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Online Behaviour Therapy Based on Exposure with Response Prevention for adults with Tourette Syndrome or Chronic Tic Disorder: A Feasibility Trial

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ABSTRACT

Objective To evaluate the feasibility, acceptability, safety, preliminary efficacy, and preliminary maintenance of TICNET, an online therapist-guided exposure and response prevention (ERP) for adults with Tourette syndrome or chronic tic disorder (TS/CTD).

Design: Single-group, unmasked feasibility trial.

Setting: A psychiatric outpatient clinic specialized in obsessive-compulsive and related disorders in Stockholm, Sweden.

Participants: Adult participants with TS/CTD were recruited nationwide by means of self- and clinical referrals.

Interventions: The 10-week online, ERP-based, therapist-supported programme TICNET consisted of eight chapters provided on a secure platform.

Primary and secondary outcome measures: The RE-AIM framework (Reach, Efficacy, Adoption, Implementation, and Maintenance) was used to assess feasibility and acceptability. Safety was measured with an adverse events questionnaire. Preliminary intervention effects on tic severity were measured with the Yale Global Tic Severity Scale – Total Tic Severity subscale. Outcome measures were collected at pre- and post-treatment, as well as at the 3-, 6- and 12-month follow-up.

Results: Out of 73 screened participants, 31 met inclusion criteria, with the most common reason for exclusion being not fulfilling the diagnostic criteria for TS/CTD. The participants completed an average of 6.5 out of 8 treatment chapters and 90% were classified as treatment completers. The therapists spent an average of 18.1 minutes/week supporting each participant. No serious adverse events were reported. The decrease in tic severity from pre- to post-treatment was statistically significant (Cohen's *d* = 0.49, 95% CI -0.46 to 1.44), and continued to decrease further during the follow-up (12-month follow-up Cohen's *d* = 1.09, 95% CI 0.14-2.04).

Conclusions: TICNET is a feasible, acceptable, safe, and potentially efficacious and durable treatment for adults with TS/CTD. The treatment warrants further testing in a well-powered, randomised controlled trial with an active comparator.

Trial registration: ClinicalTrials.gov (NCT04908969).

Keywords: Tourette syndrome, chronic tic disorder, behaviour therapy, exposure and response prevention, feasibility, adults

STRENGTHS AND LIMITATIONS

- Assesses a broad range of dimensions to inform a future full-scale trial.
- Uses the Yale Global Tic Severity Scale - a gold-standard, clinician-rated instrument to assess preliminary efficacy and maintenance.
- Three long-term follow-ups.
- The outcome assessors were often the treating clinicians, introducing potential bias to the measurements.
- Data on ADHD-comorbidity was not collected.

BACKGROUND

Tourette syndrome (TS) is characterized by motor and vocal tics present for at least one year, whereas in chronic motor or vocal tic disorder (CTD), either motor or vocal tics, but not both, are present (1). Although TS/CTD are childhood-onset disorders, a substantial proportion continue to experience impairing tics into adulthood, affecting around 0.05% of adults (2), typically individuals with most severe symptoms (3,4), with more psychiatric comorbidity in childhood (5), as well with first degree relatives with psychiatric disorders (5). These disorders are associated with reduced quality of life (6), lower educational attainment (7), and an increased risk of somatic and psychiatric morbidity and mortality (8–11).

The most common treatment for TS/CTD is pharmacotherapy, specifically antipsychotics, which show modest efficacy and often have side effects, including long-term metabolic problems (12). Non-pharmacological treatments for TS/CTD are therefore attractive alternatives. Behaviour therapy (BT) for tics is based on the idea that, while tics have a biological origin, their expression is influenced by contextual variables. Hence, BT teaches individuals skills to better manage their tics (13). Although BT for TS/CTD has shown to be effective in randomized controlled trials (RCTs) (14–18) and is recommended in treatment guidelines (19,20), it is not widely available (21,22). Internet-based interventions are known to be able to bridge the accessibility gap (23). An RCT on self-guided Internet-delivered BT (I-BT) – specifically habit reversal training (HRT) – for adults showed a superior effect compared to placebo three months after the end of the treatment (24). Two recent large-scale RCTs on therapist-guided Internet-delivered exposure and response prevention (ERP) – another variation of BT – in children and adolescents showed a decrease in tic severity (25,26), and one of them showed superiority of I-BT to therapist-guided psychoeducation (26), making ERP the most thoroughly evaluated treatment method delivered to children and adolescents via the Internet.

Despite being the preferred treatment option for TS/CTD (27), BT is generally not accessible (21) and there are no studies investigating the effects of ERP for TS/CTD in adults. The aim of the current project was to conduct a feasibility trial on therapist-guided ERP-based I-BT in adults with TS/CTD to evaluate its feasibility, acceptability, safety, preliminary efficacy, and long-term maintenance of gains.

METHODS

Design

The study was a single-group, unmasked feasibility trial of TICNET, a therapist-supported Internet-delivered ERP-based BT for adults with TS/CTD. The trial was carried out at a psychiatric outpatient clinic specialised in obsessive-compulsive and related disorders (*OCD-programmet*) at the Karolinska University Hospital in Stockholm, Sweden. The study was approved by the Swedish Ethical Review Authority (nr 2020-00479) and pre-registered at ClinicalTrials.gov (NCT04908969). The study participants and the wider public were not involved in the design of the trial. A flowchart of participant recruitment, enrolment, and follow-up is presented in Figure 1.

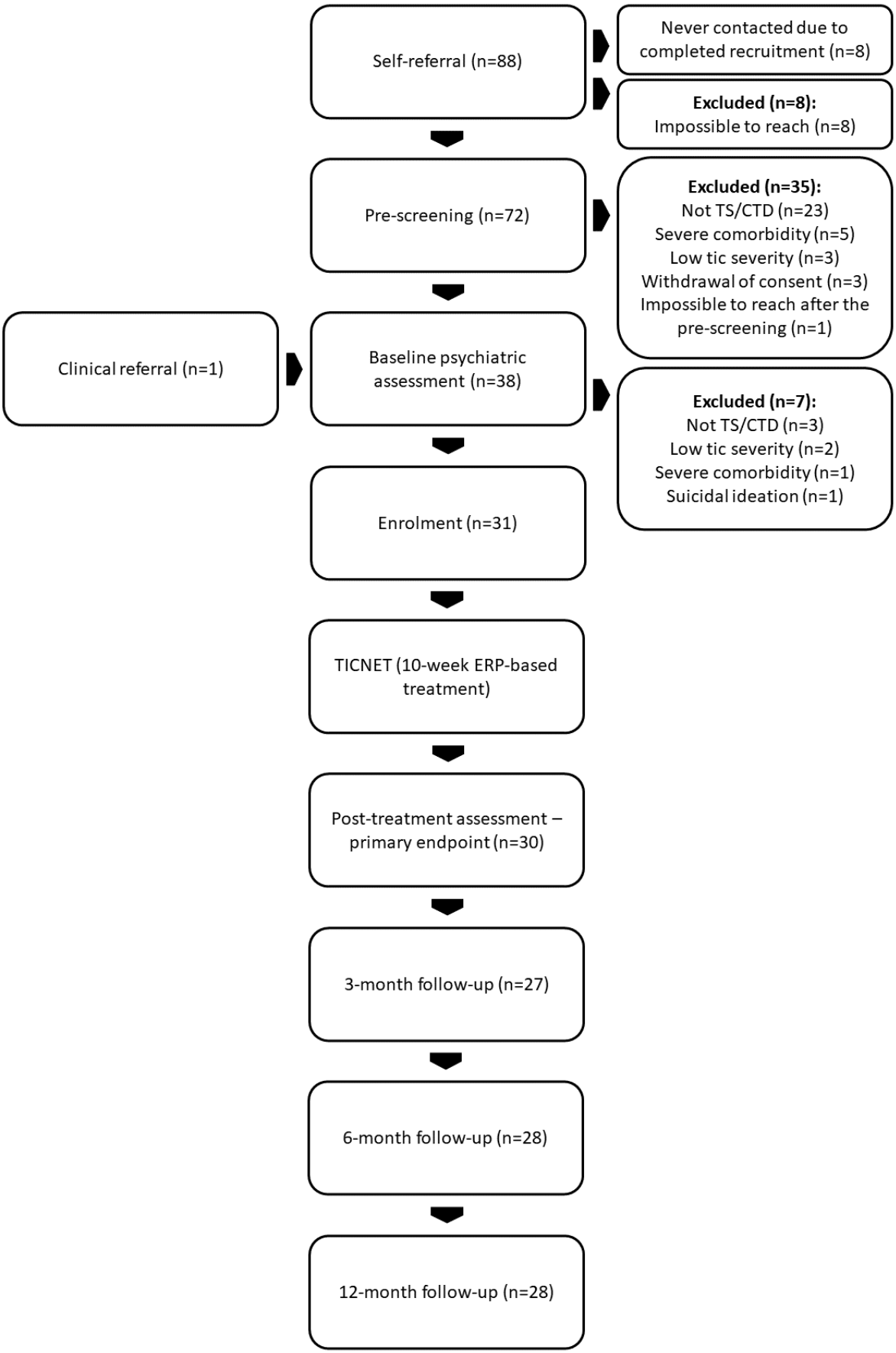

Figure 1. *Flowchart of participant recruitment, enrolment, and follow-up.*

Participants and screening procedures

Participants were recruited nationwide through self- and clinical referrals. During recruitment, information about the study was spread to interest organisations, health centres, and psychiatric outpatient clinics, as well as through advertisement in social media and a local Stockholm newspaper. For inclusion, participants had to: a) be 18 years of age or older; b) fulfil diagnostic criteria for TS/CTD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); c) have a Total Tic Severity score (TTS) of >15, or >10 for individuals with motor or vocal tics only, in the past week, as measured by the Yale Global Tic Severity Scale (YGTSS); d) be able to read and communicate in Swedish; and e) have regular access to a computer connected to the Internet, sufficient technical skills to use the treatment platform, and a mobile phone to receive text messages. Exclusion criteria were: a) severe psychiatric comorbidities such as organic brain disorder, intellectual disability, psychosis, bipolar disorder, autism spectrum disorder, anorexia nervosa or substance use disorders; b) acute psychiatric problems such as severe depression or suicidal risk needing immediate psychiatric care; c) severe tics causing immediate risk to the participants or others and requiring urgent medical attention; d) previous BT or cognitive behaviour therapy for TS/CTD for a minimum of 8 sessions with a qualified therapist within 12 months prior to assessment; e) simultaneous psychological treatment for TS/CTD; or f) initiation or adjustment of medication for TS/CTD within two months prior to assessment. All participants provided written or digital informed consent.

At the recruitment stage, the self-referred participants were guided from the study website to the secure, encrypted study platform BASS4, run by the Karolinska eHealth Core Facility at Karolinska Institutet, where they were encouraged to read detailed information about the project and to apply for the study by creating a personal account and signing the informed consent. After registration, the prospective participants were contacted via telephone by study personnel and, if the participant was deemed preliminary eligible, they received access to an online questionnaire on the platform to collect demographic data and assess common psychiatric symptoms. If there was no indication of exclusion criteria at this stage, the participant was booked for a full psychiatric assessment at the clinic via videoconferencing software, including assessment of inclusion and exclusion criteria, as well as comorbidities. Clinically referred participants were asked about their willingness to participate in the study at their first psychiatric appointment at the clinic where the full psychiatric assessment was performed.

Intervention

Upon enrolment in the study, each participant was assigned to a therapist (a licensed psychologist or a psychologist in training under supervision) who activated the treatment in the study platform within a week from the pre-treatment assessment.

The 10-week programme TICNET was provided via the platform BASS4 designed for Internet-administered treatments. The treatment consisted of eight chapters that contained psychoeducational text material, exercises, homework assignments, and worksheets for registering high-risk situations, premonitory urges (i.e., sensations typically preceding the expression of tics), and ERP practice. The treatment had a self-help format with participants

working on the chapters online, with support from a therapist through messages in the platform. The treatment further included one scheduled phone call around the time the participant had received the rationale for the ERP and was about to start their practice, to maximize the chance for the first practice to align with the rationale. The therapists were also allowed to make additional phone calls when written problem-solving was deemed insufficient. The therapists answered questions and gave feedback on homework assignments and worksheets within 24 hours. The participants were encouraged to work with one chapter a week and the subsequent chapter was opened by the therapist as soon as the previous one was completed. During the trial, bi-weekly supervision sessions were held for the therapists with an experienced clinical psychologist specialising in TS/CTD.

The central component of the treatment was ERP. During the treatment, participants received information about tics and how to work with ERP (see Table 1 for an overview of the treatment). Throughout the treatment, participants worked with exposing themselves to situations that triggered their premonitory urges and practiced suppressing their tics for increasingly longer periods of time. They learned different strategies to provoke their premonitory urges to make suppression of their tics more challenging and gradually increase the time they can suppress tics. A central tool in the treatment was the "Ticstimer", a worksheet where participants continuously recorded their ERP practice and the length of time they managed to suppress tics. Additionally, the treatment included an introduction to strategies such as HRT and applied relaxation, to give the participants a broad range of tools and make the treatment more flexible and therefore suitable for regular psychiatric settings. Treatment completion was defined as completing at least chapters 1-4.

Table 1. *Overview of the treatment chapters, delivered over 10 weeks.*

Chapter 1 – Introduction. Provides practical information about the treatment (length, homework assignments, therapist support) and introduces the psychological model for the maintenance of tics.
Chapter 2 – Register the urges. Describes the role of premonitory urges and encourages the participants to start registering the urges as a part of their training.
Chapter 3 – Exposure with response prevention. Introduces the participants to exposure and response prevention and encourages them to start using the Ticstimer (response prevention).
Chapter 4 – Proactive exposure Part 1. Encourages the participants to expose themselves to more challenging situations to provoke tics and try to suppress tics.
Chapter 5 – Proactive exposure Part 2. The participants are encouraged to get more creative to increase the difficulty level of the exercises, for example by inducing tics and then trying to interrupt them. Habit reversal strategies with incompatible movements are introduced.
Chapter 6 - Proactive exposure Part 3. The level of difficulty increases even further, as the participants are encouraged to combine different exercises and minimize avoidance of triggering situations in their everyday life.
Chapter 7 – Summary. Summarizes the core components of the treatment.
Chapter 8 – Planning forward. Planning for continued work and for relapse prevention.

Outcome measures and assessment points

The primary endpoint of the trial was post-treatment (i.e., 10 weeks from baseline). The feasibility, acceptability, preliminary efficacy, and preliminary maintenance of the effects of the treatment were assessed using the dimensions of the RE-AIM implementation framework (reach, preliminary efficacy, adoption, implementation, and maintenance) (28). *Reach* was measured by the percentage of eligible/excluded participants and the reasons for exclusion. *Preliminary efficacy* was defined as symptom change on the primary outcome measure, the YGTSS-TTS, and by other symptom-specific and non-specific measures (see below). These measures were administered at pre- and post-treatment, as well as 3, 6, and 12 months after the end of the treatment, unless specified otherwise. *Adoption* was measured by weekly questions about the treatment material and self-reported time spent on assignments, the number of treatment chapters completed during treatment, the score on the clinician-rated Internet Intervention Participant Adherence Scale (IIPAS; 5 items; score range between 0 and 20, with higher scores indicating higher patient adherence) (29) at mid- and post-treatment, the Credibility/Expectancy Questionnaire (CEQ; 5 items; score range between 0 and 50, with higher scores indicating higher credibility) (30), the Working Alliance Inventory Short-Revised (WAI-SR; 12 items; score range between 12 and 84, with higher scores indicating stronger perceived alliance between the patient and the therapist) (31) at week 4, and the Client Satisfaction Questionnaire (CSQ-8; 8 items; score range between 8 and 32, with higher scores indicating higher treatment satisfaction) (32) at post-treatment. *Implementation* was measured as the average therapist time spent per participant and week, the number of messages sent and received within the platform, and the number of additional telephone calls made by therapists. *Maintenance* was assessed using the change in symptoms and quality of life between pre-treatment and the 3-, 6- and 12-month follow-ups.

The primary outcome measure for the preliminary efficacy was the YGTSS-TTS. The YGTSS is a clinician-administered semi-structured interview with independent ratings of motor and vocal tic severity as well as a rating of tic-related impairment (33). All assessors were trained in administering the YGTSS by an experienced expert-rater by co-rating pre-recorded YGTSS administration prior to the trial. Secondary disorder-specific outcome measures were the YGTSS Impairment score, the Adult Tic Questionnaire (ATQ) (34) (also administered weekly), and the Gilles de la Tourette Syndrome Quality of Life Scale (QTS-QoL) (35).

The Clinical Global Impression - Severity (CGI-S) and Clinical Global Impression - Improvement (CGI-I) (36) scales (clinician-rated) were used to assess overall clinical severity and improvement, respectively. In line with previous trials (25,26), CGI-I scores of “very much improved” (1) or “much improved” (2) corresponded to treatment response.

The Sheehan Disability Scale (SDS) (37) and the EuroQol 5-dimensions (EQ-5D) (38) were used to evaluate general functioning and quality of life. The Montgomery-Åsberg Depression Rating Scale – Self-Rated (MADRS-S) was used to assess depressive symptoms (39) (also administered weekly).

Safety was measured at post-treatment and at the 3-month follow-up, when the participants rated a list of common adverse events and answered an open-ended question where they could report any adverse event.

Comorbidities were assessed during the pre-treatment psychiatric assessment using the MINI International Neuropsychiatric Interview (40) and the section for OCD and related disorders of the Structured Clinical Interview for DSM-5 (SCID) (41).

Data analysis

Power calculation

The power calculation was based on the only previous study testing Internet-delivered ERP for TS/CTD at the time this pilot was designed, conducted in children (42). We planned to recruit 30 participants in order to detect an effect size of *d*=0.7 (90% power, alpha 0.05), allowing for a 20% dropout.

Outcome analyses

The analyses were conducted using the statistical software R, version 4.4.0. For the measures of reach, adoption, implementation, and safety, descriptive statistics and frequencies were calculated. For each efficacy measure (YGTSS, ATQ, GTS-QoL, MADRS-S, EQ5D, and SDS) and endpoint (post-treatment, 3-, 6- and 12-month follow-up) the symptom change was evaluated using mixed-effects linear regression models with a fixed effect of time and a random intercept specification for each individual. Also, for each measure and endpoint, within-group effect sizes were calculated using Cohen's *d* by dividing the mean change between pre-treatment and the respective timepoint by the standard deviation of that measure at pre-treatment. To maximize replicability and transparency, all statistical code was uploaded to a public repository (https://osf.io/pbj4x/).

RESULTS

Recruitment and sample description (Reach)

Out of 89 individuals who applied for the study, 73 were assessed (among those n=1 clinically referred) and 42 (58% of the assessed individuals) were excluded (see Figure 1). The most common cause for exclusion was not fulfilling the diagnostic criteria for chronic tics (n=26/62% of excluded individuals), followed by having a severe psychiatric condition (n=6/14%) and low tic severity (n=5/12%). Finally, 31 participants were included in the study.

Table 2 shows the demographic and pre-treatment characteristics for the included participants. The majority were men (n=18/58.1%) with a mean age of 41.6 years (SD=15.4) and a mean total tic severity score at pre-treatment of 19.42 (SD=5.99) on the YGTSS-TTS. Just above half of participants (n=17/54.8%) fulfilled diagnostic criteria for TS, and the rest suffered from motor CTD. Only one participant had a confirmed comorbid condition - panic disorder with agoraphobia. The most common tics at pre-treatment were concentrated around the eyes (present in n=27/ 87%), nose (n=16/52%), jaws and fingers (each present in n=15/48%), and lips, neck, and shoulders (each present in n=12/39%)

Table 2. *Demographic and clinical characteristics of the included participants.*

Age, mean (SD)	41.6 (15.4)
Gender, n women (%)	13 (41.9)
Civil status, n (%)	
In a relationship	25 (80.6)
Single	5 (16.1)
Other	1 (3.2)
Employment status, n (%)	
Employed	25 (80.6)
Pension/disability pension	4 (12.9)
Student	2 (6.5)
Education, n (%)	
Secondary school	2 (6.5)
Upper secondary school	8 (25.8)
Unfinished university degree	8 (25.8)
University degree	13 (41.9)
Diagnosis (n, %)	
TS	17 (54.8)
CTD (motor)	14 (45.2)
YGTSS-TTS, mean (SD)	19.42 (5.99)
YGTSS Impairment, mean (SD)	19.03 (8.31)
ATQ, mean (SD)	31.97 (16.32)
GTS-QoL, mean (SD)	15.13 (11.14)

Abbreviations:
ATQ – Adult Tic Questionnaire
CTD - Chronic Tic Disorder
GTS-QoL – Gilles de la Tourette Syndrome - Quality of Life Scale
TS – Tourette Syndrome
YGTSS Impairment – Yale Global Tic Severity Scale – Impairment score
YGTSS-TTS – Yale Global Tic Severity Scale – Total Tic Severity subscale

Adoption

Out of 8 treatment chapters, participants completed 6.5 on average (SD=1.9; median=7.5). A total of 28 (90%) individuals were treatment completers (i.e., they completed the first four chapters containing the key ingredients of ERP). The mean credibility score on CEQ at mid-treatment was 36.6 out of 50 possible (SD=7.6). The mean treatment satisfaction score at post-treatment was 27.1 out of 32 possible (SD=3.6). The therapists' average rating of participants' treatment adherence according to IIPAS was 14.9 (SD=4.0) at mid-treatment and 13.3 (SD=5.4) at post-treatment out of 20 possible. The average rating of the usefulness of the chapters was 4.1/5 (SD=0.4), with the first chapter providing the psychological model for tics and rationale for the treatment rated as most useful (M=4.6/5, SD=0.5) and the chapters on HRT as least useful (M=3.5/5, SD=1.4).

Preliminary efficacy at post-treatment

Within-group changes in the tic-specific measures are shown in Table 3. The pre-to-post-treatment change on the primary outcome measure, the YGTSS-TTS, was statistically

significant (Figure 2, top panel). The within-group effect sizes were in the moderate range (Cohen's *d*=0.49). Changes in the YGTSS Impairment score, the ATQ (Figure 2, bottom panel), and the GTS-QoL followed a similar pattern. At post-treatment, 14 (45%) of the participants were classified as responders, according to the CGI-I.

Maintenance of gains during the follow-up

YGTSS-TTS scores continued to improve throughout the follow-up (Table 3 and Figure 2, top panel). At the 3-month follow-up, 14 (45%) participants were responders. At the 6- and 12-month follow-ups, 13 (42%) participants were classified as responders.

Table 3. *Within-group change in efficacy measures.*

		Pre	Post	FU3	FU6	FU12
YGTSS-TTS	**M**	19.42	16.47	15.07	14.57	12.92
	(SD)	(5.99)	(6.13)	(6.51)	(6.75)	(5.90)
	(df) F	-	(1,29) 22.49***	(2,55) 19.54***	(3,82) 17.70***	(4,105) 17.44***
	Cohen's *d* (95 % CI)	-	0.49 (-0.46-1.44)	0.73 (-0.22-1.68)	0.81 (-0.14-1.76)	1.09 (0.14-2.04)
YGTSS Impairment	**M**	19.03	12.67	10.74	12.50	11.67
	(SD)	(8.31)	(7.85)	(8.74)	(8.44)	(9.17)
	(df) F	-	(1,29) 22.40***	(2,55) 16.72***	(3,82) 13.73***	(4,105) 10.12***
	Cohen's *d* (95 % CI)	-	0.77 (-0.55-2.08)	1.00 (-0.32-2.32)	0.79 (-0.53-2.10)	0.89 (-0.43-2.20)
ATQ	**M**	31.97	22.77	21.25	23.61	22.70
	(SD)	(16.32)	(16.91)	(16.50)	(18.48)	(17.02)
	(df) F	-	(9,256) 4.72***	(10,283) 5.90***	(11,310) 4.93***	(12,332) 4.57***
	Cohen's *d* (95 % CI)	-	0.56 (-1.04-2.16)	0.66 (-0.94-2.26)	0.51 (-1.09-2.11)	0.59 (-1.03-2.17)
GTS-QoL	**M**	15.13	11.00	9.43	9.21	10.04
	(SD)	(11.14)	(10.27)	(7.53)	(7.65)	9.07
	(df) F	-	(1,30) 5.60*	(2,56) 5.48**	(3,83) 5.25**	(4,104) 3.97**
	Cohen's *d* (95 % CI)	-	0.37 (-1.40-2.14)	0.51 (-1.26-2.28)	0.53 (-1.24-2.30)	0.46 (-1.31-2.22)
MADRS-S	**M**	6.29	4.37	4.57	4.96	5.04
	(SD)	(4.58)	(5.14)	(4.87)	(4.64)	(3.56)
	(df) F	-	(9,256) 2.35*	(10,283) 1.96*	(11,310) 1.67	(12,332) 1.87*
	Cohen's *d* (95 % CI)	-	0.42 (-0.03-0.87)	0.37 (-0.07-0.82)	0.29 (-0.16-0.74)	0.27 (-0.18-0.72)
EQ5D	**M**	1.03	0.93	1.00	1.07	1.30
	(SD)	1.28	1.20	1.19	1.33	1.82
	(df) F	-	(1,29) 0.09	(2,55) 0.01	(3,83) 0.06	(4,106) 1.23
	Cohen's *d* (95 % CI)	-	0.08 (-0.13-0.28)	0.03 (-0.18-0.23)	0.03 (-0.17-0.23)	0.21 (0.01-0.42)
SDS	**M**	2.84	2.23	1.68	1.86	1.52
	(SD)	3.74	3.70	2.29	3.11	2.04
	(df) F	-	(1,30) 0.56	(2,58) 1.13	(3,84) 0.88	(4,105) 0.80
	Cohen's *d* (95 % CI)	-	0.16 (-0.43-0.76)	0.31 (-0.28-0.90)	0.26 (-0.33-0.86)	0.35 (-0.24-0.94)

*p<.05, **p<.005, ***p<.001
Pre – pre-treatment; Post – post-treatment; FU3 – 3-month follow-up; FU6 – 6-month follow-up; FU12 – 12-month follow-up.
All comparisons have the pre-treatment measurement as their first timepoint.

Abbreviations:
ATQ – Adult Tic Questionnaire
EQ-5D – EuroQol 5-dimensions
GTS-QoL – Gilles de la Tourette Syndrome – Quality of Life Scale
MADRS-S – Montgomery-Åsberg Depression Rating Scale – Self-Rated
SDS – Sheehan Disability Scale
YGTSS Impairment – Yale Global Tic Severity Scale – Impairment score
YGTSS-TTS – Yale Global Tic Severity Scale – Total Tic Severity subscale

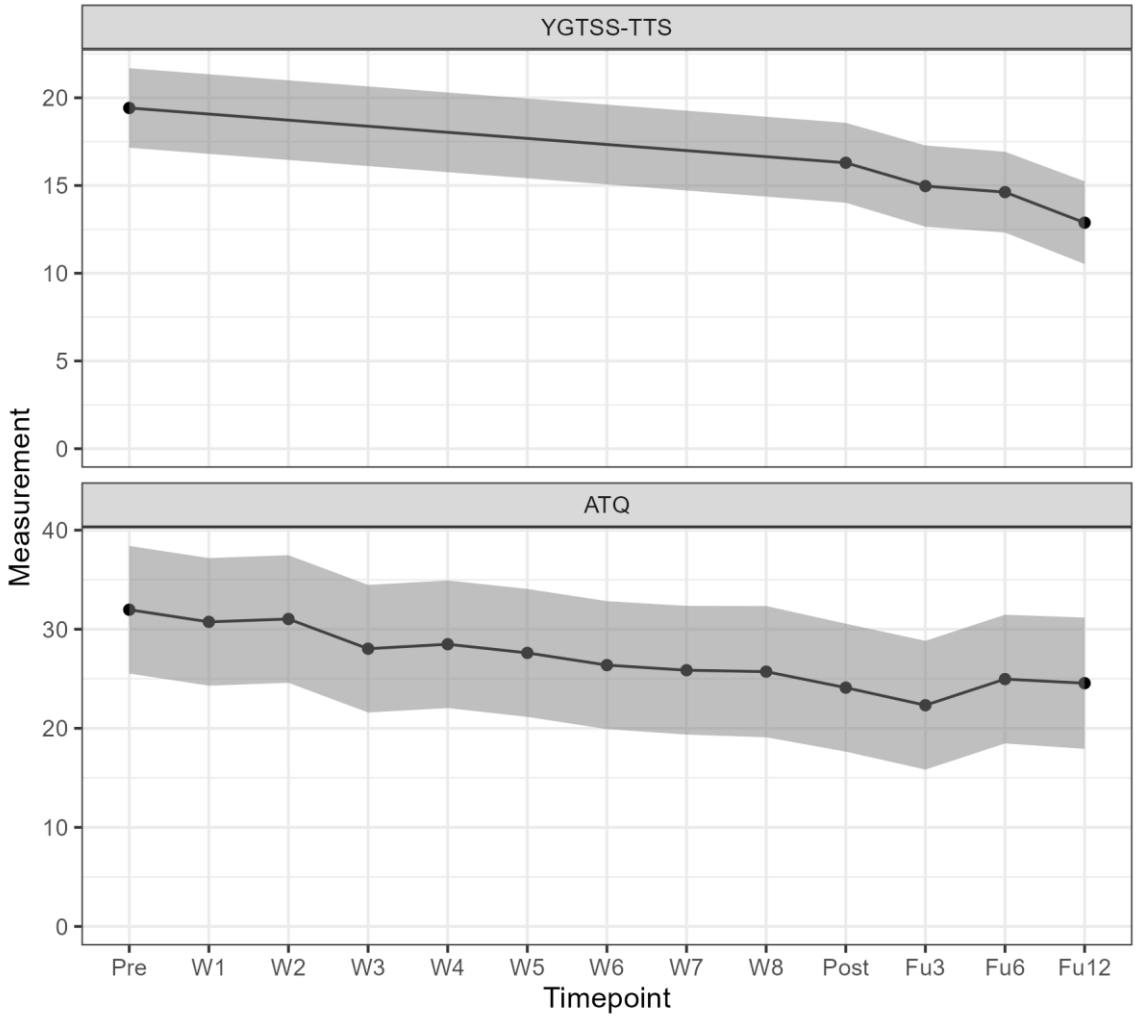

Figure 2. *Estimated means and 95% CI for the primary outcome measure Yale Global Tic Severity Scale – Total Tic Severity subscale (top panel) and the tic-specific secondary outcome measure Adult Tic Questionnaire (bottom panel) between pre-treatment and the 12-month follow-up.*
Pre – pre-treatment; Post – post-treatment; W1-W8 – weekly measurements week 1-8; Fu3 – 3-month follow-up; Fu6 – 6-month follow-up; Fu12 – 12-month follow-up.

Implementation

The average time spent by the therapists on each participant per week was 18.1 minutes (SD=9.7 minutes). A total of 11 participants (35%) received additional telephone calls during the treatment, with a median of 1 call per participant. On average, 15.0 messages (SD=11.2) were sent by the therapists to each participant during the course of the treatment. The participant rating of working alliance according to the WAI was 70.4 (SD=12.2) out of 72 possible. The participant average weekly self-reported time spent working with the treatment was 197 minutes (SD=129). In the free text answers, most of the participants found the treatment helpful, mentioned reduced shame and reduced feeling of being alone with their struggles, and were satisfied with the Internet-based format. The participants mentioned integrating the practice into their everyday life. Among the difficulties, the participants mentioned the challenges of combining the treatment with the stresses of the everyday life and challenges with understanding the structure of working materials and when navigating the treatment platform.

Safety

No serious adverse events were reported during the treatment or the follow-up period. The most common adverse events reported by the participants were fatigue, experienced often or all the time by 11 participants (35%), sleep disturbance (n=6; 19%), worry/anxiety (n=4; 13%), and feeling low (n=4; 13%). At the 3-month follow-up, the participants reported fewer adverse events, with fatigue and worsened tic symptoms being the most common (each reported by 6 participants; 19%).

DISCUSSION

The aim of this uncontrolled trial was to evaluate the feasibility, acceptability, safety, preliminary efficacy, and preliminary maintenance of TICNET, an online, therapist-guided ERP-based behavioural intervention for adults with TS/CTD. Overall, the intervention was feasible, acceptable, safe, and potentially efficacious, with reductions in tic severity being maintained for at least 12 months after treatment.

Out of the 73 screened participants, 42% were included in the study. Although the reach was lower than in a RCT for a face-to-face treatment (71%) (16), it exceeded the proportion of enrolled participants in two recent RCTs for guided Internet-delivered treatments for children and adolescents by Hollis at al. (50%) (26) and Andrén et al. (34%) (25). The two latter studies and the current study allowed participant self-referral, which is essential to achieve the high treatment accessibility, one of the greatest advantages of Internet-delivered treatments. Allowing participant self-referrals and advertising is likely to lead to higher proportions of non-eligible individuals. Most individuals with TS/CTD were included in the trial – only a small proportion was excluded due to severe comorbidities or mild tic severity – indicating that the treatment reached a relevant population. However, it is important to note that only one included participant had a current comorbid psychiatric disorder, which is highly unusual in this patient group. Thus, the Internet treatment format seems to have attracted a particular sub-population of individuals with chronic tics, which differs from most samples seen in specialist TS/CTD clinics.

The overall adoption of the treatment was good. Most participants completed almost all treatment chapters and 90% were considered treatment completers. In a recent RCT of treatment for adults, 33% of participants in the three randomization arms (face-to-face BT, unguided Internet-based BT, and placebo) were considered non-compliant (24). Despite the differences in defining compliance, our results indicate treatment compliance that was at least as good as what has been previously reported. Andrén et al. (25) reported similar compliance in their trial for I-BT children and adolescents, with the participants in the ERP group having completed 8.9 treatment chapters out of 10. Moreover, the participant adherence to the treatment in our study was in the same range as the values reported in Andrén et al: IIPAS at mid-treatment was 14.9 (compared to previously reported 14.1) and at post-treatment 13.3 (compared to 12.6). The treatment satisfaction (CSQ-8 score of 27.1) was similar to the one reported in a recent study on guided ICBT for OCD and body dysmorphic disorder (BDD) implemented in regular care (26.5 and 25.2, respectively) (43).

The change in the YGTSS-TTS between pre- and post-treatment (primary endpoint) was statistically significant and the effect-size was in the medium range, but with a wide confidence interval, reaching below zero on the lower end (Cohen's *d* 0.49; 95% CI -0.46 to 1.44). The 2.9-raw point drop in the YGTSS-TTS was comparable to that reported in a recent RCT on HRT for adults with TS/CTD (a drop of about 2.3 in both the Internet-delivered and the face-to-face arm at post-treatment; the numbers are not reported explicitly, but derived from inspecting Figure 1 in the publication) (24). A recent telehealth study on HRT saw a YGTSS-drop of 4.5 in the sample of ten adults (44). A face-to-face study from 2012 reported a larger decrease of 6.2 (16), similar to the values of 6.1 (25) and 4.5 (26) found in two recent RCTs on Internet-delivered ERP for children and adolescents. In our study, the drop in YGTSS-TTS increased at each follow-up point, reaching 6.5 points and an effect size of 1.09 (95% CI 0.14-2.04) 12 months after the end of the treatment. The lower decrease in tic severity than in other studies might be partly explained by the lower pre-treatment tic severity: the participants in our study started with less severe tics and improved to 16.5 on YGTSS-TTS, which is similar to previously reported 17.8 (16) and 16.2 (25). TS/CTD is a neurological condition, and the effect of behavioural techniques can be limited when addressing the milder tics still present after the treatment (especially during the relatively short treatment timeframe). Overall, in comparison with previous studies, the observed decrease in tic severity indicates that the treatment has the potential to bring relief to adults with TS/CTD who wish to have specialist treatment but have difficulties accessing it. The efficacy of the intervention should now be evaluated in an RCT, potentially recruiting more widely from clinical services to ensure a better representation of all people with TS/CTD.

The therapist time of 18.1 minutes per participant per week was similar to the 19.1 minutes reported in Andrén at al. (25). The study on effectiveness of ICBT for OCD and BDD conducted at our clinic reported less time spent on participant per week (9.2 and 7.2 minutes, respectively), which can partly be explained by the fact that the OCD and BDD treatments were already implemented in regular care after having been a part of an RCT conducted at the same clinic, and the clinicians were more familiar with the treatments. In our study, the time spent on each participant per week was still much lower than in face-to-face CBT, typically requiring weekly sessions of 45 to 90 minutes, suggesting that this

Internet-delivered treatment can be cost-effective. The working alliance, according to the WAI, was excellent. All in all, the adoption of the treatment by the clinic's personnel in the framework of our study was successful and only required smaller adjustments of routine procedures.

Limitations

The results require cautious interpretation given the study's limitations. This small-scale uncontrolled trial only gives an indication of the treatments' potential effects. To evaluate the treatment's efficacy, a well-powered RCT with an active comparator needs to be conducted. Also, the assessors were not blinded to the treatment that the participants received and were often treating clinician, introducing a potential bias in the assessments. The study's sample was very unusual with mild tic severity at baseline and almost no psychiatric comorbidities. Another limitation was that, although the study assessed common comorbidities at baseline, the presence of ADHD could not be assessed as this would require extensive procedures, and the project did not collect information about whether participants had previously been diagnosed with ADHD. The prevalence of ADHD – a condition that is very common in TS/CTD patients – in our sample is therefore unknown. Even with this limitation in mind, the absence of typical comorbidities, such as OCD and other prevalent disorders within this group indicates that future trials need to focus on recruiting more representative samples in order to ensure the generalizability of the results.

Conclusion

Therapist-guided Internet-delivered ERP-based BT for adults with TS/CTD is feasible, acceptable, safe, and potentially leads to a meaningful and durable reductions in tic severity and functioning, at least in individuals with mild symptoms and limited comorbidities. The intervention should be further evaluated in a well-powered RCT with an active comparator while ensuring the recruitment of more representative samples.

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AUTHOR CONTRIBUTIONS

CR initiated the project and obtained funding. EA created the treatment. PA, EA, VZI, DMC, LFC, OF, and CR planned the trial. EI had the overall responsibility for the project's progression, conducting the analyses and producing the manuscript. AB organized the work at the clinic. All authors contributed to the production of the manuscript and critically reviewed its final version.

CONFLICTS OF INTEREST

Oskar Flygare has received speaking fees from the Swedish OCD Association, Insight Events AB, WeMind Psykiatri AB, and Kry International AB, as well as reimbursement for writing articles for Inside Practice Psychiatry, all outside the submitted work. David Mataix-Cols receives royalties for contributing articles to UpToDate, Inc, and is part owner of Scandinavian E-Health AB, all outside the submitted work. Lorena Fernández de la Cruz

receives royalties for contributing articles to UpToDate, Wolters Kluwer Health and for editorial work from Elsevier, outside the submitted work. Other authors have no conflicts of interest to declare.

DATA SHARING STATEMENT

The statistical code for the analyses in uploaded at https://osf.io/pbj4x/.

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