CBIT efficacy studies (Piacentini et al., 2010; Wilhelm et al., 2012). Traditional CBIT is typically delivered during weekly, individual, outpatient therapy sessions with a clinician trained in psychotherapy. Group CBIT delivers the content of traditional CBIT in

a group format, and can include modifications such as parallel child and parent groups and small group activities (Yates et al., 2016). CBIT-Junior (CBIT-JR; (Bennett et al., 2019)) is a developmentally modified version of CBIT for younger children with chronic tics (e.g., 4-8 year olds). CBIT-JR places greater emphasis on family-focused functional assessment and intervention treatment components, and presents direct tic inhibition skills from habit reversal in a game-like fashion thought to be more easily acquired for children of these ages. As noted above, other CBIT variants leverage technology for treatment delivery, including CBIT delivered over teleconferencing (Himle et al., 2012; Ricketts, Goetz, et al., 2016) and internet-based, self-guided CBIT delivered by automated computer programs that teach the patient core CBIT skills (e.g., tichelper.com ((Conelea & Wellen, 2017; Jakubovski et al., 2016; PsycTech Ltd, n.d.). These programs generally include interactive exercises, informational videos, and self-report ratings to track symptoms over time.

Another key variation on CBIT is its “dosing.” The intensive approach compresses the full CBIT package into a shorter overall course of care by lengthening the time spent in treatment each day. For example, all eight CBIT sessions can be delivered over a small number of consecutive days (Blount et al., 2014). Additionally, one Taiwanese study showed adding a “light” version of CBIT (i.e., 4 sessions delivered across 3 months, with function-based intervention component omitted) to usual care led to greater reductions in tics and related impairment (Chen et al., 2019).

The comparative effectiveness of these different CBIT variants is largely unknown. Very few studies have directly compared the benefit of traditional CBIT to the variants described above, and those that have are small, ranging from single case reports (e.g., (Blount et al., 2014)) to randomized trials of about 20 patients (e.g., (Ricketts, Goetz, et al., 2016)). Outcomes of existing studies suggest roughly comparable benefit between traditional and non-traditional CBIT. For example, Himle et al. (Himle et al., 2012) found similar outcomes for CBIT delivered face-to-face and over telehealth. Both group CBIT and the efficacy trial showed moderate effect sizes ($d = 0.55$ for group, $d = 0.68$ for traditional; (Yates et al., 2016)). The CBIT-JR study demonstrated rates of symptom remission and treatment-responder status that were similar to the large CBIT trials (Bennett et al., 2019); however, this was a small ($n = 15$), uncontrolled pilot study, thus the results should be interpreted with those limitations in mind. At the time of the TTT Summit, trials of internet-based CBIT were ongoing, so outcomes are unknown. Further, studies of CBIT on different dosing schedules (e.g., intensive CBIT, CBIT “light”) have not compared these modified treatments to traditional CBIT. So, although the results of these studies are promising, there is still a need for further research to determine their effectiveness and acceptability to patients.

Discussion of these CBIT variants at the TTT Summit centered on a desire for research to test their comparative effectiveness. Participants recognized that each variant presents unique pros and cons that in themselves may guide patient preference (e.g., preferences around in-person

clinical interaction). However, attendees felt that information about the benefit of a given CBIT variant should also be available to patients, as this information may lead patients to prioritize differently.

Key questions identified in this domain were:

- What is the comparative effectiveness of different CBIT variants, such as traditional in-person individual CBIT, teleCBIT, group CBIT, and online self-guided CBIT?
- Are there added benefits for the patient when these CBIT variants are combined? For example, would it be beneficial to include some teleCBIT visits within the course of traditional in-person treatment? Would it be beneficial to combine group therapy with some individual CBIT sessions?
- What is the comparative effectiveness of differently “dosed” CBIT, such as intensive outpatient vs. traditional CBIT?
- Is there a minimal or optimal number of CBIT sessions when delivered in outpatient settings?
- How do these different CBIT variants and “doses” compare on outcomes beyond tic reduction, such as patient-centered outcomes, patient satisfaction, provider uptake, access, and cost?

How do CBIT formats actually work “in the real world?”

Research studies describing the CBIT variants above follow protocols that predetermine the number and length of sessions, and all participants receive this same treatment regimen. However, in the “real world” CBIT delivery is rarely this homogenized. Take, for example, the treatment schedule specified in the traditional CBIT manual. This protocol calls for 8 weekly sessions and specifies that the first two sessions are 90 minutes long, followed by six, 60 minute sessions. Strict adherence to this schedule is difficult in routine clinical practice. Most practitioners are beholden to the “billable hour,” which ranges from 45-60 minutes. The frequency and number of total sessions can vary depending on a multitude of factors, including patient and provider availability, financial/insurance constraints, and patient clinical needs (e.g., some patients simply need more or fewer sessions to benefit from CBIT skills training). In some clinical practice settings (e.g., integrated primary care settings, managed care organizations), access to behavioral health services may be especially streamlined, creating a need to condense treatment into a smaller number of sessions than employed in research studies. There is some evidence that the streamlined, 4-session “CBIT light” can provide some benefit beyond usual care, though the extent of these benefits relative to traditional CBIT is unclear (Chen et al., 2019).

Also, the content of “CBIT sessions” can also have high variability in real world practice, in part because “real world patients” are likely to present with characteristics that differ from participants that meet the carefully selected criteria of an efficacy trial. Clinicians in turn often adapt CBIT to meet individual needs. For example, they may incorporate additional treatment components to address comorbidities or treatment targets beyond the scope of CBIT (e.g., family functioning). During the TTT Summit, the benefits of this individual tailoring were recognized by affected individuals and clinicians alike. However, the variability this introduces also raised questions about how well CBIT performs in natural clinical settings.

The key overarching question in this domain was:

- How well does CBIT work “in the real world”? In other words, are outcomes in routine clinical practice similar to those reported in the efficacy trials?

How does CBIT compare to other treatments for tics?

CBIT is certainly not the only treatment option for people with tics, which can complicate treatment decision-making. Medication is the other major evidence-based treatment option for tics, with research supporting the benefit of medications such as α_2 adrenergic agonists and antipsychotics (Pringsheim et al., 2019). However, the relative efficacy of CBIT vs pharmacotherapy is understudied, making it difficult for patients and providers to make evidence-informed decisions about treatment sequencing (i.e., whether there is an ideal order for delivering CBIT and medications), combining (i.e., whether particular pairings of CBIT and medication yield greater benefits), and matching (i.e., identifying for whom particular sequences or combinations of CBIT and medication are most effective).

Tic treatment clinical trials to date have focused on testing the effect of CBIT and medication as standalone treatments. Existing meta-analysis research comparing outcomes of these monotherapy clinical trials suggest that CBIT and tic medications have a comparable effect size (McGuire et al., 2014). However, no studies have directly compared CBIT vs. medication. The closest approximation is a study in Italy that compared a package of behavior therapy for tics (combining CBIT and exposure therapy) to antipsychotic medication and to psychoeducation (Rizzo et al., 2018). Results showed that behavior therapy and antipsychotic medication were equally effective in reducing tic severity, and both were superior to psychoeducation. A similarly designed comparison that includes traditional CBIT and different classes of medication, particularly first-line α_2 adrenergic agonists, is needed to fully understand comparative efficacy of these treatments.

The effect of combined CBIT and medication is also poorly understood, despite this course of treatment being common in clinical practice. In the large CBIT trials (Piacentini et al., 2010;

Wilhelm et al., 2012), inclusion criteria allowed participants to be taking a tic medication provided that they still met the tic severity threshold and had no recent or planned medication changes. The presence of a tic medication was found to moderate outcomes, such that participants who were not on tic medication showed a greater magnitude of benefit and likelihood of positive response compared to supportive psychotherapy (Sukhodolsky et al., 2017). Importantly, however, participants on tic medication still showed improvement with CBIT, leading the authors to conclude that CBIT remains helpful for reducing tics regardless of coexisting tic medication treatment. Whether particular combinations or sequences of CBIT and medications are linked to optimal benefit remains unexplored.

There are also other options beyond these first-line treatments that patients and providers sometimes consider, including interventions that have limited or emerging research support (e.g., botulinum toxin injections, cannabis-based medications, transcranial magnetic stimulation) and approaches that have yet to be rigorously tested (e.g., diet alterations, massage therapy, vitamins/nutritional supplements, exercise (Woods et al., 2010). There is currently no research that has compared CBIT to these emerging or untested approaches. Given that many patients endorse trying alternative treatments alongside CBIT, there was also interest among TTT Summit attendees in understanding how these approaches may impact each other when delivered in combination. For example, we do not know if CBIT effects are strengthened, weakened, or unaffected if the patient is also using a cannabis-based medication. TTT Summit attendees discussed the importance of understanding CBIT efficacy in the context of these various other choices faced by patients.

Key patient-centered questions for this domain were:

- Of all of the available treatment options for tics, which ones do patients want most, and why?
- What is the comparative effectiveness of CBIT alone vs. medication alone vs. the combination?
- If given the choice between CBIT and medication, what would patients choose? Would the choice differ depending on factors such as timing, comorbidities, age, etc.?
- Can CBIT be used to help someone reduce or discontinue medication?
- What is the comparative effectiveness of CBIT vs. other forms of TS treatment, such as exposure and response therapy, newly emerging treatment options, or untested/alternative approaches?
- Are there any adjunctive treatments that boost CBIT's effects? Are there any adjunctive treatments that reduce CBIT's effects?

Are there optimal ways to time or sequence the delivery of CBIT?

For patients and providers alike, deciding how to optimally time and sequence interventions for an individual with a TD can be tricky. Typically, the first important question faced by newly diagnosed patients is whether to intervene at all. The American Academy of Neurology's current practice parameters recommend "watchful waiting" for individuals who do not experience any tic-related functional impairment (Pringsheim et al., 2019). This recommendation is based on research indicating that tics may naturally improve with time for some. However, there is no research to date that has addressed whether there is an optimal timing for initiating treatment, where "timing" can reflect a number of factors such as patient age, readiness or motivation to engage in treatment, stage of illness (e.g., first onset vs. further along in TD course), symptom severity, or comorbidity status. There is also no research to inform decisions about selecting a particular tic treatment based on these timing factors and other patient characteristics. For example, TTT Summit attendees expressed enthusiasm about the possibility of creating research-informed "patient profiles" that might help guide the question of "which treatment to deliver when?"

Also unknown is whether CBIT may have a role in buffering against development of tic-related impairment if delivered early, or if there are factors that contraindicate CBIT at particular times. For example, a concern raised by some clinicians at the TTT Summit was whether there is a risk to delivering CBIT when a person is too young or not motivated to participate, given concerns that trying CBIT and not benefitting would reduce the chances that a person would re-engage in CBIT at a "better time." Identifying timing-related factors that are linked to the greatest likelihood of CBIT success was seen as an important research priority by patient stakeholders alike.

The existence of multiple CBIT formats raises the issue of whether there are particular sequences of CBIT delivery that might maximally increase both treatment access and patient benefit. TTT Summit attendees recognized that some CBIT formats have lower access barriers, which led to interest in testing the delivery of CBIT in a stepped care model. "Stepped care" is a treatment model that aims to solve access problems by distributing evidence-based treatments in graded steps based on intensity, cost, and time demand (Ho et al., 2016). In this model, the "least restrictive" interventions are used as the first-line treatment, such as self-help or internet-based treatments. "Stepping up" to a more resource intensive treatment, such as in-person therapy, is based on response to the prior step, such that only those who do not respond to the lower-intensity treatment go on to receive the higher-intensity treatment. Stepped care models have been tested for a number of psychiatric disorders, including anxiety, depression, and OCD, and results generally show improved outcomes for patients and better cost effectiveness (Ho et al., 2016). There is no research to date testing the stepped care model in TDs. Testing a stepped care

model that includes graded steps of CBIT formats and medication was seen as a priority by TTT Summit attendees.

Key patient-centered questions raised about CBIT timing and sequencing were:

- What is the best timing for CBIT delivery vs. using a “watch and wait” approach? Possible factors that may impact timing could include patient age, severity level, tic-related impairment, and status of comorbid conditions.
- Is there a cost to delivering CBIT at the “wrong time” or “too early”? For example, could it be unhelpful or reduce treatment engagement overall?
- Can we find “profiles” to match people with TDs to care plans? For example, can we identify who would benefit most from watching and waiting, CBIT only, medication only, or CBIT plus medication?
- Can CBIT be delivered in a stepped care model? Can we tailor the entry point or sequence depending on individual profiles?
 - Possible steps could include: parent-based CBIT, online/self-guided CBIT, teleCBIT, in-person group, in-person individual, medication management.
- Do particular stepped care sequences reduce the overall amount of treatment that a given individual needs? For example, if someone does online/self-guided CBIT while on a clinic waitlist, does this reduce the number of in-person CBIT sessions needed?

Domain 4. Considering and measuring outcomes beyond tic reduction, specifically patient centered outcomes

A crucial component of patient centered research is measuring the outcomes that are most important to patients and other stakeholders. Most randomized controlled clinical trials utilize symptom reduction or symptom remission as the primary outcome for evaluating treatment efficacy. However, when considering long-term wellness following a short-term treatment, research and treatment efforts should assess change in variables that represent a broader look at life functioning. Measuring treatment efficacy based on other outcomes that are important in patients’ lives, such as the restoration and optimization of functioning in academic, occupational, social, and family life domains, and directly targeting these domains in treatment research is a new and important frontier for clinical research. Quality of life measures, and ratings of self-worth, such as self esteem, self-control and self-confidence, push treatment researchers to pursue and evaluate treatments that restore optimal functioning and promote overall health and wellbeing. Being responsive to patient-centered outcomes in this research agenda is key to the progress in the next phase of CBIT research.

While data are strong on the efficacy of CBIT to decrease the frequency of tics, stakeholders at the TTT Summit wanted to know if CBIT impacts patient-centered variables, such as self-efficacy, self-esteem, perceived control of tics, and specific functional improvements. Change in

the severity of comorbid symptoms and a decrease in impairment related to comorbid conditions, such as ADHD, OCD, anxiety disorders, mood disorders, disruptive behavior disorders, and/or substance use disorders remains a domain of significant interest to many patients and clinicians. Treatment of comorbid conditions was outside of the scope of the TTT Summit, but questions related to comorbid conditions and optimizing behavioral treatment to address these domains appeared in some large and small group discussions.

Measuring patient-centered outcomes is an important area of research in general, and specific questions related to the appropriate patient centered outcomes for future CBIT research are critical to identify and operationalize appropriate metrics for future clinical research..Large scale surveys of patients with TDs, and their family members, have identified several important variables, outside of tic reduction, that impact the lives of patients and families (Conelea et al., 2011; *Impact Survey - Tourette Association of America*, n.d.; Wolicki et al., 2019). For example, in the 2019 TAA survey (N=944), many responders endorsed that TDs negatively impacted educational experiences, occupational opportunities, and/or family finances. Moreover, an alarming number of patients with TS (32% of children and 51% of adults) reported having considered suicide or participated in self harm behaviors. Other recent research indicates that TDs are linked to a four-fold increased risk of both dying by suicide and attempting suicide, as compared to those without TDs (Fernández de la Cruz et al., 2017) These are extremely important, life changing variables that should be included in future TDs treatment outcome research.

Extant research has identified high rates of educational and social impairments related to TDs (Conelea et al., 2013, 2011; Pérez-Vigil et al., 2018; Storch, Lack, et al., 2007). Peer victimization or exclusion from peer groups is unfortunately common for youth with TDs (*Impact Survey - Tourette Association of America*, n.d.; Storch, Lack, et al., 2007; Storch, Murphy, et al., 2007; Zinner et al., 2012). The Tourette Syndrome Impact Survey (Conelea et al., 2013, 2011) found that higher tic severity was linked to greater difficulty in daily functioning, including difficulty in the domains of peer relationships, family relationships, participation in recreation and entertainment activities, avoidance of public spaces or public modes of transportation, interference with household tasks, tic related absences from school, and feeling different from others. It is important to better understand how these life variables are changed by participation in behavioral treatment, from the patients' perspective.

There is a dearth of TD treatment research studies that include outcomes such as self-esteem, self-concept, and/or self-perception. Those studies that do evaluate these outcomes tend to be small or older studies, or include samples non-specific to TDs (e.g., students defined as having “special needs”; (Brook & Boaz, 2006)). In recently published literature reviews, there were inconsistent findings on self-perception in patients with TDs, with some studies showing a negative impact of TDs on self-concept and self esteem (Cox et al., 2019; Silvestri et al., 2018). The presence of psychiatric comorbidities (specifically OCD, ADHD, and anxiety disorders) was

more likely than tic severity to be related to reported poor self-concept or poor self esteem (Silvestri et al., 2018). Loneliness, feeling isolated, and experiencing bullying are consistently reported by young people with TDs (Storch, Murphy, et al., 2007) and should be addressed in TD advocacy, education, and intervention research efforts.

The specific research questions raised within this topic focused around a central theme of assessing whether participation in CBIT improves more than “just tics,” and/or enhancing CBIT to ensure that it does. Patient-centered outcomes of interest identified at the TTT Summit included quality of life, self-confidence, self-esteem, self-control, hours spent in the classroom, and preparedness for independent adult life. Questions were also raised about whether augmenting CBIT with other interventions might improve outcomes for common comorbid problems, such as ADHD, OCD, anxiety disorders, and sensory dysregulation.

Specific questions raised in this domain included:

- Does CBIT change outcomes patients care about (e.g., hours in class, self-confidence, adult life abilities)?
- Can CBIT be combined with or augmented by other therapies to address non-tic symptoms?
- How well does CBIT improve other important outcomes, such as quality of life?
- What do youth, parents, adults, and families specifically want from tic-focused treatments?

Post-Summit Community Input

Following our analysis of TTT Summit activities, we published online an Executive Summary of the Summit and research priorities raised in TTT. We alerted the TDs community to this document via the TAA’s online newsletter (n = 59,000) and emails to individuals who previously signed up for updates on TTT (n = 61), and an announcement on Tourette’s Podcast. We invited individuals from the TDs community to share additional input by completing a simulated research funding activity, in which they pretended they were funders of research, and allocated 100 hypothetical “research dollars” to fund projects related to 14 different research questions raised in the Summit. We included questions that were deemed highest priority in a similar in-person research prioritization activity conducted in Day 2 of the Summit, as well as several questions that TTT attendees noted were particularly underrepresented in prior TDs research.

In total, 57 individuals completed the activity, including 40 individuals personally impacted by TDs, 14 healthcare professionals who work with people with TDs, and 3 who were both personally impacted and TD professionals. Detailed results of this activity can be found in Appendix E. In all, 13 of the 14 questions included received significant hypothetical funding (i.e., prioritization) from survey respondents. Respondents especially emphasized the importance of research on training general practice providers to recognize and make appropriate referrals for

TDs, training school-based providers in CBIT, evaluation effects of CBIT on patient-centered outcomes beyond tic severity and general “impairment”, understanding what makes CBIT work better for some individuals than others, researching best sequences of TD treatment (e.g., CBIT followed by medication vs. medication followed by CBIT), comparing traditional CBIT to other CBIT formats (e.g., teleCBIT, intensive outpatient CBIT), and studying the effectiveness of CBIT in neurodiverse individuals (e.g., those on the autism spectrum).

Conclusion

Researchers, clinicians, and individuals living with or otherwise impacted by TDs understand there are many questions for which we need robust, science-backed answers to guide the early detection and effective treatment of TDs in a manner that is accessible and affordable for all affected individuals. The aim of this research agenda is to provide a roadmap for researchers to answer the questions prioritized by key stakeholders in the TDs community. We aim to disseminate this research agenda broadly to academic, medical, and lay audiences. We hope the dissemination and continued discussion of this research agenda will motivate new research collaborations and novel research studies and strategies anchored in the principles of patient-centered research. Ultimately, we aspire to expedite the uptake of CBIT as the first line treatment strategy for most individuals with TDs, to improve our identification of those for whom this will be an effective treatment, and to improve the treatment to meet the needs of all individuals affected with TDs.

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Table 1. Pros and Cons of Existing Modalities of Comprehensive Behavioral Intervention for Tics (CBIT)

CBIT Modality	Modality description	Pros	Cons
Traditional CBIT	Outpatient clinic setting, psychotherapy provider, 8 hour-long individual sessions delivered weekly	<ul style="list-style-type: none"> -Demonstrated to be efficacious -Individual attention from clinician -Opportunity to deliver flexibly to address non-tic issues (e.g., comorbidities) -Largely fits within established therapy service structure 	<ul style="list-style-type: none"> -Focus on tic management -Resource intensive -Provider must seek out training -Limited access to providers, with more access challenge in rural areas -Long waitlists -Subject to limitations of established therapy structure
TeleCBIT	Traditional CBIT delivered via secure telehealth platform	<ul style="list-style-type: none"> -Outcomes about equal to traditional CBIT -Convenient: no, or low, travel time -Individual attention from clinician 	<ul style="list-style-type: none"> -Focus on tic management -Resource intensive -Often not (yet) reimbursable by insurance -Possible additional constraints for in-home version -Technology itself can be a barrier -Licensure across state lines
TicHelper	Interactive, self-guided CBIT delivered online	<ul style="list-style-type: none"> -Based on established CBIT principles -Available anywhere -No need for trained provider -Self-paced -Can be updated on an ongoing basis -Could be less expensive than face-to-face services 	<ul style="list-style-type: none"> -Requires self-motivation and accountability -Limited individual tailoring and flexibility -No individualized support from a provider -May be less relevant for cases that do not “fit the mold” -Not covered by insurance
CBIT-OT	CBIT adapted for use by occupational therapists, maintains components and structure of traditional CBIT	<ul style="list-style-type: none"> -Research shows OT can deliver CBIT successfully -CBIT techniques match well with OT training -Individual attention from clinician 	<ul style="list-style-type: none"> -Similar to cons of traditional CBIT plus: -Less integration of psychiatric comorbidities in treatment -Insurance reimbursement has been a challenge for some

		<ul style="list-style-type: none"> - Opportunity to deliver flexibly to address developmental comorbidities -OTs possibly easier to access and more cost effective than other provider types -Option for those reluctant to engage with mental health system 	<ul style="list-style-type: none"> - Lack of large-scale evidence on efficacy (i.e., unclear if response rates similar to traditional CBIT)
CBIT for medical clinics	CBIT adapted for use by nurse practitioners (NP) in medical clinics (tested thus far in neurology and developmental pediatrics)	<ul style="list-style-type: none"> -Research suggests NPs can adhere to CBIT model -Makes CBIT available at time of first diagnosis -Patient receives CBIT within established care clinic -Option for those reluctant to engage with mental health system 	<ul style="list-style-type: none"> -Research suggests potentially higher patient drop out -Still requires provider training and availability - Lack of large-scale evidence on efficacy (i.e., unclear if response rates similar to traditional CBIT)
Co-Location Model	Psychologist embedded in a medical clinic provides brief CBIT (e.g., 1-3 sessions) and develops follow-up care plan	<ul style="list-style-type: none"> -Tic and CBIT education available at time of first diagnosis -Patient receives CBIT within established care clinic -Conserve resources: provide brief CBIT for those who can benefit and triage those who need traditional model 	<ul style="list-style-type: none"> -No research on efficacy to date -Brief visits may not be enough for patient to benefit from CBIT -Comorbidities might be missed with limited interactions

Appendix A: Treating Tourette Together (TTT) Diversity and Inclusion Principles

TTT is committed to creating space for diverse voices to inform the future of behavioral research on tics. We recognize that the past two decades have brought great advances in research on behavioral treatment of TDs, brought about in large part through valuable partnerships between the Tourette Association of America, constituent members, scientists, and clinicians. We also recognize that this research has been conducted through a clinical science model that tends to under-address the needs of marginalized groups. Thus, in TTT, we aspire to the following principles regarding attendee selection and participation. The following list is not:

- prescriptive regarding whom we will invite to attend,
- exhaustive of all facets of diversity that we seek to establish in our group,
- Intended to address the many nuances related to intersecting experiences and identities
- a rank-order of priorities
- The basis of a quota system for inviting attendees

Rather, this list summarizes some key points of inclusion that we commit to keeping at the forefront of our consideration as we select our key group of attendees to give voice to the TD community broadly. Given the limited size of the Summit, and the complex and intersectional nature of identity and experience, we acknowledge that we will not fully actualize all of these principles to an optimal level; that is, these are aspirational principles that represent core our group's core values.

1. Among our professional stakeholders, we value diversity of professional experience, with regard to scope of practice, practice setting, patient population, and personal approach to clinical care. We acknowledge that TD research has often been driven by scientist-practitioners who practice predominantly in academic medical settings that may differ in crucial ways from typical community-serving healthcare settings. Thus, we resolve to seek out the voices of professionals who work with people with TDs outside of highly specialized academic medical centers in healthcare settings where most individuals with TDs are seen, and those who work with people with TDs in important non-healthcare venues (e.g., schools).
2. We value diversity of attendees' experience with behavioral and non-behavioral treatments for TDs. We seek to hear not only from individuals who have received CBIT, but also those who have not participated in CBIT, and also those who have not previously heard of CBIT. We acknowledge that hearing the voices of individuals who have **not** completed CBIT will be critical to informing ongoing research, and so we commit to

elevating these voices in our TTT discussions. With regard to healthcare providers, we value the perspectives of providers who do not have extensive expertise in providing or recommending CBIT, despite awareness of its existence.

3. Similar to #2, we value diversity in stakeholders' history of advocacy and "TD literacy". We acknowledge that a relatively small group of people have done a breathtaking amount of advocacy work to fight for increased awareness, education, and research on TDs. We stand in appreciation of these individuals and their commitment to furthering the lives of individuals with TDs. We also acknowledge that there is a much larger community of individuals with TDs who have **not** been previously involved in advocacy, and that these individuals likely have perspectives we have not yet heard. Thus, we resolve especially to give voice to newcomers to formal TD advocacy, while drawing on the contributions of more seasoned advocates.
4. We value cultural, ethnic, and racial diversity. We recognize that clinical research on TDs has historically been conducted with predominantly White individuals, with inadequate representation of ethnoracial minorities. We also recognize that health and healthcare access disparities exist in the U.S. along ethnoracial lines. Thus, we find importance in inviting the participation of individuals in historically underrepresented ethnic and racial minority groups, as well as healthcare providers who serve diverse communities.
5. We value geographic diversity. This means that we aim both to reach folks in different geographic regions and at different levels of rurality versus urbanity. We recognize that the access to and experience of treatment for those in rural areas is often inadequate and needs explicit representation.
6. We value socioeconomic diversity. We acknowledge that socioeconomic status is strongly associated with healthcare access and barriers to treatment access in the U.S.. We also acknowledge that research on behavioral treatments for TDs has largely been conducted with relatively affluent families (compared to the general U.S. population), and that CBIT is currently more accessible to individuals with higher socioeconomic status. Thus, we recognize the importance of elevating the voices of those with lower socioeconomic status in discussing future directions to expand behavioral treatment research.

Appendix B: Attendee list

Elia Abi-Jaoude
Anonymous adolescent with TS
Anonymous adolescent with TS
Anonymous Adult with TS
Anonymous parent of a child with TS
Anonymous parent of an adolescent with TS
Shannon Bennett
Tabatha Blount
Ben Brown
Lawrence Brown
Matthew Capriotti
Christine Conelea
Flint Espil
Sara Hamilton
Kelsie Hendrickson
Michael Himle
Carolyn Hunt
Emily Ivey
Cooper K.
Sue Kremer
Adam Lewin
Maggie M.
Denise Malcom
Joseph McGuire
Patty Mendoza
Mindy Meyer
Justin Mohatt
Suzanne Mouton Odum
Leo Neuringer
Alan Peterson
Kenny Phelps
John Piacentini
Juan Ramirez-Castaneda
Emily Ricketts
Heather Simpson
Jennifer Schild
Howard Schub
Diana Shineman

Jordan Stiede
Amanda Talty
Claire Teclaw
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Appendix C: TTT Summit Agenda

Treating Tourette Together (TTT) Friday August 16 - Sunday August 18, 2019 University of Minnesota, Minneapolis, MN AGENDA (subject to change)

TTT Summit Mission:

Treating Tourette Together (TTT) is a collaboration between the TAA, the Patient-Centered Outcomes Research Institute (PCORI) and leading behavioral sciences researchers. Our goal is to incorporate patient, provider, and researcher feedback into the next generation of behavioral therapy for Tourette Syndrome. This work is partially funded through a Patient-Centered Outcomes Research Institute® (PCORI®) Eugene Washington PCORI Engagement Award (EAIN-00027). Our ultimate goal is to increase access to care and decrease disability among people with Tourette and Tic Disorders.

Friday August 16: Courtyard Minneapolis Downtown (1500 Washington St.)

6:00pm to 8:00pm: Welcome Reception and Registration

Saturday August 17: University of Minnesota Masonic Children's Hospital (Wilf Family Center, South Building, 2450 Riverside Ave)

Focus on community-building, understanding and identifying strengths/weakness of CBIT modalities, and prioritizing stakeholder preferences

8:00am	Continental Breakfast and Registration
8:30am	Welcoming Remarks from the TAA: <i>Amanda Talty, President and CEO, TAA</i>
8:45am	Welcome and Overview of TTT Summit Objectives:
<i>Matt Capriotti, Sara Hamilton, Diana Shineman</i>
9:00am	Introductions and Icebreaker: <i>Carolyn Hunt</i>
9:30am	Review of "Homework" and Summit Goals: <i>Matt Capriotti</i>
9:50am	Blue Sky Thinking Small Group Break-Out #1: <i>Sara Hamilton</i>
10:15am	BREAK
10:30am	Fishbowl Session 1: Listen to patients and caregivers: <i>Ben Brown</i>
11:15am	Fishbowl Session 2: Listen to researchers and providers: <i>Sara Hamilton</i>

12:00pm	LUNCH
12:45pm	Panel Presentation and Q&A: CBIT and its Existing Adaptations <i>Christine Conelea, Michael Himle, Matt Capriotti, Shannon Bennett</i>
2:15pm	BREAK
2:30pm	Small Groups Break-Out #2: Creating SCORE Charts: <i>Sara Hamilton</i>
3:45pm	BREAK
4:00pm	Report back to large group
4:30pm	Reflection <i>Matt Capriotti, Carolyn Hunt</i>
4:45pm <i>Hamilton</i>	Closing Remarks and Review of Tomorrow's Agenda and Objectives: <i>Sara</i>
5:00pm	Close for the day
5:30pm SE)	RECEPTION AND DINNER: Graduate Minneapolis (615 Washington Avenue

Day 2: Sunday August 18: University of Minnesota Masonic Children's Hospital (Wilf Family Center, South Building, 2450 Riverside Ave)

Focus on generating content for the Research Agenda

8:00am	Continental Breakfast
8:30am	Day 1 Recap: <i>Matt Capriotti and Sara Hamilton</i>
8:45am	Icebreaker: <i>Carolyn Hunt</i>
9:00am	Overview of Research Agenda Goal: <i>Michael Himle</i>
9:30am	Small Group Breakout #3: Generating CBIT Questions: <i>Carolyn Hunt</i>
10:45am	BREAK
11:00am	Large Group Report Back: <i>Carolyn Hunt</i>
11:30am	LUNCH
12:30pm	Large Group Research Prioritization Exercise: <i>Sara Hamilton</i>
1:00pm	Small Group Break-Out #4: Design Research Agenda

2:30pm	Report back to large group: <i>Carolyn Hunt</i>
3:00pm	Evaluation and Closing remarks
3:30pm	CLOSE

Appendix D: Complete list of research questions generated by stakeholder attendees at the TTT Summit (edited only to optimize formatting and eliminate redundancies)

Domain 1: Increasing Access to CBIT

CBIT training

1. How do we best train more providers to improve access to CBIT? What are the comparative outcomes of online training versus in person training, including cost of training and post-training competency in CBIT?
2. What level of professional expertise is required to effectively deliver CBIT?
3. What is the best way to train “gateway” doctors to recognize TS? Is it feasible to use local mental health care providers as consultants?
4. Does a collaborative care model between pediatricians and mental health therapists in child psychiatry improve the identification of TS in pediatrics?
5. Does a CBIT training module in pediatrics residency programs improve knowledge, mastery, application or referrals for CBIT?
6. What are the optimal training requirements to train someone in CBIT to fidelity?
7. Do the existing CBIT training model (e.g., the Behavior Therapy Training Institute; BTII) demonstrate different post-training levels of CBIT competency for different provider groups, assessing fidelity to CBIT, number of patients treated with CBIT post-training, patient outcomes, and provider satisfaction.
8. What information will motivate providers to seek out and complete training in CBIT, including BTII testimonials, patient testimonials, information on the prevalence of TS, and/or a financial pitch including number of new referrals and revenue generated post CBIT training?
9. Is it better to train 1000 people to achieve 50% tic reduction or to train 50 people to achieve 100% tic reduction?
10. Does training in CBIT make money or save money for providers and/or institutions?

CBIT in Other Care Settings

11. Is it feasible, acceptable, cost-efficient and effective to deliver CBIT in schools via a brief, condensed, or group format?
12. Are there optimal ways to tailor CBIT depending on provider type? For example, is there an optimal way to abbreviate CBIT so that it can be delivered by a primary care doctor/pediatrician?
13. Is it feasible, acceptable cost-efficient and effective to provide CBIT in primary care contexts?
14. Is the provision of CBIT in primary care settings as effective as the current gold standard CBIT?

15. If CBIT is modified for different providers and settings, how will the outcomes compare? For example, would brief instruction in CBIT by a pediatrician work as well as a longer single session with a nurse practitioner or co-located psychologist?
16. What is the utility and acceptability of a CBIT self-help toolkit?
17. Does the development and dissemination of a parent TS screening tool in primary care improve early detection of tic disorders?

Domain 2: Increasing CBIT's Effectiveness

What patient factors predict positive outcomes in CBIT (for whom does CBIT work)?

1. How do patients who do not respond well to CBIT differ from responders on variables such as engagement and treatment readiness, patient characteristics, patient resiliency or grit, parent support (for children), comorbidity status, and sensory regulation, among others?
2. How do we conceptualize, measure, and assess "CBIT readiness," and does this predict outcome?
3. Would individually tailoring CBIT improve outcomes, and how can this be done?
4. What other patient-focused research methods can be used to better understand factors related to treatment response (e.g., focus-groups with responders, non-responders, and drop-outs)?
5. What is the best way to define treatment response? Is it best to treat to response or remission?
6. What parenting factors influence CBIT response in children?
7. Does age matter, especially when treating children? Does CBIT work better for pre-pubescent teens? Does it work for younger children? What modifications are necessary or beneficial for different age groups or developmental levels?
8. What types and dimensions of tics respond best to CBIT (motor vs. vocal, simple vs. complex, tics associated with urges versus those that are not, frequent vs. infrequent tics, recent onset vs. established tics, etc.)?
9. Can we identify subgroups of people who might benefit from augmented treatments (e.g., medications, adjunctive therapeutic techniques, motivational strategies, addressing comorbid symptoms)?
10. In the CBIT studies, why was the response rate lower for adults than for children?

Sociodemographic moderators of treatment

11. Does CBIT work for racial and ethnic minority individuals?
12. Do the common CBIT delivery models (in person, teleCBIT or online CBIT) work differently for individuals in urban vs. rural geographic locations or for individuals of higher or lower socioeconomic strata?

What CBIT components are necessary and sufficient for positive outcomes, and how should they be delivered?

13. What treatment components are necessary and sufficient for positive treatment response (competing response training/HRT vs. function-based strategies)?
14. What parts of CBIT really cause change?
15. Are there components of CBIT that are less effective, and can these be removed or used “as needed” (e.g., behavioral rewards, social support)?
16. Does treatment fidelity predict positive response (what parts of treatment can be applied flexibly or “as needed”)?
17. What parts of treatment do patients find most useful and what parts of treatment do they use or not use? What do CBIT recipients wish had been different about the treatment?
18. Would additional therapy modules or techniques improve outcomes (e.g., including strategies for addressing comorbid symptoms, sensory regulation, motivation, etc.)?
19. Are there specific CBIT components that can be implemented by parents with minimal child engagement? Would a “parent-only” CBIT protocol be effective?
20. Can CBIT be delivered in a condensed format (e.g., single or fewer sessions)? Is a shorter course of treatment sufficient for some individuals? If so, for whom?
21. Are there modifications to the CBIT protocol that potentially make tics worse or that are detrimental?
22. What constitutes a sufficient / insufficient dose of CBIT?
23. Does intermittent HRT practice make tics worse via intermittent negative reinforcement?
24. Does degree of social support change CBIT outcome?

Domain 3: Optimizing How CBIT Fits into Individuals’ Broader Care for TDs

Are there differences between existing CBIT “makes and models”?

1. What is the comparative effectiveness of different CBIT variants, such as traditional in-person individual CBIT, teleCBIT, group CBIT, and online self-guided CBIT?
2. Are there added benefits for the patient when these CBIT variants are combined? For example, would it be beneficial to include some teleCBIT visits within the course of traditional in-person treatment? Would it be beneficial to combine group therapy with some individual CBIT sessions?
3. What is the comparative effectiveness of differently “dosed” CBIT, such as intensive outpatient vs. traditional CBIT?
4. Is there a minimal or optimal number of CBIT sessions when delivered in outpatient settings?

5. How do these different CBIT variants and “doses” compare on outcomes beyond tic reduction, such as patient-centered outcomes, patient satisfaction, provider uptake, access, and cost?

How do CBIT formats actually work “in the real world?”

6. How well does CBIT work “in the real world”? In other words, are outcomes in routine clinical practice similar to those reported in the efficacy trials?

How does CBIT compare to other treatments for tics?

7. Of all of the available treatment options for tics, which ones do patients want most, and why?
8. What is the comparative effectiveness of CBIT alone vs. medication alone vs. the combination?
9. If given the choice between CBIT and medication, what would patients choose? Would the choice differ depending on factors such as timing, comorbidities, age, etc.?
10. Can CBIT be used to help someone reduce or discontinue medication?
11. What is the comparative effectiveness of CBIT vs. other forms of TS treatment, such as exposure and response therapy, newly emerging treatment options, or untested/alternative approaches?
12. Are there any adjunctive treatments that boost CBIT’s effects? Are there any adjunctive treatments that reduce CBIT’s effects?

Are there optimal ways to time or sequence the delivery of CBIT?

13. What is the best timing for CBIT delivery vs. using a “watch and wait” approach?
Possible factors that may impact timing could include patient age, severity level, tic-related impairment, and status of comorbid conditions.
14. Is there a cost to delivering CBIT at the “wrong time” or “too early”? For example, could it be unhelpful or reduce treatment engagement overall?
15. Can we find “profiles” to match people with TDs to care plans? For example, can we identify who would benefit most from watching and waiting, CBIT only, medication only, or CBIT plus medication?
16. Can CBIT be delivered in a stepped care model? Can we tailor the entry point or sequence depending on individual profiles?
 - a. Possible steps could include: parent-based CBIT, online/self-guided CBIT, teleCBIT, in-person group, in-person individual, medication management.

17. Do particular stepped care sequences reduce the overall amount of treatment that a given individual needs? For example, if someone does online/self-guided CBIT while on a clinic waitlist, does this reduce the number of in-person CBIT sessions needed?

Domain 4: Investigating CBIT's Impact on Outcomes that Matter to People Living with TDs

1. Does CBIT change outcomes patients care about (e.g., hours in class, self-confidence, adult life abilities)?
2. Does CBIT change outcomes for youth in the classroom?
3. Can CBIT be combined with or augmented by other therapies to address non-tic symptoms?
4. How well does CBIT improve other important outcomes, such as self-esteem and/or quality of life?
5. What do youth, parents, adults, and families specifically want from tic-focused treatments?

Appendix E. Post Summit Community Input

Table 1. Questions from community input exercise by rank of mean “funding dollars” allocated. Color denotes statistically significant differences within each respondent category (green=highest, yellow=medium, orange= lowest). All= all respondents, Impacted= individuals with TS and their family members

Full Question	Question Abbreviation	All Rank (n=58)	Impact ed Rank (n=44)	Professiona l Rank (n=14)
Many people with TS have to see more than one doctor, or wait a long time, to get diagnosed and connected to quality care. What is the best way to train general doctors (such as pediatricians and family doctors) to recognize TS and provide appropriate education, resources and referrals?	TrainGateway	1	1	2
Children spend a lot of time in school. Can we train school-based providers (e.g., guidance counselors, school OTs) to provide CBIT effectively in school settings?	SchoolCBIT	2	2	4
TS impacts many aspects of a person’s life. Can we evaluate the effect of CBIT on things that patients care about other than tic severity and general “tic-related problems”? These could include self-esteem, confidence, perceived control over tics, time spent in class, ability to drive, etc.	Other Outcomes	3	6	3
CBIT in its current form does not work for everyone. Can we improve CBIT outcomes by figuring out what makes it work more, or less, well for some people? This would include looking at numerical information from studies, and also talking with people who have received CBIT about ways to improve it.	ImproveCBIT Outcomes	4	4	5
People with TS are likely to use multiple kinds of scientifically-backed treatments, such as medications and CBIT. What are the best sequences of treatment for TS (for example, CBIT followed by medication, or vice versa)? And, can we identify who will benefit from one treatment sequence instead of another?	TxSequencing	5	5	6
Currently, there are not enough CBIT providers for all of the people with TS who want CBIT. What are the most effective ways to train more providers in CBIT?	TrainCBIT Providers	6	3	8
Many patients live too far from CBIT providers for weekly visits. Can we evaluate whether other CBIT formats work just as well, such as doing CBIT over videochat or doing a short, intensive “CBIT Bootcamp” (called “intensive outpatient treatment” by healthcare providers)?	CBITFormats	7	9	1
CBIT has not been studied much for people with TS plus neurodevelopmental differences and disabilities (e.g., autism, sensory processing disorders, intellectual disability). How effective is CBIT for these [neurodiverse] individuals?	Neurodiverse	8	7	11
Many patients who want CBIT have to wait a long time on waitlists to get it. Can we help people with TS find relief more quickly by having patients start with an online, self-help version of CBIT, and then move on to CBIT with a therapist if self-help is not effective for them?	SelfHelpFirst	9	8	10
Most participants in CBIT studies have been White and of high socioeconomic status. How effective is CBIT for patients from minority racial and ethnic backgrounds (for example, African Americans and Latinos) and low-income people?	MinorAndLow Income	10	10	7
Many people with TS take tic-reducing medications but wish they did not have to. Can CBIT be used as a tool to get off of these [tic-reducing] medications?	CBITtoStopMeds	11	11	12
How well does CBIT work compared to medication alone, and the combination of CBIT and medication used simultaneously?	CBITMedCombo	12	12	9

CBIT involves a number of different parts. Can we make CBIT more efficient by identifying its most “active ingredients”?	IDActiveIngred	13	13	13
Many people with TS do not feel that CBIT is a good fit for them. Can we create a “CBIT Readiness Interview” to explain what CBIT is, discuss concerns, assess for whom it will have the best chance to work, and possibly increase patients’ desire to do CBIT?	ReadyInterview	14	14	14

Table 2. Detailed descriptive statistics for community input activity. SE= standard error; CI=confidence interval; LL=lower limit; UL= upper limit.

		All (n=58)				Impacted (n=44)				Professional (n=17)			
Question Abbreviation	All Rank	Mean	SE	95% CI LL	95% CI UL	Mean	SE	95% CI LL	95% CI UL	Mean	SE	95% CI LL	95% CI UL
TrainGateway	1	13.9	2.3	9.3	18.5	14.8	2.8	9.1	20.5	12.0	2.4	7.3	16.7
SchoolCBIT	2	11.6	2.1	7.4	15.9	12.6	2.6	7.4	17.8	11.3	3.4	4.5	18.0
Other Outcomes	3	8.5	1.4	5.6	11.3	8.2	1.8	4.7	11.7	10.5	3.0	4.6	16.4
ImproveCBIT Outcomes	4	8.2	1.6	4.9	11.4	8.2	2.0	4.3	12.1	8.6	3.1	2.4	14.7
TxSequencing	5	8.0	1.5	5.1	11.0	8.2	1.8	4.6	11.8	8.2	2.9	2.4	14.0
TrainCBIT Providers	6	7.7	1.5	4.8	10.6	7.8	1.6	4.5	11.1	7.5	2.4	2.6	12.4
CBITFormats	7	7.6	1.1	5.4	9.8	7.1	1.8	3.5	10.8	7.1	2.1	3.0	11.3
Neurodiverse	8	6.7	1.5	3.8	9.6	7.1	1.2	4.7	9.6	6.3	2.5	1.3	11.2
SelfHelpFirst	9	6.7	1.0	4.6	8.8	6.2	1.2	3.8	8.5	5.9	2.5	1.0	10.8
MinorAndLow Income	10	6.1	1.2	3.7	8.5	5.8	1.5	2.9	8.7	5.4	2.0	1.4	9.3
CBITtoStopMeds	11	5.4	1.3	2.8	7.9	5.7	1.6	2.6	8.8	5.3	2.2	0.8	9.8
CBITMedCombo	12	4.3	0.9	2.5	6.2	3.8	1.0	1.9	5.7	4.4	2.0	0.5	8.3
IDActiveIngred	13	3.2	0.8	1.7	4.8	3.0	0.9	1.2	4.8	3.9	1.4	1.1	6.7
ReadyInterview	14	2.0	0.6	0.8	3.2	1.5	0.6	0.3	2.7	3.6	1.6	0.4	6.8