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# Is Comprehensive Behavioral Intervention for Tics (CBIT) effective in decreasing tic severity in individuals with chronic tic disorders?

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### A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies Philadelphia College of Osteopathic Medicine Philadelphia, Pennsylvania

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## ABSTRACT

**Objective:** The objective of this selective EBM review is to determine whether or not "Is Comprehensive Behavioral Intervention for Tics (CBIT) effective in decreasing tic severity in individuals with chronic tic disorders?"

**Study Design:** A systematic review of three randomized controlled trials (RCTs) published between 2010 and 2016.

**Data Sources:** All three RCTs were discovered using PubMed. The articles were published in English in peer-reviewed journals and selected based on applicability to the clinical question.

**Outcome Measured:** A reduction in tic severity was the outcome measured in all three studies using the Yale Global Tic Severity Score (YGTSS). Scores range from 0-100 with higher scores indicating stronger tic severity. The mean change from baseline was calculated once intervention was received.

**Results:** In the RCT led by Wilhelm et al., CBIT led to a reduction in tic severity compared with the control group (P < 0.001), indicated by a mean change from baseline of 6.2. In the RCT by Piacentini et al., CBIT led to a reduction in tic severity compared with the control group (P < 0.001), indicated by a mean change from baseline of 7.6. Lastly, Ricketts et al. demonstrated a reduction in tic severity with CBIT-VoIP (voice over internet protocol), indicated by a mean change from baseline of P < 0.01 in the CBIT treatment group.

**Conclusion:** All three studies in this review demonstrated that CBIT led to significantly reduced tic severity as measured by the YGTSS. This suggests CBIT is an effective and beneficial method of treatment for chronic tic disorders. Further studies should explore online administration, treatment duration, and maintenance therapy.

Key Words: tic, comprehensive behavior therapy

#### INTRODUCTION

Chronic tic disorders involve repeated, brief, rapid movements or vocalizations. The tics typically present as rapid movements such as blinking and/or vocalizations such as grunting. In order to classify as a chronic disorder, tics must be recurring. A more specific diagnosis of Tourette syndrome (TS) can be made when individuals have both motor and vocal tics for greater than one-year duration.<sup>1</sup> Tics typically begin in childhood, with severity peaking in early adolescence, and declining in young adulthood. It is estimated that the prevalence of TS in children is 6 cases per 1,000; this analogizes to about 300,000 cases of TS among children in the United States.<sup>2</sup> The estimated prevalence of TS in adults is 1 per 2,000.<sup>2</sup> There is not an exact estimate available regarding annual health care utilization, however treatment of chronic tic disorders is multifaceted and includes neurology, psychology/psychiatry, speech therapy, and more subspecialty appointments, resulting in an immense amount of healthcare visits each year.<sup>3</sup> Similarly, the total healthcare cost of tic disorders has not been identified, but it is estimated that \$117 million is spent annually on risperidone, a medication commonly used to treat tic disorders.<sup>3,4</sup>

Tic disorders are complex neurological disorders thought to be caused by a combination of genetic and environmental factors, although the exact etiology is unknown. Many scientists believe them to be attributable to an abnormal release and uptake of dopamine. Chronic tic disorders are commonly associated with other psychiatric disorders including obsessive compulsive disorder and attention deficit hyperactivity disorder, leading to further psychosocial complications and difficulty maintaining a productive, independent, and/or self-sufficient lifestyle.<sup>2</sup> Current treatment for chronic tic disorders is complex and multidimensional, usually involving both behavioral therapy and pharmacotherapy. Some pharmacologic options include

alpha-adrenergic agonists, such as clonidine and guanfacine, antipsychotics such as risperidone, haloperidol, and pimozide, antiepileptics such as topiramate, stimulants such as methylphenidate, SSRIs such as fluoxetine, and anxiolytics such as clonazepam. Other alternative methods include botulinum injections (Botox), psychotherapy, and deep brain stimulation (DBS).

Medications play an effective role in treating chronic tic disorders but are not without consequences, often causing undesirable side effects. For example, antipsychotics can cause sedation and weight gain. The limitations of pharmacologic therapy highlight the importance of, and need for, alternative therapies. Comprehensive Behavioral Intervention for Tics (CBIT) is a nonpharmacologic treatment consisting of three key elements: training the patient to be more aware of their urge to tic, training patients to incorporate competing behavior when the urge to tic arises, as well as altering daily activities in ways which will help to reduce volume of tics.<sup>3</sup> This paper evaluates three randomized controlled trials (RCTs), assessing the efficacy of CBIT as a management for chronic tic disorders.

#### **OBJECTIVE**

The objective of this selective EBM review is to determine whether or not "Is Comprehensive Behavioral Intervention for Tics (CBIT) effective in decreasing tic severity in individuals with chronic tic disorders?"

#### **METHODS**

Studies were chosen based on credibility, applicability to the clinical question, and incorporation of patient-oriented outcomes. Further, they were selected if they fulfilled criteria based on population, intervention, comparison, and outcome measured. It was required that all studies were directed at patients clinically diagnosed with chronic tic disorders. The studies referenced in this review were found on PubMed using keywords "tic" and "comprehensive behavior therapy". It was required that the studies employed randomization and were published in peer-reviewed journals. All articles selected were in the English language. Inclusion criteria consisted of RCTs published after 2009. Studies published prior to 2009 were excluded. Statistical analyses utilized in these studies include the mean change from baseline in the Yale Global Tic Severity Score (YGTSS) as well as evaluating statistical significance using p-values.

The population of the studies targeted in this selective EBM review were patients diagnosed with a chronic tic disorder of moderate or greater severity. The demographics and characteristics of these studies can be found in Table 1. The intervention used in each study was CBIT. Authors Wilhelm et al. and Piacentini et al. compared CBIT with psychoeducation and supportive therapy (PST), whereas Ricketts et al. utilized a wait-list control group for comparison. The outcome measured that is discussed in this selective EBM is a reduction in tic severity.

#### **OUTCOME MEASURED**

All three studies utilized the YGTSS, a rating determined by a physician based on a semi structured interview regarding tic number, frequency, intensity, complexity, and interference in the preceding week. The total tic score is calculated by totaling several component scores, including the overall impairment rating, total motor tic score (0-25), and total phonic tic score (0-25).<sup>8</sup> The overall impairment rating is on a 50-point scale, 0 indicating no impairment and 50 indicating severe impairment.<sup>8</sup> Scores range from 0-100 with higher scores indicating stronger tic severity. The outcome measured in this review is a reduction in tic severity as measured by the YGTSS.

Study	Туре	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Wilhelm <sup>5</sup> (2012)	RCT	122	16- 69	Patients at least 16 years old who meet diagnostic criteria for Tourette or chronic tic disorder of moderate or greater severity, English fluency, IQ > 80	History of substance abuse, schizophrenia, or pervasive developmental disorder, ≥ 4 previous sessions of habit reversal training	17	CBIT VS. PST
Piacentini <sup>6</sup> (2010)	RCT	126	9-17	Patients 9-17 years old who meet diagnostic criteria for Tourette or chronic tic disorder of moderate or greater severity, English fluency, IQ > 80	History of substance abuse, pervasive developmental disorder, psychosis, unstable medical condition, $\geq 4$ previous sessions of habit reversal training	12	CBIT VS. PST
Ricketts <sup>7</sup> (2016)	RCT	20	8-16	Patients 8-17 years old who have residence within the state of Wisconsin, a DSM-IV-TR diagnosis of chronic tic disorder or Tourette syndrome, unmedicated or on stable medication for tics, English fluency	YGTSS >30, WASI- Vocabulary subtest T-score <37, diagnosis of substance abuse, conduct disorder, pervasive developmental disorder, mania, or psychotic disorder, previous habit reversal training for tics, lack of functional and accessible computer or internet speed	1	CBIT-VoIP (voice over internet protocol) VS. waitlist control

Table 1. Demographics & Characteristics of Included Studies

#### RESULTS

All three studies in this review enrolled individuals diagnosed with a chronic tic disorder of moderate or greater severity and evaluated the safety and efficacy of CBIT. Wilhelm et al. conducted a randomized controlled trial using blinded raters. The authors enrolled patients 16 years or older with a chronic tic disorder of moderate or greater severity. The study was conducted over 10 weeks and compared CBIT with psychoeducation and supportive therapy (PST). The primary outcome analyzed was the change in tic severity at the end of week 10. The cohort was comprised of 122 patients who were randomized in a 1:1 ratio to either CBIT or PST, and then stratified based on whether or not tic suppressing medication was prescribed, further improving accuracy.<sup>5</sup> In total, 63 patients received CBIT while 53 patients received PST.<sup>5</sup> Although both patients and therapists were aware of treatment assignment, independent evaluators were masked to treatment conditions throughout the entirety of the trial. Both groups received eight sessions of either CBIT or PST for 10 weeks duration. Adverse events ranged from mild to severe, including myalgias, headaches, anxiety or depression, irritability, and sleep problems, however there was no evidence the adverse events were secondary to either intervention.<sup>5</sup> In both groups, four subjects experienced tic worsening. Seven subjects discontinued treatment in the CBIT group, and 10 subjects discontinued in the PST group, but sufficient reason for discontinuation was not identified. Those individuals were not included in the final analysis.<sup>5</sup>

Assessments for efficacy and improvement in the YGTSS were observed after week 10 of treatment. The authors used mean values to measure outcomes prior to and after treatment. The results were statistically significant (P < 0.001) in both interventions. The CBIT group showed a decrease in mean values with  $24.0 \pm 6.5$  prior to treatment and  $17.8 \pm 7.3$  at 10 weeks,

resulting in a mean change from baseline of  $6.2.^{5}$  The PST group demonstrated a decrease in mean values with  $21.8 \pm 6.6$  prior to treatment and  $19.3 \pm 7.4$  at 10 weeks, resulting in a mean change from baseline of  $2.5.^{5}$  The results are summarized in Table 2 below. CBIT was found to be superior to the control treatment, PST, as reflected by the 3.7-point difference between groups.<sup>5</sup> These results compute to a 25.8% decrease from baseline to week 10 versus an 11.5% decrease for the control PST treatment.<sup>5</sup> The presence of tic suppressing medication at baseline did not moderate treatment outcome as measured by the YGTSS.

Table 2. YGTSS Change in Tic Severity from Baseline to Week 10 Follow-Up<sup>5</sup>

	Before Treatment	Week 10	Mean Change	P-value
	$(Mean \pm SD)$	$(Mean \pm SD)$	from Baseline	
CBIT group	$24.0\pm6.5$	$17.8 \pm 7.3$	6.2	< 0.001
PST group	$21.8\pm6.6$	$19.3 \pm 7.4$	2.5	< 0.001

Piacentini et al. conducted a trial with a very similar design as Wilhelm et al. but focused on children and adolescents from age 9-17 years old. Piacentini et al. conducted a randomized controlled trial using blinded raters. The authors enrolled patients 9-17 years old with a chronic tic disorder of moderate or greater severity. The study was conducted over 10 weeks and compared CBIT with psychoeducation and supportive therapy (PST). The primary outcome analyzed was the change in tic severity at the end of week 10. The cohort was comprised of 126 patients who were randomized in a 1:1 ratio to either CBIT or PST, and then stratified based on whether or not tic suppressing medication was prescribed, further improving accuracy. In total, 61 patients received CBIT while 65 patients received PST.<sup>6</sup> Although both patients and therapists were aware of treatment assignment, independent evaluators were masked to treatment conditions throughout the entirety of the trial. Both groups received eight sessions of either CBIT or PST for 10 weeks duration. Adverse events ranged from mild to severe, including irritability and explosive behavior, myalgias, headaches, disruptive behavior, and fatigue, however there was no evidence the adverse events were secondary to either intervention.<sup>6</sup> One individual in the CBIT treatment group experienced tic worsening versus four in the PST treatment group. Five subjects discontinued treatment in the CBIT group and seven discontinued in the PST group. All 126 subjects were included in primary data analysis, but a worst-case analysis was not preformed.<sup>6</sup>

Assessments for efficacy and improvement in the YGTSS were observed after week 10 of treatment. Mean values with a 95% CI were used to measure outcomes both prior to and after treatment. The results were statistically significant (P < 0.001) in both interventions. The CBIT group showed a decrease in mean values with 24.7 (23.1 – 26.3) prior to treatment and 17.1 (15.1 – 19.1) at 10 weeks, resulting in a mean change from baseline of 7.6.<sup>6</sup> The PST group demonstrated a decrease in mean values with 24.6 (23.2 – 26.0) prior to treatment and 21.1 (19.2 – 23.0) at 10 weeks, resulting in a mean change from baseline of 3.5.<sup>6</sup> The results are summarized in Table 3 below. This 4.1-point difference between groups is clinically meaningful, indicating CBIT was superior to the control treatment, PST, with a 51% decrease from baseline to week 10 compared with a 30% decrease for the control treatment.<sup>6</sup> The presence of tic suppressing medication at baseline did not moderate treatment outcome as measured by the YGTSS.

Table 5. 10155 Change in The Seventy from Dasenne to Week 10 Follow-Op					
	<b>Before Treatment</b>	Week 10	Mean Change	<b>P-value</b>	
	Mean (95% CI)	Mean (95% CI)	from Baseline		
<b>CBIT group</b>	24.7 (23.1-26.3)	17.1 (15.1-19.1)	7.6	< 0.001	
PST group	24.6 (23.2-26.0)	21.1 (19.2-23.0)	3.5	< 0.001	

Table 3. YGTSS Change in Tic Severity from Baseline to Week 10 Follow-Up<sup>6</sup>

Ricketts et al. also conducted a randomized controlled trial of subjects diagnosed with a chronic tic disorder. Subjects ranged from 8-16 years old. Tic scores were measured by blinded raters. The study was a 10-week RCT comparing CBIT-VoIP (voice over internet protocol) to a

waitlist control group. Participations in the CBIT-VoIP received CBIT by method of video conference. The primary outcome analyzed was the change in tic severity at the end of week 10. Treatment consisted of two 1.5-hour sessions followed by six one-hour sessions occurring over a 10-week period. The cohort was comprised of 20 patients who were randomized to either CBIT-VoIP or waitlist control group, and then stratified with respect to medication status and gender.<sup>7</sup> A total of 12 patients were assigned to receive CBIT-VoIP while eight patients were allocated to the waitlist.<sup>7</sup> Patients were informed of group assignment via phone after baseline and independent evaluators were masked to treatment conditions throughout the entirety of the trial. Adverse events were not indicated. One subject discontinued treatment in the CBIT-VoIP group, however, no one discontinued waitlist position. All 20 subjects were included in data analysis.<sup>7</sup>

Assessments for efficacy and improvement in the YGTSS were observed after week 10 of treatment. Mean values were used to measure outcomes both prior to and after treatment. The results were statistically significant (P < 0.01) in the CBIT-VoIP group, whereas the waitlist control group was not precise (P = 0.15).<sup>7</sup> The CBIT-VoIP group showed a decrease in mean values with 25.75 prior to treatment and 18.50 at 10 weeks, resulting in a mean change from baseline of 7.25.<sup>7</sup> The waitlist control group demonstrated a decrease in mean values with 22.0 prior to treatment and 20.25 at 10 weeks, resulting in a mean change from baseline of 1.75.<sup>7</sup> The results are summarized in Table 4 below.

	Before Treatment Mean	Week 10 Mean	Mean Change from Baseline	P-value
<b>CBIT-VoIP</b> group	25.75	18.50	7.25	< 0.01
Waitlist group	22.00	20.25	1.75	0.15

Table 4. YGTSS Change in Tic Severity from Baseline to Week 10 Follow-Up<sup>7</sup>

#### DISCUSSION

Chronic tic disorders are a life-altering condition for which there is currently no cure, supporting the need for new treatment methods. Compared to pharmacologic treatments, nonpharmacologic treatments are beneficial in that they lack systemic side effects; however, they are more time-consuming to complete and thus patient and family compliance is more challenging. Additionally, because it is a newer development, there are a limited number of healthcare professionals trained on providing proper and effective CBIT to patients. Another barrier to CBIT may be cost. Limited insurance coverage, high co-pays, and travel costs associated with frequent sessions can be significant, rendering it an unaffordable option for some patients and families.

This review evaluated the efficacy of Comprehensive Behavioral Intervention for Tics as a treatment resulting in a reduction in tic severity in those with chronic tic disorders. All three studies found statistically significant improvement in the Yale Global Tic Severity Score after intervention with CBIT, with a substantial mean change from baseline in CBIT groups, a statistically significant p-value and large effect sizes. This proves not only that CBIT is more effective than the control groups of PST and waitlist, but to a significant magnitude. Ricketts et al. was especially promising, as CBIT was still determined to be effective when administered via VoIP, eliminating the time and cost commitment of travel. The results from this study support the efficacy of this therapy and indicate an improvement in quality of life.

All three studies had limitations. Patients were unable to be kept "blind" to treatment, leaving the potential for a false sense of improvement and bias due to subjects being aware of their treatment intervention. This bias most likely would be in favor of CBIT and could compromise results, falsely indicating a greater reduction in tics by CBIT than actually produced in practice. The use of blinded raters alleviates some of this concern but does not eliminate the risk of bias altogether. Additionally, Ricketts et al. used a small sample size, affecting the validity and reliability of these results. Lastly, Wilhelm et al. and Piacentini et al. did not perform worst case analyses for missing outcome data from subjects lost during their respective trials. This factor also introduces bias within these studies and make them less valid.

#### CONCLUSION

This systematic review showed Comprehensive Behavioral Intervention for Tics to be effective in decreasing tic severity in individuals with chronic tic disorders. Wilhelm et al., Piacentini et al., and Ricketts et al. all found CBIT to cause a statistically significant mean decrease in YGTSS after 10 weeks of treatment. The chance for any improvement in tics in those with chronic tic disorders is deserving of further exploration as quality of life can be much improved with a decrease in frequency and severity of tics. In order to further demonstrate the potential CBIT has, additional trials should be performed with an even larger sample size and duration. It would be beneficial to conduct further studies to determine the minimum number of treatment sessions required to reduce tic severity, as well as investigate long-term maintenance sessions to keep tic severity low. Additionally, it would be of great benefit to further explore the administration of CBIT online as it makes treatment more compatible with a busy lifestyle.

Another possibility to be explored is initiating CBIT immediately upon diagnosis. CBIT may be more beneficial if started earlier because recognizing the urge of a tic early, as well as learning how to prevent it quickly, may train the brain to resist tics at a more formative stage of the disease and potentially slow progression. This way, tic disorders may never have the chance to become severe. Early intervention would require individualized therapy such that it accounts for differences in a child's various phases of development. Implementing personalized delivery strategies can lead to better absorption, and thus an increased effectiveness of CBIT.

There is currently a trial of Internet based CBIT being sponsored by Tel Aviv Medical Center in a sample of children and adolescents 8-17 years old with chronic tic disorders.<sup>9</sup> It was estimated to be completed in 2020 however is still ongoing. If found to be effective, this has the potential to significantly reduce overall cost and treatment burden placed on those with living with a chronic tic disorder. Hopefully, future studies will be able to identify the most successful implication and utilization of CBIT, so those with chronic tic disorders can have an improved quality of life with minimal limitations due to their symptoms.

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