

**A 12-MONTH FOLLOW-UP STUDY EVALUATING
GROUP INTERVENTIONS FOR CHILDREN WITH
TOURETTE SYNDROME**

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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OVERVIEW

This thesis consists of three parts: a systematic literature review, an empirical paper and a critical appraisal. It aims to contribute to the evidence base for psychological interventions for Tourette Syndrome (TS). TS is a neurodevelopmental condition characterised by the presence of both motor and vocal tics. Tics typically first present in childhood and are associated with psychiatric co-morbidity, social and emotional difficulties, impaired school functioning and a diminished quality of life.

The literature review explores the efficacy and effectiveness of currently available psychological interventions for TS. It reviews both traditional behavioural approaches as well as newer adaptations of existing treatment protocols.

The empirical paper evaluates the long-term outcomes of two group treatments (Comprehensive Behavioural Intervention for Tics and psychoeducation) for children with TS. It assesses the effect of these treatments on tic severity, neuropsychological functioning, quality of life and school attendance.

Finally, the critical appraisal reflects on the process of conducting the research study. Specifically, it comments on the unique advantages and disadvantages of joining a larger research project, further explores the strengths and limitations of the study's methodology and finally reflects on the experience of working with children with a neurodevelopmental disorder.

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PART 1: LITERATURE REVIEW

PSYCHOLOGICAL INTERVENTIONS FOR TOURETTE SYNDROME:

A SYSTEMATIC REVIEW

ABSTRACT

Aims

This review aims to summarise and evaluate the empirical support for currently available psychological interventions for Tourette syndrome (TS).

Method

A systematic search of three databases (Embase, PsychINFO and Ovid Medline) was conducted and a narrative synthesis of the data was reported.

Results

Sixteen citations were identified for inclusion in the review, consisting of both controlled and uncontrolled trials of psychological interventions for TS. Interventions included established behavioural treatments and cognitive behaviour therapy (CBT), as well as third wave CBT approaches and adapted behavioural protocols utilising novel treatment delivery methods.

Conclusions

Treatment efficacy was reported across the range of psychological interventions, with traditional behavioural methods demonstrating the greatest treatment response. Newer approaches which address practical issues such as limited clinician availability will require high quality evaluation before conclusions about 'a best approach' can be made.

1. INTRODUCTION

Diagnosis and epidemiology

Tics are sudden, involuntary and repetitive movements or vocalisations. They are considered neurodevelopmental in nature and tend to wax and wane with time. A diagnosis of Tourette syndrome (TS) may be given where two or more motor tics and at least one vocal tic occur consistently or on and off for a period of one year. Where only motor or vocal tics are present, a diagnosis of chronic tic disorder (CTD) may be offered (American Psychiatric Association, 2013). Diagnostic criteria are similar in the International Classification of Diseases, 10th Revision (ICD-10; World Health Organisation, 1992). This review will refer to both chronic tic disorders and Tourette syndrome, collectively (TS), as it summarises and evaluates the research evidence supporting psychological interventions for tic disorders.

Tourette Syndrome has an estimated prevalence rate of approximately 1% amongst 5-18 year olds (Robertson, 2008) with prevalence higher amongst males than females (Knight et al., 2012). Comorbid psychiatric disorders are common amongst individuals with TS, with co-occurrence rates for attention deficit hyperactivity disorder (ADHD) and obsessive compulsive disorder (OCD) typically ranging between 25% and 50% (Abramovitch, Dar, Mittelman & Wilhelm, 2015). Tourette Syndrome and its comorbidities have also been associated with poor quality of life (Storch et al., 2007) and more recent psychological interventions have placed a focus on the management of these adverse psychosocial effects.

Psychopharmacotherapy

Traditionally, drugs such as antipsychotics (risperidone, haloperidol and pimozide) and alpha-2 agonists (guanfacine and clonidine) have been used in the management of tic disorders. Weisman, Qureshi, Leckamn, Scahill and Bloch (2013) conducted a meta-analysis of five randomised, placebo-controlled trials evaluating the efficacy of these drug treatments. Results found a significant treatment effect (standardised mean difference = 0.58) for antipsychotics compared to placebo. A modest treatment effect for alpha-2 agonists was also found, however subgroup analysis of the stratified data found this effect to be significant only for participants with comorbid ADHD symptoms. These findings suggest that certain tic medication may not be suitable or effective for all TS patients. Antipsychotics have also been associated with unpleasant side effects such as restlessness, weight gain and depression (Scahill et al., 2006), and it has been estimated that as much as 80% of individuals discontinue use of TS medication due to unwanted side effects (Peterson, Campise and Azrin, 1994).

Furthermore, whilst drug treatment may significantly reduce certain tic symptoms, some tics may persist and without adequate learned coping mechanisms, may remain bothersome. For individuals with symptoms that do not respond to drug treatment or for those that struggle with the unpleasant side effects of medication, psychological treatment may prove to be a more viable and sustainable option.

Behavioural interventions

Literature on the efficacy of psychological interventions for tics spans several distinct behavioural models which have followed the chronology of treatment in other disorders such as depression and anxiety. Historically, these have included operant conditioning models involving contingency management methods (Roane, Piazza, Cercone, & Grados, 2002), as well as Massed Negative Practice (MNP).

MNP is an approach that involves the deliberate voluntary repetition or 'over-rehearsal' of target tics with the aim of promoting muscle fatigue, leading to the reduction of tic expression (Franklin, Walther & Woods, 2010). These behavioural approaches have largely been trialled and documented within single case studies (Nicassio, Liberman, Patterson, Ramirez, & Sanders, 1972; Wagaman, Miltenberger, & Williams, 1995) with few controlled, experimental trials undertaken.

The most commonly evaluated and arguably most widely applied behavioural approach to date is Habit Reversal Training (HRT). Developed and first proposed by Azrin and Nunn (1973), HRT consists of self-monitoring components and awareness building as well as relaxation and competing response training (Azrin & Peterson, 1988, cited in Dutta & Cavanna, 2013). It aims to attune the patient's awareness to the premonitory urge, a sensory experience that signals the onset of a tic. The patient is then taught to inhibit the production of the tic when they notice the premonitory urge by applying an incompatible movement, vocalisation or breathing pattern that inhibits the tic. These tic blocking gestures are referred to as 'competing responses'. Several randomised controlled trials (RCTs) have demonstrated significant improvement in tic symptoms following a course of HRT when compared to supportive psychotherapy treatment (Deckersbach, Rauch, Buhlmann and Wilhelm, 2006; Wilhelm et al., 2003). HRT has also been found to achieve greater reductions in tics compared to MNP (Azrin, Nunn & Frantz, 1980).

Exposure and Response Prevention (ERP) was developed as an 'extension to habit reversal' (Verdellen, Keijsers, Cath & Hoogduin, 2004). ERP encourages exposure to the premonitory urge that precedes the tic whilst suppressing the tic for as long as the patient feels able to. Suppression time is gradually extended during and beyond treatment. The approach is designed to promote habituation to the urge, reducing the subjective intensity of the premonitory urge and consequently,

increasing the length of time the patient is able to suppress the tic. Treatment effects of ERP have been found to be comparable to that of HRT (Verdellen et al., 2004).

Newer studies have applied an adapted behavioural protocol that combines several of the above-mentioned behavioural techniques including habit reversal training, as well as psychoeducation, contingency management, behavioural rewards and function-based interventions. This combination of behavioural techniques is referred to as a 'Comprehensive Behavioural Intervention for Tics' (CBIT; Himle et al., 2012) and has been associated with positive treatment outcomes in both children (Piacentini et al., 2010) and adults (Wilhelm et al., 2012).

McGuire et al.'s (2014) meta-analysis reviewed the efficacy of behavioural interventions for TS including HRT, ERP and CBIT treatment trials. Overall, a medium to large treatment effect of behaviour therapy was identified (standardised mean difference = 0.67), comparable to that of antipsychotic medication.

Cognitive behavioural interventions

During the 2000s, an emphasis was placed in research studies on cognitive elements of treatment. CBT includes treatment components such as cognitive restructuring alongside standard behavioural techniques. Cognitive restructuring involves identifying and adapting patients' expectations and behavioural patterns in 'high tic risk situations', described by O'Connor (2005) as specific times or places where tics have been observed to occur more frequently (e.g. at the end of the day). Other CBT approaches, such as Storch et al.'s (2012) 'Living With Tics' (LWT) protocol have employed cognitive restructuring tools to target distorted beliefs about

the meaning of having tics and the impact they have on the patient's everyday life with the aim of improving quality of life outcomes (Storch et al., 2012). Several studies have demonstrated positive treatment outcomes from Cognitive Behaviour Therapy (CBT) for TS (Morand-Beaulieu, O'Connor, Sauvé, Blanchet & Lavoie, 2015; O'Connor et al., 2001).

The cognitive behavioural approach to tic management has paved the way for the development of protocols based on third wave CBT methods. Reese et al. (2015) demonstrated the feasibility of a mindfulness-based stress reduction treatment aimed at targeting tic-related anxiety and frustration, whilst Franklin, Best, Wilson, Loew and Compton (2011) adapted an HRT protocol to include Acceptance and Commitment Therapy (ACT) components that aimed to promote the acceptance of tic-related urges. They found that this combined approach demonstrated comparable effectiveness to HRT.

Challenges and future directions for psychological interventions

Despite the positive outcomes associated with psychological interventions for TS, treatment is not widely available or accessible due to the limited number of trained practitioners (McGuire et al., 2015). To address this problem, several novel treatment delivery approaches have been developed. The structured, component-based nature of CBIT has allowed for its adaptation for alternative treatment delivery models such as telemedicine (Himle, Olufs, Himle, Tucker & Woods, 2010; Himle et al., 2012; Ricketts, Bauer, Ran, Himle & Woods, 2014) and as an intensive outpatient treatment package (IOP; Blount, Lockhart, Garcia, Raj & Peterson, 2014). IOP uses a combination of intensive, week-long, face to face sessions as well as telehealth-facilitated follow up appointments to overcome the challenges of

treatment availability for families in remote locations. Preliminary findings from a small-N case series demonstrated significant reductions in tic severity following IOP treatment, which were maintained at 6-7 month follow up (Blount et al., 2014). In addition, delivery by non-therapist health professionals such as school psychologists (Clarke, Bray, Kehle & Truscott, 2001), occupational therapists (Rowe, Yuen & Dure, 2013), and physicians and nurse practitioners (Ricketts et al., 2015a) further aims to widen the availability of behavioural treatment for TS.

This systematic review evaluates the quality of the research evidence supporting the currently available range of psychological interventions for tic disorders.

2. METHOD

2.1 SEARCH METHODOLOGY

2.1.1 Electronic search strategy

An electronic search was conducted to identify relevant peer-reviewed journal articles. Using Ovid, the search was run simultaneously on the following databases: Embase (1974 to 2015 October 16), PsychINFO (1806 to October Week 2 2015) and Ovid Medline (1946 to October Week 2 2015).

Search terms were determined by an initial look at the existing literature and preliminary 'trial' searches. The original search terms were then refined to ensure that the search strategy was both appropriately specific and sensitive. The following search terms were used: "Tourette* OR tic OR tics" featured in the title AND "behavio* OR mindfulness OR acceptance OR cognitive" featured as a keyword AND "treatment OR therapy OR intervention" featured as a keyword. Results were limited to the English language and to human subjects.

This search strategy produced 1583 citations, 597 of which were identified as duplicates and excluded using the Ovid 'De-duplicate' tool (see Figure 1 for flow diagram illustrating study selection process).

2.1.2 Citations from other sources

Four additional citations were identified for inclusion through personal correspondence with authors of the already included citations. This allowed for inclusion of very recently published articles and those that had been accepted for publication and were 'in press'.

2.2 SELECTION OF STUDIES

A preliminary review of the titles and abstracts led to the exclusion of 948 citations that were not specifically studying TS/CTD, did not focus on the effectiveness of a psychological intervention, or were not a treatment trial. The remaining 42 citations underwent a more detailed full text evaluation and 26 were excluded on the basis of study design issues which included duplicated samples, small sample case series that did not offer aggregated outcome data and the absence of a tic severity outcome measure. The remaining citations underwent a critical appraisal of methodological factors. Studies were scored using a point system developed from a combination of several existing critical appraisal tools (Centre for Evidence-based Medicine; Critical Appraisal Skills Programme, 2013; Evidence-Based Behavioral Practice; Health Evidence Bulletins, Wales; The Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions; The Scottish Intercollegiate Guidelines Network). A set of questions relating to study quality that were deemed relevant to the aims of this review were compiled from these existing quality assessments. Points were awarded for each quality factor that was fulfilled by a study, with a maximum of 17 points available. Quality criteria were split into three categories: methodological factors, statistical factors and confounding factors.

Points were awarded according to the following quality criteria:

- description of intervention;
- use of control group;
- group allocation process;
- characteristics of the evaluator;
- suitability and validity of measures;
- reporting of inclusion and exclusion criteria;
- reporting of demographic data;
- representative sample;
- reporting of outcome data including estimates of random variability;
- considerations of sample size and power analysis;
- use of statistical correction for multiple statistical tests;
- consideration of potential confounding variables and correction for these.

Five citations were excluded from the systematic review on the basis of a low appraisal score. The cut-off appraisal score for inclusion was set at 'eight or above' which was determined when reading each paper in full independent of the technical assessment and noting that each paper identified as having significant study design issues had scored seven or less points during the critical appraisal.

2.3 DATA MANAGEMENT

2.3.1 Data extraction

Personal correspondence was made with eight authors of included articles to either acquire the full text of the article or to check whether subject samples were unique to the study where this was not clear.

Data from each study was inputted into a standardised table. Data included the following information:

- sample size;
- demographics;
- comorbidity data;
- medication status;
- treatment type;
- number of treatment sessions;
- control group;
- outcome measures;
- critical appraisal score.

2.3.2 Data synthesis

Due to the inclusion of both controlled and non-controlled study designs, a narrative data synthesis approach was used.

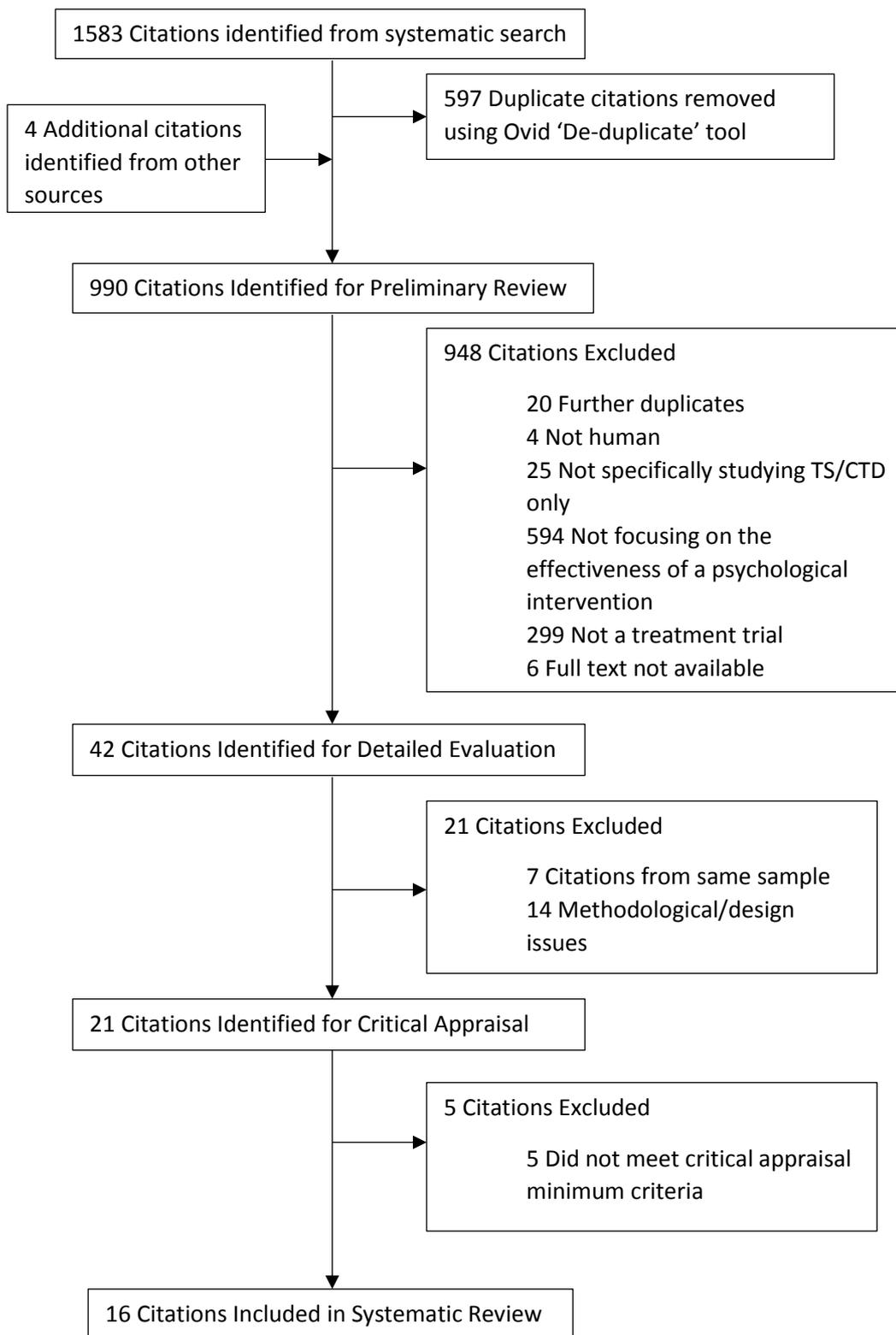


Figure 1. Study selection and rationale for exclusion

3. RESULTS

3.1 SEARCH RESULTS

Sixteen journal articles met inclusion criteria (see Table 1 for a full list of included studies). Articles were grouped into four main categories based on the type of psychological intervention they were investigating. Categories included: behavioural treatment (N=6), cognitive behavioural treatment (N=4), third wave cognitive behavioural treatment (N=2) and novel delivery modalities of behavioural treatment (N=4).

3.2 DESCRIPTION OF STUDIES

3.2.1 Outcome measures

Most studies (N=14) used the Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) as a primary outcome measure of tic severity. Other measures of tic severity included the Parent Tic Questionnaire (PTQ; Chang, Himle, Tucker, Woods & Piacentini, 2009) and the Adult Tic Questionnaire (ATQ; which is directly modelled on the PTQ), the Clinicians Global Impression – Improvement Scale (CGI-I; Guy, 1976), the Clinicians Global Impression – Severity Scale (CGI-S; Guy, 1976), the Tic Symptom Hierarchy Tracker (TSHT; Woods, 2008), Subjective Units of Distress (SUDS; Woods, 2008), direct observation, Premonitory Urge for Tics Scale (PUTS; Woods, Piacentini, Himle & Chang, 2005), Tourette Syndrome Global Scale (TSGS; Harcherik et al., 1984), Child Tourette's Syndrome Impairment Scale (CTIM-P; Storch et al., 2007a), and a daily tic diary.

Aside from tic severity, studies also measured the impact of the intervention on quality of life/life satisfaction (Deckersbach et al., 2006; McGuire et al. 2015; Storch et al., 2012), psychosocial functioning (Deckersbach et al. 2006; McGuire et al.

2015; Morand-Beaulieu et al., in press; O'Connor et al. 2001; Piacentini et al. 2010, Storch et al., 2012), impulsivity (Morand-Beaulieu et al., 2015) work and social adjustment (Franklin et al., 2011; Reese et al., 2015) occupational performance (Rowe et al. 2013) and working alliance (Himle et al. 2012).

3.2.2 Study samples

Eight studies measured the efficacy of an intervention within a child/adolescent population only, six studies focused on an adult population only, and two studies included both adult and child subjects in their treatment trials.

Sample populations were drawn from several different countries including the USA (12), Canada (2), The Netherlands (1) and Japan (1).

Table 1
Characteristics of Studies Included in Systematic Review

Study	N	Mean age	% male	% with OCD	% with ADHD	% on tic medication	Treatment	Control group	No. of sessions	Outcome measures	Critical appraisal score	Critical appraisal rating
Deckersbach et al., 2006	 30	35	 57%	 30%	 0%	 53%	 (HRT)	Supportive psychotherapy	14	YGTSS, CGI-I, SDI, SOS-10, VSP task	14	●●●
Franklin et al., 2011	 13	15	 85%	 8%	 46%	N/A	 (HRT + ACT)	HRT	HRT + ACT = 10, HRT = 8	YGTSS, CGI-I, WSAS	10	●●
Himle et al., 2012	 18	12	 94%	 22%	 28%	 28%	 CBIT (Tele-health)	CBIT (Face to face)	8	YGTSS, CGI-S, CGI-I, PTQ, WAI, TAQ	13	●●●
McGuire et al., 2015	 24	11	 75%	 38%	 42%	 54%	 (LWT)	Waitlist	10	YGTSS, CTIM-P, PedsQL, CY-BOCS, MASC	15	●●●

Study	N	Mean age	% male	% with OCD	% with ADHD	% on tic medication	Treatment	Control group	No. of sessions	Outcome measures	Critical appraisal score	Critical appraisal rating
Morand-Beaulieu et al., 2015	 20	38	 65%	 0%	 5%	 10%	 ●	N/A	14	YGTSS, TSGS, BDI, BAI, VOICI, BIS-11	9	 ●
Nonaka et al., 2015	 7	15	 71%	 0%	 0%	 100%	 ● (CBIT)	N/A	8	YGTSS, PUTS, SUDS	9	 ●
O'Connor et al., 2001	 54	39	 61%	 0%	 0%	N/A	 ●	Waitlist	12	Daily tic diary, SSI, LES, STAI, BDI, GHQ, MOCI, EPI	11	 ●●
Piacentini et al., 2010	 126	12	 79%	 19%	 26%	 37%	 ● (CBIT)	Supportive therapy and education	8	YGTSS, PTQ, CGAS	14	 ●●●
Reese et al., 2014	 18	35	 56%	 44%	 11%	 44%	 ● (Mindfulness based stress reduction)	N/A	8 (+ 4hr retreat)	YGTSS, CGI-I, ATQ, WSAS, FFMQ	10	 ●●

Study	N	Mean age	% male	% with OCD	% with ADHD	% on tic medication	Treatment	Control group	No. of sessions	Outcome measures	Critical appraisal score	Critical appraisal rating
Ricketts et al., 2015a	 9	12	 66%	 11%	 11%	 44%	 (CBIT-NP)	N/A	6	YGTSS, KBIT, CGI-S, CGI-I	11	
Ricketts et al., 2015b	 20	12	 58%	 5%	 20%	 35%	 (CBIT-VoIP)	Waitlist	8	YGTSS, MINI-Kid, WASI, CGI-I, PTQ, CPTR, TAQ	13	
Rowe et al., 2013	 30	12	 70%	 33%	 23%	 17%	 (CBIT)	N/A	8	COSA, SUDS, PTQ, TSHT	9	
Storch et al., 2012	 8	12	 75%	N/A	N/A	 38%	 (LWT)	N/A	10	YGTSS, CGI-S, CGI-I, Direct observation, CBCL, CTIM-P, MASC, PHSCS, PedsQL	9	

Study	N	Mean age	% male	% with OCD	% with ADHD	% on tic medication	Treatment	Control group	No. of sessions	Outcome measures	Critical appraisal score	Critical appraisal rating
Verdellen et al., 2004	 43	21	 79%	 14%	 30%	 40%	 (ERP)	HRT	ERP = 12, HRT = 10	YGTSS, TF-institute, TF-home	14	●●●
Wilhelm et al., 2003	 29	35	 55%	N/A	N/A	 48%	 (HRT)	Supportive psychotherapy	14	YGTSS, CGI-I	12	●●
Wilhelm et al., 2012	 122	32	 64%	 18%	 28%	 25%	 (CBIT)	Supportive treatment	8	YGTSS, CGI-I, ATQ	15	●●●

Note. Gender: ■ = male, ■ = female

OCD comorbidity: ■ = comorbid diagnosis, ■ = no comorbid diagnosis

ADHD comorbidity: ■ = comorbid diagnosis, ■ = no comorbid diagnosis

Tic medication: ■ = taking tic medication, ■ = not taking tic medication

N/A = Not Available or Not Applicable

Treatment: ● = BT, ● = BT using novel treatment delivery method, ● = CBT, ● = third wave CBT

Population sample:  = Demographic data available for recruited sample,  = Demographic data available for analysed sample

YGTSS = Yale Global Tic Severity Scale, CGI-I = Clinical Global Impression – Improvement scale, SDI = Sheehan disability inventory, SOS-10 = Schwartz

Outcome Scale, VSP = visuospatial priming, WSAS = Work and Social Adjustment Scale, CGI-S = Clinical Global Impression – Severity Scale, PTQ = Parent Tic Questionnaire, WAI = Working Alliance Inventory, TAQ = Treatment Acceptability Questionnaire, CTIM-P = Child Tourette's Syndrome Impairment Scale, PedsQL = Pediatric Quality of Life Inventory-Child Version, CY-BOCS = Children's Yale–Brown Obsessive Compulsive Scale, MASC = Multidimensional Anxiety Scale for Children, TSGS = Tourette Syndrome Global Scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, VOCI = The Vancouver Obsessional Compulsive Inventory, BIS-11 = Barratt Impulsiveness Scale, PUTS = *Premonitory Urge for Tics Scale*, SUDS = *Subjective Units of Discomfort*, SSI = Social Self-esteem Inventory, LES = Life Experience Survey, STAI = Speilberger State-trait Anxiety Inventory, GHQ = General Health Questionnaire, MOCI = Maudsley Obsessional–Compulsive Inventory, EPI = Eysenck Personality Inventory, CGAS = Children's Global Assessment Scale, ATQ = Adult Tic Questionnaire, FFMQ = Five Facet Mindfulness Questionnaire, KBIT = Kaufman Brief Intelligence Test, MINI-Kid = Mini International Neuropsychiatric Interview – Kid, WASI = Wechsler Abbreviated Scale of Intelligence, CPTR = Children's Perception of Therapeutic Relationship, COSA = Child Occupational Self-Assessment, TSHT = Tic Symptom Hierarchy Tracker, CBCL = Child Behavior Checklist, PHSCS = Piers-Harris Children's Self-Concept Scale, TF-institute = tic frequency observed at the institute, TF-home = tic frequency monitored at home
Critical appraisal: *** = scoring ≥ 13, ** = scoring 10 – 12, • = scoring ≤ 9

3.3 CRITICAL APPRAISAL

Critical appraisal scores ranged between 9 and 15 with a median score of 11.5.

Wilhelm et al. (2012) and McGuire et al. (2015) achieved the highest scores of 15.

Articles scoring below 8 were not included in this review.

3.3.1 Methodological factors

Reporting of demographic data and inclusion/exclusion criteria

Tourette syndrome is a heterogeneous disorder in which the severity of symptoms is partially influenced by patient demographics such as age and gender. TS has a higher prevalence amongst males with a typical ratio of 4:1 (Robertson, 2008) and tends to peak in severity in early adolescence, with research describing a 'bell-shaped' severity curve. Tic severity may also be influenced by stress factors, comorbid conditions, and medication status. Clear reporting of sample demographic data is therefore integral to the accurate interpretation of any study findings. The majority of studies included in this review (N=12) presented clear demographic data with mean values and measures of variance. The remaining studies presented partial data, typically omitting information on comorbidity and/or medication. All studies (N=16) reported inclusion and exclusion criteria, which typically included diagnosis, age, symptom severity, medical and treatment history, and IQ.

Description of the intervention

All 16 studies were deemed to have offered a comprehensive description of the treatment protocol used, including a description of the treatment components, total number of sessions and therapist qualifications.

Use of a control group

Ten studies used a control group which consisted of either a supportive

psychotherapy intervention (N=4), an alternative tic intervention (N=1), a waitlist group (N=3) or a treatment controlling for one aspect of the trialed intervention such as Himle et al.'s (2012) study which investigated the effect of treatment modality whilst controlling for type of treatment (CBIT) or Franklin et al.'s (2011) study which investigated the additive effect of ACT treatment components to an HRT intervention.

Eight controlled studies reported using a random allocation process to assign participants to groups, with four of these studies reporting stratification by medication status and one study also stratifying by gender (Ricketts et al., 2015b). Pre-randomisation stratification can be considered a useful technique for smaller sample sizes as a way of avoiding chance imbalances in baseline characteristics that randomisation can sometimes create (Schulz & Grimes, 2002). Franklin et al. (2011) allocated participants to groups by consecutive referral whilst O'Connor et al.'s (2001) study used partial randomisation with every third participant randomised.

Almost all the controlled studies reported testing for significant differences between the baseline characteristics of each group, with the exception of Franklin et al. (2011) who do not make reference to this process.

Validity of tic severity outcome measures

Fourteen studies used the Yale Global Tic Severity Scale (YGTSS) as the primary outcome measure. The YGTSS is a gold standard clinician-rated measure of tic severity with good validity as well as good interrater reliability (Leckman et al., 1989; Walkup, Rosenberg, Brown & Singer, 1992, cited in Deckersbach et al., 2006). In place of the YGTSS, Rowe et al. (2013) used the PTQ, TSHT and SUDS and O'Connor et al. (2001) asked participants to complete a daily tic diary with measures of tic frequency, intensity and subjective degree of control over tics, as well as using video recording for direct observation.

Criteria		Deckersbach et al., 2006	Franklin et al., 2011	Himle et al., 2012	McGuire et al., 2015	Morand-Beaulieu et al., 2015	Nonaka et al., 2015	O'Connor et al., 2001	Piacentini et al., 2010	Reese et al., 2014	Ricketts et al., 2015a	Ricketts et al., 2015b	Rowe et al., 2013	Storch et al., 2012	Verdellen et al., 2004	Wilhelm et al., 2003	Wilhelm et al., 2012	
Methodological factors	Intervention	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
	Demographic data	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Inclusion/exclusion criteria	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Participant recruitment	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Control condition	●	●	●	●	●	●	●	● ^a	●	●	●	●	●	●	●	●	●
	Independent evaluators	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Validity of outcome measures	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Criteria		Deckersbach et al., 2006	Franklin et al., 2011	Himle et al., 2012	McGuire et al., 2015	Morand-Beaulieu et al., 2015	Nonaka et al., 2015	O'Connor et al., 2001	Piacentini et al., 2010	Reese et al., 2014	Ricketts et al., 2015a	Ricketts et al., 2015b	Rowe et al., 2013	Storch et al., 2012	Verdellen et al., 2004	Wilhelm et al., 2003	Wilhelm et al., 2012	
Statistical factors	Consideration of sample size and statistical power	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	
	Reporting of statistics	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Estimates of random variability	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Correction for multiple comparisons	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
	Statistical analysis of baseline group differences	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Confounding factors	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Criteria	Deckersbach et al., 2006	Franklin et al., 2011	Himle et al., 2012	McGuire et al., 2015	Morand-Beaulieu et al., 2015	Nonaka et al., 2015	O'Connor et al., 2001	Piacentini et al., 2010	Reese et al., 2014	Ricketts et al., 2015a	Ricketts et al., 2015b	Rowe et al., 2013	Storch et al., 2012	Verdellen et al., 2004	Wilhelm et al., 2003	Wilhelm et al., 2012
Total quality count																

Note. Intervention: ● = not described, ● = partially described, ● = fully described

Demographic data: ● = not reported, ● = partially reported, ● = fully reported

Inclusion/exclusion criteria: ● = not reported, ● = reported

Participant recruitment: ● = process not described, ● = process described, ● = process described and representative sample obtained

Control condition: ● = no control group, ● = use of control group, ● = use of control group with participant randomisation

Independent evaluators: ● = evaluators not independent or difficult to determine, ● = independent evaluators

Validity of outcome measures: ● = outcome measures lack validity, ● = valid/gold standard outcome measures used

Consideration of sample size and power: ● = not considered, ● = considered

Reporting of statistics: ● = unclear reporting, ● = clear reporting

Estimates of random variability: ● = not reported, ● = reported

Correction for multiple statistical comparisons: ● = statistical corrections not reported, ● = statistical corrections reported

Statistical analysis of baseline group differences: ● = not carried out, ● = reported

Confounding factors: ● = not statistically considered and accounted for, ● = statistically considered and accounted for

^a This study used partial randomisation with every third participant randomised. This information was omitted from the publication of the study and obtained through personal correspondence with the author.

3.3.2 Statistical factors

Consideration of sample size and power analysis

Four studies reported considerations of power and sample size. Wilhelm et al. (2012) and Piacentini et al. (2010) considered attrition rate (estimated at 10%), significance level (0.05), power (80%) and an estimate of effect size (0.55) to justify their sample sizes. Franklin et al. (2011) acknowledge that their study was “not powered to conduct traditional significance testing” and present their study as a feasibility report, based on findings from an exploratory analysis. Storch et al. (2012) acknowledged that due to their small sample size, reported effect sizes would be of more worth than the reported p values. Sample sizes ranged from seven (Nonaka et al., 2015) to 126 (Piacentini et al., 2010).

Reporting of statistical results

Most of the studies presented clear results of statistical analyses and reported mean scores and measures of random variability. Twelve studies reported effect sizes, with the majority using Cohen’s d (N=7) or Partial Eta Squared (N=2), whilst Ricketts et al. (2015a) reported r values from a Wilcoxon Signed-Rank test. Piacentini et al. and Wilhelm et al. (2012) also provide specific descriptions of their effect size calculations.

Verdellen et al. (2004) also include a measure of ‘percentage of patients who improved’ (PPI) in each treatment group, based on a 30% improvement on the YGTSS, whilst Nonaka et al. (2015) report the number of patients who demonstrated 25% YGTSS improvement. These percentages are in line with research that suggests a 25% improvement on the YGTSS would reflect a clinically meaningful change (Jeon et al., 2013).

Multiple statistical comparisons

Wilhelm et al. (2012) acknowledge that no adjustments were made for multiple comparisons when testing secondary outcomes, whereas no other studies comment on the need for, or use of, such corrections.

3.3.3 Confounding factors

Most studies considered medication status, baseline tic severity and/or comorbidity as potential confounding variables and used preemptive or post-hoc methods to either reduce the impact of these or statistically control for them. All control group studies used a statistical approach to test for significant baseline differences between groups, with the exception of Franklin et al. (2011) who did not make reference to this approach. As previously mentioned, five control group studies also used a stratified allocation process to 'match' participants on baseline characteristics.

Six studies conducted post hoc statistical analyses to measure for any potential influence on outcomes from confounding variables by either incorporating these factors as covariates in the initial or secondary analyses or performing a statistical adjustment. Deckersbach et al. repeated their analysis including baseline medication status and comorbidity as covariates, whilst Wilhelm et al. (2003) included baseline measures of tic severity and impairment as covariates. Wilhelm et al. (2012) and Piacentini et al. report that neither medication status nor baseline tic severity moderated treatment outcome on the YGTSS.

Piacentini et al. and Himle et al.'s studies were conducted across multiple sites and both therefore included 'site of treatment' as a variable in the initial analyses with neither finding any significant differences in treatment outcome across sites.

Verdellen et al. compared eight sessions of HRT to 10 sessions of ERP and

adjusted for the unequal number of treatment sessions in the statistical analysis by obtaining weighted gain scores.

Six studies conducted an 'intention to treat' analysis to control for a potential dropout effect (Deckersbach et al., 2006; McGuire et al., 2015; Piacentini et al., 2010; Ricketts et al., 2015b; Verdellen et al., 2004; Wilhelm et al., 2012). Eight studies conducted analysis on completers only, and three studies reported no dropouts (Franklin et al., 2011; Rowe et al., 2013; Storch et al., 2012).

3.4 OUTCOMES

3.4.1 Behavioural treatment

Six studies investigated the efficacy of behavioral treatment for TS. Wilhelm et al. (2012), Piacentini et al. (2010) and Nonaka et al. (2015) examined the efficacy of CBIT, Deckersbach et al. (2006) and Wilhelm et al. (2003) examined the efficacy of an HRT intervention, whilst Verdellen et al. (2004) compared treatment response to HRT versus ERP.

Habit Reversal Training

Most of the studies in this review investigated the efficacy of behavioural treatment for TS. The earliest of these studies being an RCT conducted by **Wilhelm et al. (2003)** that investigated the efficacy of HRT for TS by randomly assigning 32 adult participants to either 14 sessions of HRT or supportive psychotherapy. Outcome was measured using the YGTSS and analysis found that at post-treatment and at 10-month follow-up, HRT patients had significantly lower tic severity and functional impairment scores compared to the comparison group. This effect was maintained when statistically controlling for baseline severity and impairment. The authors concluded that habit reversal training should be considered an effective behavioural treatment for TS.

This study benefits from the use of a comparison group that controlled for non-treatment related effects such as therapist contact. It does however also have limitations. Participants were recruited in part through newspaper advertisements, an opportunity sampling method that carries a self-selecting bias and therefore may not be wholly representative of the general TS population. Although a gold standard tic severity measure was used, raters were not blind to group allocation, leaving the outcome measure vulnerable to bias from rater expectations. Nevertheless, this study paved the way for larger studies to follow suit and address some of these key validity issues.

Deckersbach et al. (2006) were able to replicate much of Wilhem et al.'s methodology with a sample of 30 adult participants. This RCT compared the efficacy of HRT and supportive psychotherapy on tic severity, life satisfaction and psychosocial functioning. Furthermore, participants were asked to complete a pre-treatment visuo-spatial priming task to measure behavioural response inhibition, in order to investigate whether baseline response inhibition would be a predictor of treatment response. Outcome measures included the YGTSS and CGI-I as measures of clinical change, as well as the Sheehan disability inventory (Leon et al., 1992, cited in Deckersbach et al., 2006) which measured psychosocial functioning and the Schwartz Outcome Scale (SOS-10; Blais et al., 1999, cited in Deckersbach et al., 2006) which measured life satisfaction. Results indicated that the HRT group demonstrated significantly lower levels of tic severity mid-treatment (8 weeks) and post-treatment when compared to the control group. These outcomes were maintained when controlling for baseline tic severity, comorbidity and medication. This suggests that a shorter treatment protocol of eight sessions may be just as effective as a longer course of treatment. Both groups showed improvement on psychosocial functioning and life satisfaction measures, highlighting the potential

benefits of supportive psychotherapy as a treatment approach for TS where HRT may not be available. Patients demonstrating greater inhibitory priming at pre-treatment showed greater tic severity improvements following HRT, suggesting that inhibitory processes may mediate treatment response.

This study would benefit from a larger sample and similar to the study by Wilhelm et al., did not use rater-blinded outcome measures leaving it at risk of rater-bias.

Exposure and Response Prevention

Verdellen et al. (2004) compared the efficacy of two behavioural treatments: HRT and ERP. They conducted an RCT with 43 TS patients allocated to either 10 sessions of HRT or 12 sessions of ERP. A cross-over design was used meaning that after treatment completion, participants were offered the alternative approach as an additional treatment and findings from this second phase of the study were analysed separately to assess for any additional treatment benefits. The impact of treatment on tic severity was measured by the YGTSS and a tic frequency count during an observation of a 15 minute videotaped session in the clinic, as well as a tic frequency count by a family member during a 15 minute direct observation at home. Unlike the previously mentioned studies, assessors were blind to treatment allocation.

Multivariate analysis showed that both treatment groups significantly improved on measures of tic severity and there were no significant differences between treatments suggesting that both ERP and HRT are good behavioural treatment options for TS.

The second phase of the study showed additional improvement in patients receiving ERP following HRT, but no additional improvement in patients receiving HRT following ERP suggesting that ERP may offer supplementary therapeutic benefits.

Tic frequency measures were weakly related ($r = 0.25$) suggesting low reliability of one or more measures. Video and direct observation can be limited by the impact of context-specific tics and although the comparison group will have controlled for this variable to some extent, context-specific observational assessments may still inevitably prove less reliable than standardised measures of tic severity.

Although Verdellen et al. controlled for unequal treatment lengths (10 versus 12 sessions) through the use of weighted gain scores, no statistical adjustment was applied to account for unequal session duration times. Descriptions of treatment protocols in this article mention that each ERP session lasted 120 minutes, whilst HRT sessions are described as lasting 60 minutes meaning that even when controlling for number of treatment sessions, participants in the ERP group would have received twice as much patient-therapist contact time compared to the HRT group.

Comprehensive Behavioural Intervention for Tics

The largest RCT included in this review was conducted by **Piacentini et al. (2010)**. It investigated the efficacy of an eight session Comprehensive Behavioural Intervention for Tics (CBIT) compared to a control group offering supportive psychotherapy and education. Clinical outcomes were measured using the YGTSS and CGI-I in a sample of 126 children.

Following 10 weeks of treatment, scores on the YGTSS improved significantly more in the CBIT group compared to the supportive psychotherapy group, with a group difference effect size of 0.68, whilst the CGI-I recorded a significantly larger percentage (52.5%) of 'improvers' (those rated as 'very much improved' or 'much improved') compared to the control group (18.5%), suggesting a clinically meaningful improvement for participants completing the CBIT treatment. Woods et

al. (2011) conducted a further analysis on the same sample, examining the effects of CBIT on secondary psychiatric symptoms as well as psychosocial symptoms. Results found that positive response to treatment at 10 weeks was also associated with an improvement in secondary psychiatric and psychosocial symptoms at 6-month follow-up, highlighting the potential added benefits of CBIT.

This was a large sample study with good demonstrable power, low attrition rate and independent, blinded raters. Interventions were matched for treatment duration and length and potential confounds such as medication status and baseline tic severity were considered in the analysis.

Wilhelm et al. (2012) conducted a similarly large RCT with 122 adult participants comparing the efficacy of eight sessions of CBIT to an eight session control group offering 'supportive treatment'.

Results found CBIT to be more effective at reducing symptoms on the YGTSS than the control condition. The analysis also found a significantly greater proportion of improvers as measured by the CGI-I in the CBIT group compared to the control condition. The analysis controlled for possible site effects as well as baseline tic severity and medication status.

It is worth noting that the authors report on six participants who scored above 30 on the severity ratings of the YGTSS at baseline (the inclusion threshold for the study). This score indicates a very high level of severity in these participants. It is stated that three of the six participants were then accepted onto the trial following a panel review. The reason for this is not elaborated on in the article suggesting a possibility of bias as a result of pseudo-systematic selection methods.

A comparison between the two largest CBIT studies, Piacentini et al. and Wilhelm et al. (2012) suggests that CBIT may be more effective for children than adults, with Piacentini et al. demonstrating comparatively larger effect sizes on both the YGTSS

and CGI-I with a similar methodology and sample size.

Nonaka et al. (2015) present a small, yet important, study that evaluates the feasibility of a CBIT intervention in a non-Western population. Seven Japanese subjects were offered nine sessions of CBIT and evaluated both pre- and post-intervention to assess for treatment effects. TS symptoms were measured using the YGTSS, PUTS and a subjective units of distress scale (SUDS). Analysis showed a significant improvement on the YGTSS and SUDS, but not on the PUTS suggesting that subjects may continue to experience a similar level of premonitory urges despite an overall reduction in tic expression and distress.

It is worth noting that one participant dropped out of the study after the third treatment session due to finding it too difficult to talk about their tics. This participant was not included in the analysis and therefore the possibility of a dropout effect should be considered.

As this is a small study with no control group, it is difficult to determine how much of the change seen in these measures can be attributed to treatment effects. TS symptoms typically fluctuate over time (Robertson, 2008) and natural recovery is common, particularly in adolescence. Without a control group, it is difficult to determine how much of the symptom change may be as a result of the natural waxing and waning of the symptoms. Despite these limitations, it is the only non-Western study included in this review, and contributes evidence to the cross-cultural validity of CBIT.

3.4.2 Cognitive behavioural treatment

The majority of studies included in this review focus on behavioural treatment such as HRT and CBIT, however, there are also a number of studies that have based their trials on a cognitive behavioural treatment protocol. Four CBT studies have

been included in this review, implementing either the O'Connor et al. (2005) protocol (cited in Morand-Beaulieu et al., 2015) or the 'Living with Tics' protocol (a broad-ranging CBT approach developed by Storch et al., 2012). These two tic treatment protocols are comparable as they both augment traditional behavioural techniques with cognitive restructuring components.

'Living With Tics'

Storch et al. (2012) reported on a sequential case series of eight youth that underwent CBT treatment for tics using the 'Living with Tics' (LWT) protocol. The LWT protocol consists of modules that include psychoeducation and cognitive restructuring targeting distorted beliefs. The focus of this approach is to improve quality of life rather than directly reduce tic severity, however an introduction to HRT strategies is also included with the aim of contributing to the individual's self-efficacy. This is a needs-assessed modular intervention in which the choice of modules and time devoted to each module is tailored to the individual needs of the child.

Tic severity was measured pre- and post-treatment using the YGTSS, the Clinical Global Impression-Severity (CGI-S) scale and via direct observation. In addition to this, changes over time in child behavior, impairment, self-concept, anxiety and quality of life were measured. Significant improvements were seen on the CGI-severity scale as well as the impairment subscale of the YGTSS, but not on the overall YGTSS total score, suggesting improvement in impairment but not in overall tic severity. No significant change was recorded from direct observation.

Furthermore, the study found significant improvement in anxiety, self-concept and quality of life following treatment completion.

This study suggests that augmenting traditional behavioural treatment with cognitive components can help to address emotional and cognitive symptoms associated with

TS that may not be directly addressed by traditional behavioural treatment.

This was a small case series designed to investigate the feasibility and acceptability of the LWT protocol: a new CBT protocol for tics. Due to the small sample size, there are limitations to the extent that statistical significance testing could accurately measure change over time. Raters were not blinded and the study was susceptible to the vulnerabilities typical of uncontrolled treatment testing. Limitations of this study were addressed in a larger trial of LWT by **McGuire et al. (2015)**.

McGuire et al.'s study evaluated the efficacy of the LWT protocol relative to a waitlist control group with a sample of 24 children and adolescents. Similar outcome measures were used as in Storch et al.'s study with the addition of the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS).

Significant improvement was demonstrated on the YGTSS impairment scale and quality of life scale, as demonstrated in Storch et al.'s findings. No significant change was seen on the YGTSS total tic score or anxiety scale. Furthermore, after the waitlist participants were offered LWT treatment, an open-trial analysis was conducted on a larger sample of 19 subjects which found significant improvement on all measures following treatment, suggesting that previous analyses may have been under-powered to find smaller effects of treatment.

The use of a non-active control group leaves this study vulnerable to bias as it would be difficult to control for any clinical change attributable to non-specific therapeutic components and use of an active control could be an important future adaptation to this study. It is also important to acknowledge that only waitlist participants classed as 'completers' (N= 10/12) were later offered the active treatment and only 7 out of these 10 participants accepted and undertook this treatment and hence were included in the open-trial analysis. Using completers only increases the risk of a dropout effect and reasons for why the other three participants declined participation

at this stage were not provided. This leaves the potential for a self-selecting bias in the open-trial analysis, suggesting that results should be interpreted with caution.

This is, however, the first modular intervention for children with TS which reports a potentially effective, broad ranging treatment which also takes into account co-occurring conditions.

One of the earliest trials, conducted by **O'Connor et al. (2001)**, looked at the effectiveness of a CBT treatment program for individuals with chronic tic disorders (CTD) and habit disorders (HD). Forty-four adult participants diagnosed with chronic tic disorder completed a daily tic diary recording frequency, intensity and self-perceived ability to control tics at pre- and post-treatment. Fourteen of these participants were placed in a waitlist control group to control for the natural fluctuations in tic severity. Video observations were also recorded and independently-rated.

Following a 12-session treatment programme, the intervention group demonstrated a significantly greater decrease in tic frequency and intensity and an increase in self-perceived degree of control compared to the control group. There was also a significant decrease in symptoms on accompanying questionnaires in the CBT condition including the Beck Depressive Inventory (BDI), the General Health Questionnaire (GHQ), and the Spielberger State-trait anxiety Inventory (STAI). A significant increase in self-esteem was also reported on the Social Self-esteem Inventory (SSI).

This study was one of the first controlled trials to investigate the efficacy of CBT as a tic treatment. Although it used a waitlist control group as part of the experimental design, baseline group differences between the intervention and waitlist group were not tested for, making it difficult to attribute any changes observed in the treatment condition to the intervention rather than pre-existing group differences. O'Connor et

al. also note the initial exclusion of subjects with 'severe' or 'extreme' TS and/or comorbid psychiatric conditions. Most studies in this review have included participants with comorbidities such as OCD or ADHD given the high prevalence of these co-occurring with TS. This exclusion makes findings from O'Connor et al.'s study less generalisable to the TS population.

Morand-Beaulieu et al. (2015) observed the effect of CBT on tic severity, inhibition and motor activation in a pre-post design. A stimulus-response compatibility inhibition task was used to measure change in inhibition, whilst electrophysiological recordings, such as event related potentials (ERPs), measured motor cortical activation. Tic severity was measured by the YGTSS and TSGS.

Twenty adult patients attended a 14-session course of CBT that included traditional components of HRT as well as elements of cognitive restructuring practiced in 'high tic-risk situations'. Results found that tic symptoms, as measured by the YGTSS and TSGS, significantly improved following CBT whilst CBT also appeared to have a normalising effect on cortical motor activation. There was no significant change in inhibitory function.

It should be noted that this study had a high dropout rate (30%), which may in part have been due to the large amount of testing involved as part of the assessment procedure or the lengthy treatment protocol. The likelihood of a drop out effect may therefore need to be considered when evaluating findings.

The authors also highlight the impact of having a wide age range of participants when measuring certain ERPs that would be dependent on brain maturation and therefore, developmental stage. Despite the limitations, these findings contribute evidence to the range of benefits associated with CBT treatment for tics and highlight the need for research to further explore potential neuropsychological treatment outcomes.

3.4.3 Third wave cognitive behavioural treatment

Two studies investigated the efficacy of third wave CBT approaches, augmenting standard protocols with components of ACT (Franklin et al., 2011) and mindfulness-based stress reduction (Reese et al., 2015).

Franklin et al. (2011) piloted an HRT protocol combined with components of ACT (HRT+ACT) and compared against an HRT-only control. Thirteen adolescents and young adults received either 10 sessions of HRT or 12 sessions of HRT+ACT.

Tic severity was measured using the YGTSS and findings suggest that both groups demonstrated significant improvement in tic symptoms over time, but found no significant difference between the two interventions. CGI-I scores did however indicate that the HRT condition may have been slightly more effective than the HRT+ACT condition, indicating that ACT components may not have necessarily provided additional therapeutic benefits.

It is important to consider these results in the context of the study's limitations. Firstly, as is the case for most feasibility studies, this study was underpowered. Secondly, the two treatment groups did not have an equal amount of treatment sessions and this disparity does not appear to be addressed in the statistical analysis, making direct comparison between interventions difficult. Thirdly, the study mentions using five different therapists to administer treatment, one of which had significantly more experience in ACT than the others. The authors considered expertise as a potential confound and conducted a post-hoc comparison between YGTSS scores achieved by the 'beginner' versus 'intermediate' ACT therapists. This comparison was depicted visually on line graphs and based on a visual inspection of the line graph the authors note that there appears to be a difference in clinical change achieved by the beginner versus intermediate therapists, in favour of the latter. This suggests the importance of controlling for therapist expertise in any

future studies in this area. The authors also note that potential moderators such as psychiatric comorbidity were not considered in the analysis due to a lack of statistical power.

Reese et al. (2015) investigated the efficacy of a Mindfulness-Based Stress Reduction intervention for tics (MBSR-tics). Eighteen subjects were offered eight treatment sessions and a 4 hour retreat as part of an uncontrolled open trial. Treatment outcomes were measured using the YGTSS, CGI-I, adult tic questionnaire (ATQ), the work and social adjustment scale (WSAS) as well as the Five Facet Mindfulness Questionnaire (FFMQ) to measure change in self-reported mindfulness.

Results show significant symptom reduction on the YGTSS tic severity score ($d=1.03$) and tic-related impairment ($d=1.17$) with treatment gains maintained at 1-month follow-up. These clinical changes accompany significant increases in self-reported mindfulness as measured by the FFMQ, and further analysis demonstrates how increases on the FFMQ were positively predictive of clinical change on the YGTSS ($r=0.57$, $p=0.018$).

The authors acknowledge the need for blind assessment as well as a valid control condition to test whether clinical change is in fact attributable to mindfulness skill acquisition specifically and not just a result of the relatively large amount of therapy hours offered (20 hours). Despite the large amount of sessions, this is a relatively cost effective intervention given the group format and provides general support for the future use of group-based tic treatment.

3.4.4 Novel treatment delivery modalities

Four studies addressed the issue of limited treatment availability by piloting novel treatment delivery methods. All four studies adapted the standard CBIT protocol. Of

these four studies, two investigated the feasibility of using communication technology to deliver behavioural treatment remotely. Ricketts et al. (2015) tested preliminary efficacy and feasibility of a voice-over internet protocol, whilst Himle et al (2012) observed response to a behavioural treatment delivered via videoconference technology.

A further two studies addressed the accessibility issue by piloting the delivery of behavioural treatment by health professionals other than psychologists. Ricketts et al. (2015) observed treatment response to an abbreviated version of the CBIT protocol administered by nurse practitioners in developmental paediatrics and neurology clinics, whilst Rowe et al. (2013) observed response to a CBIT protocol administered by trained occupational therapists.

Treatment delivery within novel clinical settings

To increase the availability of behavioural treatment for the TS population, recent studies have tested the feasibility of non-psychology health professionals delivering CBIT in outpatient clinics. As TS patients are often first referred to neurology and paediatric clinics for assessment and consultation regarding their tic symptoms, **Ricketts et al. (2015a)** conducted a study evaluating the acceptability of an abbreviated CBIT protocol (CBIT-NP) delivered by either a nurse practitioner or physician with specialist neurology and/or developmental paediatric expertise.

Nine youth completed six sessions of CBIT-NP each lasting 20-25 minutes. Measures of tic severity including the YGTSS and CGI-S were taken pre- and post-treatment. Results identified a significant reduction on the YGTSS total tic score and impairment score as well as a significant reduction in global impairment as measured by the CGI-S, with 56% of the sample classified as treatment responders.

This study highlights the potential efficacy of a relatively short course of behavioural

treatment for tics. Due to the limited time available in each session, a greater emphasis was placed on homework tasks to be completed in between sessions. As a result, homework non-adherence may pose a significant barrier to the effectiveness of CBIT-NP.

It is important to note that the study was uncontrolled and the sample size was small. Furthermore, evaluators were not blinded to pre- or post-treatment conditions and were aware of the study's hypotheses. The study suffered a 36% attrition rate which raises questions about the acceptability of this treatment despite good satisfaction ratings reported by treatment completers. Addressing these issues could help refine a protocol that not only increases treatment availability but due to its clinical setting, may also help patients receive appropriate treatment sooner.

Similarly to Ricketts et al., **Rowe et al. (2013)** explored the delivery of behavioural treatment by non-psychology practitioners, piloting an eight session CBIT protocol delivered by an occupational therapist. Thirty children took part in this study and were evaluated pre- and post-treatment using the PTQ, SUDS and the Tic Symptom Hierarchy Tracker (TSHT) which all measured tic severity, as well as the Child Occupational Self-Assessment (COSA) which measured changes in occupational performance. Following treatment, a significant reduction in scores on the PTQ and SUDS was observed as well as a significant improvement in self-perceived occupational performance.

This study did not benefit from a control condition, making it difficult to determine the specific effect of the intervention above and beyond generic therapeutic effects such as those garnered from therapist-contact. Additionally, it is important to note that tic outcomes were not independently rated, making them vulnerable to experimenter bias. The authors also question the validity of the COSA as a measure of occupational performance in patients with tic disorders as it was not originally

designed to be used for this purpose.

Nonetheless, these findings support the feasibility of non-psychologist health professionals, such as occupational therapists, administering CBIT. This treatment approach demonstrates the potential and opportunity for experts with different training backgrounds to transfer their skills and contribute to the delivery of TS interventions. In this example, occupational therapists could use their knowledge of functional performance to expand the focus of behavioural tic treatment to secondary outcomes such as improved general functioning and quality of life outcomes in addition to focusing on tic symptom improvement.

Remote treatment delivery using communication technology

To further address the limited availability of behavioural treatment for tics, studies have evaluated the efficacy of novel treatment delivery modalities to help increase therapy provision. **Himle et al. (2012)** explored the effectiveness of CBIT delivered via videoconference technology by recruiting twenty children to a randomised controlled pilot trial comparing videoconference delivery to traditional face to face CBIT.

Clinical change was measured using the YGTSS, CGI-I and Parent Tic Questionnaire (PTQ). The analysis took into consideration 'site' as a variable in this multi-site trial as well as condition and time. Results identified a significant improvement in tic symptoms for both conditions on both the clinician-rated YGTSS and parent-rated measure, with no significant difference between the two delivery modalities and no effect of site. Whilst the sample size is small, these results provide some evidence for the comparable efficacy of videoconference CBIT and face to face CBIT, and present a promising treatment alternative that can help overcome geographical barriers to treatment provision. Crucially, children and adults

found both forms of delivery acceptable and there were no significant differences on working alliance scales as one might predict when comparing a face to face contact to telehealth.

Building on these findings, **Ricketts et al. (2015b)** investigated the efficacy of voice over internet protocol-delivered CBIT (CBIT-VoIP), a telehealth delivery modality that can be set up at a patient's home using an ordinary computer, internet connection and web camera. Twenty youth were randomised to either CBIT-VoIP or a waitlist control. The CBIT-VoIP group received CBIT delivered by a Master's level trained therapist via Skype software.

Outcomes were measured using the YGTSS and PTQ. The CBIT-VoIP group demonstrated a significantly greater improvement in tic severity over time (28.2%) compared to the control group. This is a similar tic severity reduction to that observed in the original VOIP trial (33%; Himle et al., 2012) and in a large study of face to face CBIT (30.8%; Piacentini et al., 2010). Differences between the intervention and control group on impairment score change, however, did not meet significance, in contrast to the original VOIP trial (Himle et al., 2012) where a significant reduction in impairment was observed. The authors hypothesised that this may have been due to a delayed therapeutic influence on psychosocial functioning.

Results found a significantly larger proportion of CGI-I treatment 'responders' in the CBIT-VoIP condition relative to the control, however the proportion of responders in the CBIT-VoIP condition (33%) was still significantly lower than both the original VOIP trial (80%; Himle et al., 2012) and the large face to face CBIT trial (52.5%; Piacentini et al. 2010). This may have been in part due to technical difficulties recorded in a large proportion (37.6%) of CBIT-VoIP sessions. Future studies evaluating telehealth delivery of CBIT could benefit from implementing changes to

the internet protocol to reduce the likelihood of technological difficulties.

Therapists also reported difficulties with child and parent focus and homework adherence in the intervention condition. These difficulties may have arisen as a result of this study being largely conducted from the subjects' homes without specialist technology, unlike Himle et al (2012)'s study, which used a similar methodology within a university setting with specialist equipment. Rickett et al.'s methodology strengthens the ecological validity of this study and presents a treatment approach that can be easily implemented with the wider treatment-seeking TS population. Adaptations to the protocol such as adding internet programs for homework completion and improving the sound and visual quality could contribute to better future treatment adherence and outcomes. This study could also benefit from an active control condition such as face-to-face CBIT, in order to enable a more specific measurement of the effect of treatment modality whilst controlling for therapeutic contact.

3.4 SUMMARY

This review draws together empirical support for established behavioural approaches with an emerging evidence base for new and adapted psychological interventions, evaluating the quality of the evidence base as a whole so that conclusions can be made for best practice.

Literature findings from the systematic search illustrate a shift in experimental focus within the area of TS. Where older studies have focused on measuring the efficacy of traditional behavioural approaches such as HRT and ERP, more recent studies have focused on evaluating treatment outcomes for adapted and enhanced multi-component approaches such as LWT (McGuire et al., 2015) and HRT+ACT (Franklin et al., 2011) that draw together multiple therapeutic tools, as well as novel

treatment delivery methods (Ricketts et al., 2015a), with the aim of improving both outcomes and treatment accessibility. This shift in empirical focus addresses some of the current challenges that behaviour therapy for tics faces, such as limited or partial patient therapeutic response and treatment availability (McGuire et al., 2015).

Findings from this review highlight a discrepancy in the quality of research in psychological interventions for TS. Behavioural approaches such as HRT and CBIT appear to be supported by larger, more rigorous RCTs, whilst there is a noticeable lack of RCTs supporting the more recently developed third wave therapeutic approaches. Treatments such as mindfulness-based stress reduction for tics could benefit from controlled trials with larger samples. This in turn would enable direct comparisons to be made more confidently across the evidence base. The most rigorous of the studies included in this review are Piacentini et al. (2010) and Wilhelm et al. (2012), benefiting from large samples enabling well-powered designs with statistical consideration for potential confounds such as medication and baseline tic severity. These two studies reported similarly large effect sizes, demonstrating significant reductions in tics and tic-related impairment in individuals following behavioural treatment. Slightly larger effect sizes were observed in the child sample (Piacentini et al.) compared to the adult sample, producing results comparable to that of large placebo-controlled drugs trials of antipsychotic medication (Sallee et al., 2000). These findings support the use of behavioural therapy for TS and set a high quality standard for future research.

4. DISCUSSION

4.1 CONCLUSIONS

This review includes studies with a broad range of research quality investigating a variety of different therapeutic approaches. Despite this, positive outcomes still appear to be demonstrated across the range of treatments. These findings are supported by research studies that have explicitly compared two different treatment protocols (Franklin et al., 2011; Verdellen et al., 2004) and found comparable results. Studies evaluating traditional behavioural methods demonstrated the greatest treatment response overall, however these traditional approaches are also supported by more rigorous empirical research. Given that the body of high quality RCTs sits within traditional behavioural approaches, newer approaches will require high quality evaluation before conclusions about 'a best approach' can be made.

4.2 METHODOLOGICAL ISSUES

Conclusions made from this review should be considered in the context of the collective limitations of the studies included. Firstly, as mentioned previously, considerable sample size variation across studies was observed. Most of the studies included in this review described themselves as pilot or feasibility studies to reflect the relatively small sample sizes, which is naturally a limitation of the literature overall. Sample sizes ranged from 7 (Nonaka et al., 2015) to 126 (Piacentini et al., 2010), indicating varying levels of study quality and suggesting that direct comparisons between studies should be made with caution.

Secondly, it is important to acknowledge the lack of cross-cultural empirical evidence in this area of research, with most of the study samples included in this review representative of North American populations and only one of an Asian and

one of a European population. At present, there is no available data from studies in Africa.

The review consisted of ten controlled trials and seven uncontrolled pilot studies. By including both controlled and single group studies, this review offers a broad reflection of the current literature available. Studies that do not have a control group do however present significant challenges when drawing comparative conclusions amongst patient populations that experience regular disease status fluctuation and natural recovery (Paulus et al., 2014). These challenges are relevant to TS populations for whom symptoms regularly wax and wane and for whom (natural or treatment-aided) recovery by the age of 18 is common. However, it can be argued that the potential for natural recovery diminishes with increasing disease duration (Ip et al., 2013) and therefore studies that exclude recently diagnosed participants may be less prone to the potential for natural recovery amongst participants during the treatment trial. Studies included in this review excluded participants exhibiting tic symptoms for a duration of less than one year, theoretically reducing the risk of natural recovery during the study and increasing the possibility of capturing a meaningful treatment effect (Ip et al., 2013).

This review is broad-reaching of study methodology. Higgins and Green (2011) discuss the importance of undertaking, and therefore reporting on, non-randomised or uncontrolled trials, acknowledging that these studies evaluate initial feasibility that contributes to the development of future RCTs. These studies therefore hold an important functional purpose as part of the evidence base. Paulus et al. add that findings from pre-post design studies may also play a part in contextualising the findings of studies using alternative methodology.

4.3 CLINICAL IMPLICATIONS

This review found positive results across a range of therapeutic approaches, suggesting that clinicians and patients may have some choice when deciding on the best course of psychological treatment for TS. However, it is important to consider that different protocols will place an emphasis on different treatment outcomes, with HRT focusing more heavily on direct improvement of tic symptoms and the LWT protocol placing an emphasis on quality of life outcomes and co-occurring conditions (e.g. anger, self-esteem, behaviour). It will therefore be important to determine the patient's clinical needs and specific therapy goals before any final treatment decisions are made.

Certain treatment protocols may also be more compatible to patients with comorbid disorders such as OCD or ADHD, offering transferable therapeutic skills. One example of this is ERP, a tic treatment that is also typically used to manage OCD symptoms (Abramowitz, 1996) and may prove a more intuitive treatment choice for individuals with comorbid TS and OCD. Comorbid ADHD on the other hand, has been found to be a significant moderator of behavioural treatment effect in individuals with TS (McGuire et al., 2014; Theule, Ward, Cheung & Lee, 2015), highlighting the importance of acknowledging individual factors such as patient comorbidity and treatment history when deciding upon a course of treatment. Further research into individual treatment mediating factors may improve successful treatment prescribing for patients.

Evidence supporting newer treatment modalities such as telehealth (Himle et al., 2012; Ricketts et al., 2015b) offers practical solutions to the issues of limited clinician availability. These approaches have also contributed to the development of further innovative treatment delivery solutions such as intensive outpatient programmes.

4.4 FUTURE RESEARCH

Future research would benefit from a focus on high quality, well-powered studies that benefit from active controls, particularly when looking to replicate findings from some of the newer pilot studies emerging amongst the evidence base. As psychological treatments for TS continue to be developed, adapted and refined, and given the large variety of approaches demonstrating positive results, dismantling studies may help contribute to our understanding of the key active mechanisms of change within TS treatment. Recent meta-analytic data has considered the influence of separate therapeutic components (e.g. psychoeducation, relaxation training, contingency management) on psychosocial treatment efficacy. Theule et al. (2015) found a positive relationship between tic reduction and the inclusion of contingency management components, whilst interestingly, the inclusion of psychoeducation components corresponded to reduced treatment efficacy. The authors theorise that psychoeducation may take time away from the practice of tic management skills, leading to poorer outcomes. Future research would benefit from a further exploration of these ideas.

A small body of emerging new research offers support for alternative approaches to cognitive behavioural therapies for TS such as exercise and music therapy. Packer-Hopke (2014) found that a six-week aerobic exercise programme led to improvements in TS symptoms and quality of life in a small study of five TS participants, whilst a larger trial of 18 youth demonstrated an improvement in mood and anxiety levels as well as a reduction in tics during and post-exercise (Nixon, Glazebrook, Hollis & Jackson, 2014). Listening to music, live performance of music and musical mental imagery have all also been found to significantly reduce tic frequency (Bodeck, Lappe & Evers, 2015). Further research is needed to robustly explore the potential benefits of these novel approaches as well as the opportunity

for incorporating these components into established modular treatments such as CBIT or LWT, with the aim of enhancing outcomes.

Tourette Syndrome research offers potential for future development in many areas including cross-culturally, via alternate delivery methods, using modular protocols, novel treatment components and multidisciplinary approaches. Large tic treatment trials and meta-analytic data have made a strong case for psychological treatments (Richards & Black, 2015). Robust, high quality research studies are now needed in order to support empirical expansion that addresses existing barriers to the clinical application of these methods.

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PART 2: EMPIRICAL PAPER

**A 12-MONTH FOLLOW-UP STUDY EVALUATING GROUP
PSYCHOLOGICAL INTERVENTIONS FOR CHILDREN WITH TOURETTE
SYNDROME**

Dabrowski, J. (2016, June). *What are the long-term outcomes of group-based CBIT and psychoeducation?* Poster session presented at the 9th European Conference on Tourette Syndrome and Tic Disorders, Warsaw, Poland.

ABSTRACT

Aims

Tourette Syndrome (TS) is a neurodevelopmental disorder characterised by the presence of both motor and phonic tics. It is often associated with psychiatric co-morbidity, social and emotional difficulties, impaired school functioning and a diminished quality of life. Comprehensive Behavioural Intervention for Tics (CBIT) is a behavioural therapy with strong empirical support for its effects on tic severity when offered as an individual therapy, and emerging evidence for its effectiveness in a group format. Psychoeducational (PE) group interventions provide children with information about tics and target impairing psychosocial and co-morbid difficulties typically associated with TS. The objective of this study was to compare the long-term effects of CBIT and PE groups.

Method

Twenty-eight participants with TS were assessed 12 months after completing a course of either group-based CBIT or PE. Participants completed measures assessing tic severity, self-reported quality of life (QOL) and neuropsychological functioning. School attendance data was also collected.

Results

Both groups demonstrated long-term improvement in tic severity which included significant continued improvement during the follow-up period ($p = 0.012$, $\eta_p^2 = 0.22$). Long-term improvements were found for measures of self-reported QOL ($p = 0.004$, $\eta_p^2 = 0.25$) and both groups showed significant post-treatment improvement in school attendance ($p = 0.004$, $\eta_p^2 = 0.30$). An association between tic suppression ability and self-report QOL was observed at follow-up ($r = -.52$, $p = 0.016$). No systematic effects of either treatment were found on neuropsychological measures.

Conclusions

Group-based interventions were associated with lower tic severity, improved quality of life and more frequent school attendance 12 months post-treatment. These results support the implementation of CBIT and PE group treatments for children with TS.

1. INTRODUCTION

Diagnosis and epidemiology

Tourette Syndrome (TS) is characterised by the presence of two or more motor tics and at least one phonic tic for a period of one year. Tics are sudden, rapid, involuntary movements or vocal sounds that are often preceded by an aversive sensory experience, termed the premonitory urge (PU), which signals their onset. Common tics include eye blinking, sniffing and neck movements (McGuire et al., 2015). Where only either motor or vocal tics are present, a diagnosis of chronic tic disorder (CTD) is described (American Psychiatric Association, 2013; ICD-10). The prevalence of TS is estimated at approximately 1% amongst 5-18 year olds (Robertson, 2008) with prevalence at least three times higher amongst males than females (Bitsko et al., 2014). Symptoms typically first present at ages 6-8 years (Peterson, Pine, Cohen & Brook, 2001) and reach peak severity between 10-12 years, with an improvement in symptoms usually seen throughout late adolescence and adulthood (Pappert, Goetz, Louis, Blasucci, & Leurgans, 2003).

Neurobiology

The neurobiological nature of TS has been examined with the help of brain imaging and neurophysiological studies. Findings from these studies implicate the cortico-striatal-thalamo-cortical (CSTC) pathways (Felling & Singer, 2011; Mink, 2001). An fMRI study conducted by Wang et al. (2011) demonstrated greater neural activity in motor pathways in TS subjects (sensorimotor cortex, putamen) compared to non-TS subjects, whilst decreased activity was observed in areas associated with the inhibitory control of motor pathways (caudate, anterior cingulate cortex). It was concluded that tics are likely generated by an increase in activity within the motor pathways and a decrease in activity in areas associated with inhibitory control. Diminished performance on neuropsychological tests of inhibitory control supports

this theory of TS (Deckersbach, Rauch, Buhlmann & Wilhelm, 2006; Watkins et al., 2005).

Conversely, Ganos et al. (2014) found no difference in action inhibition between TS and non-TS subjects, whilst Jackson et al. (2011) reported enhanced inhibition in TS subjects. They propose that enhanced inhibitory processes in TS subjects are evidence of compensatory adaptations to the prefrontal cortex developed as a result of repeated attempts at tic suppression and control.

Conflicting findings make the neuropsychological correlates of TS difficult to determine and may be due to the variety of neuropsychological tests used, the broad range of ages tested, varying patient tic suppression ability, and the possible neural discrepancies between the causes and consequences of the disorder. Comorbidity may also play a mediating role, with some studies suggesting that inhibitory dysfunction is present only in TS patients with a comorbid disorder (Ozonoff, Strayer, McMahon & Filloux, 1998; Roessner, Becker, Banaschewski & Rothenberger, 2007).

Despite research implicating several brain regions (e.g. caudate nucleus, sensorimotor cortex, anterior cingulate cortex), a principal site of tic generation is yet to be identified, leaving questions unanswered about the fundamental causes of TS (Felling & Singer, 2011; Gerard & Peterson, 2003).

Comorbidity

Comorbid conditions are common amongst individuals with TS with ~50% presenting with a diagnosis of co-morbid obsessive compulsive disorder (OCD) or attention deficit hyperactivity disorder (ADHD; Abramovitch, Dar, Mittelman & Wilhelm, 2015; Bloch et al., 2006; Gaze, Kepley & Walkup, 2006). Other commonly, co-occurring difficulties include rage attacks, disruptive behaviour and social difficulties (McGuire et al., 2013; Sukhodolsky et al., 2003). These co-occurring

conditions compound the degree of functional, social and emotional impairment, impacting on the individual's overall quality of life (QOL; Specht et al., 2011; Storch et al., 2007). Indeed, research has shown that individuals with TS exhibit a significantly reduced QOL when compared to the non-TS population (Eddy et al., 2011; Müller-Vahl et al., 2010; Storch et al., 2007).

Quality of Life

Further key contributors to a diminished QOL include a perceived pressure to adapt to society's expectations, negative self-perception and the experience of being bullied (Cutler, Murphy, Gilmour & Heyman, 2009; Khalifa, Dalan & Rydell, 2010).

Tic severity has also been found to be predictive of QOL (Cutler et al., 2009; Elstner, Selai, Trimble & Robertson, 2001; Evans, Seri & Cavanna, 2016), however Storch et al. (2007) found this effect to be present only in children with low levels of externalising behaviours. Recent research has identified a link between the ability to suppress tics and quality of life, finding that an individual's satisfaction with their ability to control their tics is positively associated with enhanced QOL (Matsuda, Kono, Nonaka, Fujio & Kano, 2016). The authors argue that teaching strategies to patients to help them develop a sense of perceived control over their tics is key to improving QOL.

Previously, interventions for individuals with TS were concerned primarily with the reduction of tic severity. In recent years, however, adaptations have been made to psychotherapeutic treatments to broaden the focus of therapy. Storch et al. (2012) developed a modular treatment protocol ('Living with Tics') that incorporates behavioural treatment with modules that focus on psychoeducation, problem-solving, distress tolerance and coping at school, with the aim of improving tic-related impairment and resilience as well as tic severity.

Psychoeducation is a therapeutic approach that aims to increase the child's understanding of TS as well as target the associated impairing psychosocial and co-morbid difficulties. Topics can include self-esteem, school, anger, attention and OCD (Murphy & Heyman, 2007). It has been described as a significant therapeutic component when it comes to improving QOL, aiming to resolve misunderstanding around the diagnosis and alleviate anxiety (Cutler et al., 2009). Psychoeducation facilitated in a group format has also been described (Murphy & Heyman, 2007) and offers the added benefit of peer support as well as facilitating the sharing of information amongst individuals. Nussey, Pistrang and Murphy (2014) found that a classroom-based psychoeducational group was associated with more positive perceptions of TS in both children with TS, and their teachers and classmates.

As the focus on QOL outcomes grows, it becomes increasingly important to determine the specific therapeutic components responsible for measurable psychosocial improvement.

School functioning

Storch et al. (2007) identified school to be the most commonly reported area of impairment amongst children with TS. Concentration in the classroom can be affected by the distracting nature of the tics and attempts to suppress tics during lessons may lead to fatigue and frustration (Packer, 2005). Children with TS are vulnerable to social isolation and bullying as a result of their symptoms, with one study reporting that up to 45% of children with tics experienced 'teasing' from peers (Debes, Hjalgrim & Skov, 2010). Certain practical tasks in the classroom, such as handwriting, can also be affected by frequent motor tics and a fifth of children have been shown to experience a level of tic severity that made functioning at school at times unfeasible, affecting school attendance (Leckman et al., 1998). These findings suggest that an improvement in tic severity may lead to an improvement in school

attendance rates, however, these are yet to be formally evaluated as a TS treatment outcome in children.

Treatment

Pharmacotherapy has traditionally been used to manage the symptoms of TS. Drug treatments such as typical and atypical antipsychotics (e.g. haloperidol, risperidone) and alpha-2 adrenergic agonists (e.g. clonidine, guanfacine) have been shown to significantly reduce tic severity (Weisman, Qureshi, Leckamn, Scahill and Bloch, 2013).

The European clinical guidelines for TS suggest that medication can lead to a 25 to 50% reduction in tic symptoms. However, it is acknowledged that unlike psychotherapeutic interventions, medication does not offer long-term coping mechanisms to support and sustain improvement post-treatment (Roessner et al., 2011). Furthermore, little is known about the impact of medication on the equally impairing psychosocial symptoms of TS (Woods et al., 2011).

Treatment guidelines endorse behavioural therapy (BT) and psychoeducation as first line interventions for mild to moderate TS, recommending pharmacotherapy where behavioural interventions are not sufficient or unavailable (Steeves et al., 2012; Van de Griendt, Verdellen, van Dijk & Verbraak, 2013).

Habit Reversal Training (HRT; Azrin and Nunn, 1973) is arguably the most empirically supported behavioural approach, demonstrating medium to large treatment effects that are equivalent to effect sizes seen in drug trials of antipsychotic medication (Dutta & Cavanna, 2013; McGuire et al., 2014). Habit reversal training includes self-monitoring and awareness building components which aim to attune the patient's awareness to the premonitory urge in order to facilitate early tic detection. Patients are then taught to apply a specific physically

incompatible movement or sound termed the 'competing response', in order to effectively block the production of the tic.

Habit reversal training can be combined with relaxation training and functional analysis to create a multi-component intervention termed the 'Comprehensive Behavioural Intervention for Tics' (CBIT; Woods et al., 2008).

Treatment outcomes

Evidence supports the efficacy of CBIT when delivered face-to-face as an individual treatment (Piacentini et al., 2010; Wilhelm et al., 2012), as well as via telehealth (Himle et al., 2012; Ricketts et al., 2015). There is also emerging evidence for the efficacy of group-based CBIT (Yates et al., 2016). These latter protocols aim to increase the availability of behavioural treatments that can often be limited in their accessibility (McGuire et al., 2015).

In addition to tic severity outcomes, Deckerbach et al. (2014) examined the effect of behavioural treatment on neuropsychological functioning, finding that TS adult patients demonstrated a significant decrease in motor pathway (putamen) activation when comparing fMRI findings from pre- and post- treatment. These findings indicate a degree of neuroplasticity and suggest that repeated practice of tic suppression (a key therapeutic component of BT) may lead to structural and functional changes to affected CSTC pathways. Further support for this comes from Morand-Beaulieu, O'Connor, Sauvé, Blanchet and Lavoie (2015) who found that CBT had a normalising effect on pre-treatment motor pathway abnormality detected in TS patients. Behavioural Inhibition was also monitored but remained unchanged post-treatment.

Behavioural protocols have been found to significantly improve secondary psychosocial symptoms such as QOL (Woods et al., 2011), with findings indicating that children show a reduction in tic-related impairment following BT. Similarly,

Deckersbach Rauch, Buhlmann and Wilhelm (2006) found improvements in life satisfaction ratings following a course of HRT in adult patients.

Long-term outcomes

Few studies have investigated the long-term durability of behavioural interventions. Of those studies that have carried out follow-up assessments, Wilhelm et al (2003) report the longest follow-up period (10 months) and describe a maintenance of post-treatment improvement. Similarly, stability of treatment effects on tic severity has been reported at 6 month follow-ups in both children and adults (Himle et al., 2012; Piacentini et al., 2010; Wilhelm et al., 2012), whilst continued improvements have also been demonstrated for TS-related psychosocial symptoms (Woods et al., 2011).

It should be noted that much of the available follow-up data suffer high attrition rates (~30%) and has been limited to 'treatment-responders' only, suggesting a need for a conservative interpretation of findings. Furthermore, little is known about the long-term efficacy of newer, adapted behavioural protocols designed to increase treatment availability, and at present, no follow-up observations have been conducted beyond 10 months. Due to the waxing and waning nature of tics, short-term follow-ups may indirectly capture fluctuations in the natural course of symptom presentation and longer observation periods to account for these fluctuations have been recommended (Roessner et al., 2011).

The present study

Empirical support for the efficacy of behavioural interventions for TS, as well as the psychosocial benefits associated with group-based psychoeducation, makes a case for the potential benefits of group-based BT.

A recent pilot randomised controlled trial (RCT) conducted by Yates et al. (2016) evaluated treatment outcomes for group-based CBIT and psychoeducation in order

to address the issue of limited treatment availability and explore the potential added psychosocial benefits of peer support. Improvements in tic severity and quality of life were reported for both treatment groups, with greater tic severity improvements for the CBIT group. Improvements in measures of behavioural inhibition were also observed in both group conditions and reported separately (Edwards, 2015). Good group attendance indicated the acceptability and feasibility of group treatment approaches, offering an effective treatment option for resource-limited services. Presently however, little is known about the long-term efficacy of group-based TS interventions.

Aims and Objectives

This study aims to examine the long term efficacy of group treatments (CBIT and PE) for TS by evaluating 12-month follow-up outcomes in patients originally assessed at post-treatment by Yates et al. (2016) and Edwards (2015). In doing so, the study also aims to contribute to the limited long-term evidence base for CBIT and PE tic treatments.

Rationale

This study will investigate whether improvements in tic severity and QOL following group treatment (as reported in Yates et al., 2016) are sustained after a 12-month follow-up period, as indicated by existing individual BT research (McGuire et al., 2015; Piacentini et al., 2010). It will also aim to clarify the effect of behavioural treatment on inhibitory processes, an association which has to date produced conflicting findings (Edwards, 2015; Morand-Beaulieu et al., 2015). This study will investigate whether post-treatment improvements in a measure of behavioural inhibition (as reported in Edwards, 2015) are sustained at 12 months.

Additionally, based on recent research indicating a relationship between self-perceived tic control and QOL (Matsuda et al., 2016), an objective measure of tic suppression ability will be examined as a potential predictor of QOL outcomes.

Finally, this study will aim to investigate the relationship between tic treatment and school attendance in children. This relationship has yet to be formally evaluated however existing research linking tic severity to school attendance (Leckman et al., 1998) indicates the potential for improvement in attendance following treatment.

Hypotheses

Hypothesis 1: Improvements in tic severity will be maintained at 12-month follow-up for both the CBIT group and the PE group, with the CBIT group exhibiting greater improvements than the PE group.

Hypothesis 2: Improvements in QOL will be maintained at 12-month follow-up in both CBIT and PE groups.

Hypothesis 3: Long-term quality of life (QOL) outcomes will be associated with tic suppression ability.

Hypothesis 4: Improvements on a test of attention and inhibitory control will be maintained at 12-month follow-up in both groups.

Hypothesis 5: Children in both groups will improve on school attendance in the 12 months post-treatment compared with the 12 months prior to group treatment.

2. METHOD

2.1 THE WIDER PROJECT

This follow-up study is part of a wider project that investigated the short-term effects of group-based interventions for TS. The original study was designed and developed as part of two D.Clin.Psy theses. Edwards (2015) investigated the effects of group

interventions on tic severity and neuropsychological functioning, whilst Yates et al. (2016) explored the impact of these interventions on tic severity and quality of life outcomes. The original study provided the Time 1 and Time 2 outcomes cited in this report. This study explores tic severity, quality of life and neuropsychological outcomes at 12 months post-treatment. It also examines the impact of group treatment on school attendance, an additional element to the wider project that was not previously investigated.

The wider project includes contributions from three trainee clinical psychologists, including the author. A breakdown of trainee contributions is provided in Appendix A.

2.2 DESIGN

This follow-up study is part of a pilot randomised controlled trial (RCT) designed to test the feasibility and acceptability of a future larger, multi-site RCT. This study has a cross-sectional design, collecting data at a single time point (time 3). The data, however, forms part of a larger longitudinal data set and will be analysed together with previously collected data from time 1 (pre-treatment) and time 2 (post-treatment).

The project has a single-blinded, randomised and controlled design. Participants were pre-allocated to either CBIT or PE group treatment using a randomisation method as part of the original study. Group allocation was maintained for the follow-up. Data analysis used a repeated-measures design with three time points (pre-treatment, post-treatment and 12-month follow-up).

2.3 ETHICAL CONSIDERATIONS

All participants received a letter informing them about the study followed by a phone call a few weeks later offering the opportunity to ask any study-related questions. Families were informed that they were under no obligation to participate in the

follow-up study and that their decision would not affect their clinical care. Families that chose to participate gave verbal consent to the study during the telephone call and parental written consent and child written assent was obtained at the start of the follow-up assessment. Children were given the opportunity to ask any questions prior to the assessment and were reminded that they could opt-out of the study at any time. See Appendix B for further details of ethical considerations.

2.4 ETHICAL APPROVAL

The original study was approved by London Queen Square Research Ethics Committee and the hospital's research and development department. The original ethics application included a planned follow-up study and this was approved. Prior to commencement of the follow-up, modifications to the original protocol were made and these were submitted as a major amendment by the author and were reviewed and accepted by the ethics committees (see Appendices C and D).

2.5 AFFILIATIONS AND FUNDING

This trial was registered on the National Institute for Health Research Portfolio Database (ISRCTN: 50798741). Funding for the follow-up trial was provided by University College London and Tourettes Action, UK (a national TS charity).

Tourettes Action did not contribute to any aspect of the study's design, execution, data analysis or reporting. University College London provided guidance and supervision for this project.

2.6 PARTICIPANTS

A total of 33 participants took part in the original trial. Participants were children that had been referred to and seen by the tic disorder clinic in the preceding 5 years to the study. Eligible participants were aged 9-13 years (to coincide with the peak tic severity period), with a primary diagnosis of TS or CTD, a baseline score of >13 on

the Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) and a full-scale IQ >80. Exclusion criteria included a current or lifetime diagnosis of psychosis or substance abuse and children who had previously received more than four sessions of behavioural treatment for tics or had attended a psychoeducational session at the tic clinic within the past 2 years. Families whose level of English language proficiency would render it difficult to follow sessions were also excluded. Children who were successfully recruited were assigned to either CBIT or PE group treatment arms. The treatment interventions commenced in October 2013 and January 2014. Participants were randomised and stratified to ensure equal group allocations for age and gender.

All participants who participated in the original trial were eligible for inclusion in the follow-up study unless they had withdrawn during the trial¹. Twenty-nine of the original study participants were contacted for follow-up recruitment and 28 participants agreed to participate². Recruitment for the follow-up study took place between October 2014 and January 2015.

2.7 INTERVENTIONS

Both group treatments consisted of eight sessions conducted on a once-weekly basis. The first two sessions of each group were 90 minutes long, with the remainder of sessions running for 60 minutes each. Sessions comprised of psychologist-led components as well as interactive group discussions and activities. Both treatment groups included the same initial session on psychoeducation about tics and both included a relaxation training component. Groups were matched on overall structure, therapist exposure, use of reward strategies and the amount of homework set each week. In order to maintain consistency across groups, a

¹ Four participants withdrew from the original trial prior to post-treatment assessment (time 2).

² One participant was uncontactable having moved address and changed telephone number without informing the clinic.

Paediatric Neuropsychologist (TM) with over 10 years of experience of working at the specialist tic clinic, facilitated both treatment groups.

Alongside the child CBIT and PE groups, parents attended four parallel intervention group sessions that were linked to either the child CBIT group or the PE group depending on their child's group allocation. Parent group sessions included either CBIT-specific or PE-specific content designed to complement the content of their child's group, including information about tics, group discussions and advice on the use of reward strategies with their child.

The CBIT group treatment was developed from a combination of the individual CBIT treatment protocol (Woods et al., 2008) and the HRT parent workbook (Verdellen, van de Griendt, Kriens & van Oostrum, 2011). The PE group treatment was based on a protocol developed by Murphy and Heyman (2007). See Appendix E for further details on the content of interventions.

2.8 OUTCOME MEASURES

Measures used in the current study are reported. Several additional measures were administered during the follow-up assessment in accordance with the wider project but did not form part of the current study. These additional measures are cited in the assessment protocol (see Appendix F).

2.8.1 Tic severity

Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989)

The YGTSS is a semi-structured, clinician-administered interview with good internal consistency, inter-rater reliability and validity in paediatric TS populations. It is considered the gold-standard measure of tic severity (Storch et al., 2005; Abramovich et al., 2015) and is the primary outcome measure for this study. The YGTSS collects information on tic symptoms over the last week and scores these

for number, frequency, intensity, interference and complexity. There is also a separate impairment scale. See Appendix G for a copy of the YGTSS.

The lead assessor (a trainee clinical psychologist) was trained in YGTSS administration by a consultant clinical psychologist (TM) who has over 10 years of experience administering the YGTSS at a national tic clinic. TM also trained the YGTSS assessors at Time 1 and Time 2.

- *Inter-rater reliability*

All YGTSS interviews were audio recorded and 10% were later re-rated to test for inter-rater reliability. A random number generator website (<https://www.randomizer.org/>) was used to identify the three YGTSS interviews that would be double rated by a consultant clinical psychologist (TM). An overall agreement percentage was obtained by calculating the mean difference between scores for each double-rated YGTSS interview. Percentage agreement was calculated at 96% indicating strong inter-rater reliability.

Video Observation of tic expression and tic suppression

Video observations were carried out in order to calculate tic suppression ability. Children were seated in front of a laptop that screened 20 minutes of a Simpsons episode whilst the in-built laptop webcam captured a video of the participant's head and upper torso area. The Simpsons episode was carefully chosen and matched to the two previous episodes watched by participants at T1 and T2. Further details of the episode selection process are provided in Appendix H.

After 15 minutes, the episode was paused and the video recording was ended. Participants were then asked to attempt to suppress their tics as much as they felt able to for the following 5 minutes, after which they would receive a small reward (a bouncy ball). The episode and video recording was then continued for a further 5 minutes.

The protocol used for video observation in this study closely followed the methodology used in the original study, which was based on a protocol described and reported by Himle et al. (2006). In addition, the principal investigators from the original study trained the follow-up assessor in order to increase stability and consistency of observation methods.

Tic frequency was measured for each condition by calculating the average number of tics observed per minute. The percentage change in tic frequency between the tic expression and tic suppression conditions was then calculated in order to calculate a measure of suppression ability,

2.8.2 Quality of life

The Gilles de la Tourette syndrome-quality of life scale for children and adolescents (C&A-GTS-QOL; Cavanna et al., 2013).

The C&A-GTS-QOL is an Italian 27-item measure of health-related quality of life in children with TS. It consists of four subscales (psychological, physical, obsessive-compulsive and cognitive) as well as a separate life satisfaction scale. This study used an English translation of the measure which has been shown to have good acceptability, reliability (Cronbach's alpha > 0.7) and validity (Su et al., 2016). See appendix I for a copy of the C&A-GTS-QOL.

2.8.3 Neuropsychological functioning

Neuropsychological functioning was measured using the NIH Toolbox (www.nihtoolbox.org), which is a set of brief, computerised measures used to measure changes in neurological function over time. These measures are nationally standardised to the US population, normed for ages 3-85 years and demonstrate good convergent and discriminant validity (Weintraub et al., 2013; Beaumont et al., 2013).

For the administration of the first two tests (the Dimensional Change Card Sort test and the Flanker Inhibitory Control and Attention Test), children were seated at a table in front of a computer screen and keyboard. The assessor controlled the computer screen from a laptop that ran the online NIH Toolbox software. Each task included a set of standardised instructions and a brief practice period. Visual stimuli were presented on the screen and remained there until a response was made. Participants were asked to respond with their dominant hand using either the right or left arrow buttons on the keyboard. Age-adjusted scaled scores were automatically calculated and made available in an online database.

The Dimensional Change Card Sort test (DCCS) and Flanker Inhibitory Control and Attention Test were chosen as measures of executive function and attention. Specifically, they measured an individual's ability to switch focus between multiple aspects of a task (set shifting) and the individual's ability to inhibit any automatic responses that may delay task completion. The 9-Hole Pegboard Test was chosen as a measure of motor dexterity. Specifically, it measures finger coordination and the individual's ability to skilfully handle objects under time pressure.

Dimensional Change Card Sort test (DCCS)

This is a measure of cognitive flexibility and takes approximately four minutes to administer. Participants were shown a picture in the centre of the screen followed by a set of two further pictures that appeared below. Participants were asked to select one picture from the pair that matched the original central image according to one of two rules (colour or shape). Participants were asked to match first according to shape and then according to colour. A third round of trials involved participants switching between shape and colour rules at random dependent on instructions on the computer screen.

Flanker Inhibitory Control and Attention Test

This is a measure of attention and inhibitory control and takes approximately three minutes to administer. It is a timed task and requires the participant to attend to a central stimulus (arrow pointing either left or right) whilst inhibiting attention to any stimuli flanking it. Flankers are either congruent or incongruent and the participant is asked to respond in accordance with the central stimulus.

Pegboard Dexterity Test

This is a measure of manual dexterity and takes approximately four minutes to administer. It measures the time taken for an individual to accurately place nine pegs one at a time into a nine-hole pegboard, and then remove each peg one-by-one.

2.8.4 School attendance

School contact information was obtained from families during the follow-up assessment. Each participant's school was then contacted in order to obtain school attendance data (% attendance) for the full academic year prior to group attendance (September 2012 – July 2013) and the full academic year following group participation (September 2014 – July 2015).

2.8.5 Significant life events, medication changes and further treatment

Participants were asked to provide information about any medication changes, significant life events or further psychological treatment of tics that may have occurred in the 12 months between the end of the intervention and the follow-up assessment. Information was recorded on a separate questionnaire (see Appendix J) completed by the parent.

2.9 PROCEDURE

Participants were informed about the 12-month follow-up assessment during the original study and each family was asked whether they would like to be contacted to participate in the follow-up at the T2 assessment. All families agreed to be contacted.

Families were initially sent a letter outlining details of the follow-up study (see Appendix K) accompanied by both a parent and child information sheet (see Appendices L and M). This was followed up three weeks later with a telephone call which offered the opportunity for families to ask questions about participation in the study. If they agreed to participation, a home-based follow-up assessment was organised over the telephone.

The complete battery of tests was administered by the same assessor in a single session based in a quiet room at the child's home. Assessments lasted approximately 3 hours. The assessor followed the same structured assessment protocol used in the original study in order to maintain consistency and reliability of assessment.

Prior to the assessment, the assessor checked that both the parents and children had understood the information provided about the assessment and checked whether they had any questions. Children were shown a visual plan of the day (see Appendix N) and consent and assent forms (see Appendices O and P) were completed and collected.

All follow-up assessments were carried out approximately 12 months after the post-treatment assessment (time 2) and within 30 days of the 12-month mark, with the exception of one participant who attended the PE group³. Assessments were

³ For this case, the time 2 assessment was delayed by 14 weeks. The time 3 assessment was conducted in line with the original time 1 assessment, and therefore 10 months after time 2.

completed by March 2015 and school attendance data collection was completed by December 2015.

2.10 RANDOMISATION AND BLINDING

Participants were randomised to treatment groups at the start of the original study. Families were not blind to treatment allocation due to the distinguishable topics and concepts covered within group sessions. The principal assessor was not involved in any aspect of the original study and remained blind to group allocation throughout the follow-up study.

Blinding was maintained by ensuring that participant group allocation details were stored separately from the main database in a password-protected file that the principal assessor did not have access to during the study. The assessor informed families when arranging follow-up assessments and again at the start of the assessment that they were blind to treatment allocation and explained the importance of not disclosing which group the child had participated in.

- *Success of blinding*

The success of blinding is considered a key determinant of a clinical trial's validity (Bang, Ni & Davis, 2004). Blinding success was calculated for each treatment arm using Bang's Blinding Index (BI; Bang et al., 2004; Williamson, Harvill & Stamey, 2013) based on the assessors allocation guesses for each participant. Bang's BI is treatment arm-specific and has a range of -1 to 1, where 0 represents perfect blinding, 1 represents complete unblinding (every group allocation guessed correctly) and -1 indicates complete opposite guessing (every group allocation guessed incorrectly) which could also be an indicator of unblinding.

A BI of 0.38 was calculated for the CBIT condition, indicating that 38% of allocation guesses were correctly guessed beyond chance. For the PE condition, Bang's BI was calculated as -0.15, indicating that 15% of guesses were incorrect beyond chance. There is no specific range of BI that indicates acceptable blinding (Kolahi, Bang and Park, 2009) although smaller values (positive or negative) will indicate strength of blinding. Bang's blinding indices for the two treatment conditions indicate that for the majority of participants, blinding was successful, however blinding may have been unsuccessful for a few cases in the CBIT condition (see Table 1).

Table 1

Number of subjects by actual group allocation and guessed group allocation

Actual allocation	Guessed allocation			Total n (%)
	n (%)			
	CBIT	PE	Don't know	
CBIT	8 (28.6)	3 (10.7)	4 (14.3)	15 (53.6)
PE	5 (17.9)	3 (10.7)	5 (17.9)	13 (46.4)
Total	13 (46.4)	6 (21.4)	9 (32.1)	28 (100.0)

Note. Blinding index (CBIT:PE) = 0.38 : -0.15

2.11 SAMPLE SIZE AND POWER

The sample size for the follow-up study was limited to participants that had completed the original study (N = 29). There was one dropout between T2 and T3, therefore the follow-up study had a predetermined sample of N = 28. A medium effect size ($f=0.25$) was estimated based on results from the original study (Yates et al., 2016). A post hoc analysis was used to estimate achieved power for a repeated measures mixed model ANOVA with two groups and one primary outcome measure (YGTSS) taken at three time points. Power calculations were made using

“G*Power3” statistical software (Faul, Erdfelder, Lang & Buchner, 2007) based on an alpha level of 0.05, nonsphericity correction at 1 and correlation among repeated-measures at 0.5. The analysis estimated power = 0.81 for this study, which is by convention considered sufficient to minimise the risk of incurring a type II error (Cohen, 1992).

2.12 STATISTICAL ANALYSIS

Data was analysed using IBM SPSS version 21.0. A completers-only analysis (N=28) was conducted in accordance with previous follow-up analyses (Wilhelm et al., 2003; Deckersbach et al., 2006) in which only participants for whom data was available at all three time points were included. A responders-only analysis (participants who had responded positively to treatment) was also considered in line with previous studies (Woods et al., 2011, Piacentini et al., 2010), however was ultimately not used in this study in order to preserve sample size and statistical power.

Prior to outcome analysis, data was screened for missing values, tests of normality were conducted, and statistical outliers were removed where appropriate. Where the assumption of normality was not met, this was corrected for and described alongside any reported results.

Baseline descriptive data was analysed and independent samples *t*-tests and Fischer’s Exact tests were used to check for any significant baseline group differences. Parametric tests were used throughout the main analysis having established that data met the relevant test assumptions.

The primary hypothesis was analysed using 2 x 3 mixed model repeated measures Analysis of Variance (ANOVA) tests, with ‘group condition’ as the between subjects factor (CBIT, PE) and ‘time’ as the within-subjects factor (pre-treatment, post-treatment and 12-month follow-up). Partial eta-squared effect sizes (η_p^2) were

reported⁴. Secondary hypotheses were analysed using 2 x 3 mixed model repeated measures ANOVA tests and Pearson's correlations⁵. Where multiple comparisons were made using one outcome measure, significance levels were adjusted using Bonferroni corrections to control for an inflated familywise error rate.

3. RESULTS

Follow-up assessments took place between November 2014 and March 2015 with all participants remaining in their pre-assigned group conditions. Twenty-eight participants took part in the follow-up study out of a total of 33 participants recruited at time 1. The five dropouts⁶ did not significantly differ from completers on measures of baseline tic severity ($d = 0.18$, $p = 0.73$). Participants ranged in age from 10 - 14 years (mean = 12.06, $SD = 1.38$).

3.1 CONSIDERATION OF POTENTIAL CONFOUNDS

3.1.1 Attendance rates

Of the 28 follow-up participants, 26 were considered treatment 'attenders' (attending at least five out of eight treatment sessions). The two participants attending less than five sessions were both from the PE group and attended two and four sessions, respectively. Children in the CBIT group attended a mean of 7.53 sessions ($SD = 0.52$) with a mode of 8 sessions, compared with 7.2 sessions ($SD = 1.9$) in the PE group with a mode of 8 sessions. Difference in group attendance between the two

⁴ Rules of thumb taken from Murphy and Myors (2004) suggest effect size magnitudes: 0.01 = small effect size, 0.06 = medium effect size, 0.14 = large effect size.

⁵ Rules of thumb taken from Cohen (1988) for Pearson's correlation coefficient suggest effect size magnitudes: 0.1 = small effect size, 0.3 = medium effect size, 0.5 = large effect size.

⁶ The five dropouts consisted of four participants that did not complete the original study and one participant that completed the original study but was not recruited for the follow-up.

conditions was considered small and therefore no adjustments were made during analysis.

3.1.2 Tic medication changes

Four participants (3 CBIT, 1 PE) reported tic medication changes over the previous 12 months. Three participants had stopped taking medication due to an improvement in tic symptoms and one participant reported reducing their dosage. Previous studies have found no evidence of tic medication acting as a moderator to behavioural treatment outcomes (Piacentini et al., 2010; McGuire et al., 2014) and therefore the four changes in medication status were not statistically accounted for in analysis.

3.1.3 Significant life events

Seven participants reported significant life events during the follow-up period. Four participants reported family-related issues, one participant reported stress caused by school exams, one reported a depressive episode, and one participant reported being off school for three months due to physical illness. The analysis was re-run to exclude participants that reported significant life events. Where changes to findings were observed, these are reported.

3.1.4 Further psychological treatment

Thirteen participants engaged in psychological treatment unrelated to the study during the follow-up period. The focus of therapy varied amongst participants (3 generalised anxiety, 1 phobia, 4 OCD, 1 low mood, 2 anger, 1 'physical symptoms not related to TS' and 1 ASD). No participants reported engaging in further psychological therapy for tics specifically.

Exposure and response prevention, a therapy typically used to manage OCD symptoms, is also an evidence-based treatment for tics (Verdellen et al., 2011). It is

therefore possible that participants benefitting from ERP treatment for OCD symptoms during the follow-up period (PE = 4, CBIT = 0) may have experienced additional therapeutic benefits to tic symptoms. For this reason, all analyses were re-run excluding the four participants that had received ERP for OCD. Where changes to findings were observed, these are reported.

3.1.5 Age

Tic symptoms gradually remit throughout adolescence for the majority of individuals (Hassan & Cavanna, 2012). This natural remission should be taken into consideration when investigating the long-term effects of treatment and efforts should be made to distinguish natural remission from the effects of the intervention when evaluating treatment efficacy.

The mean age of participants in this study was 10.80 ($SD = 1.39$) at baseline (T1) and 12.06 ($SD = 1.38$) at follow-up (T3). Peak severity of tic symptoms has typically been observed at approximately 10-12 years (Bloch et al., 2006; Leckman et al., 1998). In accordance with the literature, the current sample of participants was assessed across three time points all within the 'peak period' of tic symptoms. This suggests that an effect of natural remission would not necessarily be expected. In addition, age-matched randomisation across groups should further obviate any effect.

3.2 NORMALITY, OUTLIERS AND MISSING VALUES

Outcome variables were screened to check for normal distribution using Kolmogorov-Smirnov tests of normality. All data was normally distributed with the exception of T2 CBIT group data for the DCST and Flanker neuropsychological outcome variables. This data was normalised following the removal of an outlier (participant #33). Two further statistical outliers (participant #2, PE group; participant #3, CBIT group) were found and removed from the tic counting data.

Follow-up tic counting data and neuropsychological outcome data was missing for participant #11 who only agreed to complete the questionnaires at T3, and school attendance data was not available for participants #3, #7 and #11⁷.

3.3 BASELINE CHARACTERISTICS

Baseline characteristics for the 28 follow-up participants are presented as categorical and continuous data in Tables 2 and 3, respectively. Participants in the two conditions did not differ significantly on demographic or clinical characteristics, with the exception of baseline tic suppression ability (calculated as a percentage using tic frequencies from suppression and non-suppression video observations). At baseline, the PE group demonstrated significantly better suppression ability than the CBIT group ($p = 0.01$). This significant baseline difference between groups should be held in mind and related results should be interpreted with caution.

⁷ Attendance data missing due to schools not responding to data requests.

Table 2

Categorical descriptive data and group differences for participant characteristics at baseline

Demographic and clinical characteristics	Group						Fisher's Exact Test
	All (n = 28)		Psych-Ed (n = 13)		CBIT (n = 15)		p^*
Male gender (n, %)	21	75%	10	76.9%	11	73.3%	1.00
Ethnicity (n, %)							1.00 ^a
White British	19	67.9%	9	69.2%	10	66.7%	
Other White	6	21.4%	3	23.1%	3	20%	
British Indian	1	3.6%	1	7.7%			
Black British	1	3.6%			1	6.7%	
Mixed/ multiple ethnic	1	3.6%			1	6.7%	
Tic disorder (n, %)							0.48
TS	26	92.9%	13	100%	13	86.7%	
CMTD	2	7.1%			2	13.3%	
Right handed (n, %)	24	85.7%	11	84.6%	13	86.7%	1.00
Comorbidity (n, %)							
ADHD diagnosis	6	21.4%	4	30.8%	2	13.3%	0.37
OCD diagnosis (based on parent impairment rating reaching clinical cut-off, see below)	8	28.6%	5	38.5%	3	20%	0.41
Other diagnoses ^b							
ASD	2	7.1%	1	7.7%	1	6.7%	
Anxiety/panic	2	7.1%			2	13.3%	
Dyspraxia	2	7.1%	1	7.7%	1	6.7%	
Dyscalculia	1	3.6%	1	7.7%			
Epilepsy	1	3.6%					
Month group began (n, %)							0.71
September	15	53.6%	6	46.2%	9	60%	

Demographic and clinical characteristics	Group						Fisher's Exact Test p^*
	All (n = 28)		Psych-Ed (n = 13)		CBIT (n = 15)		
November	13	46.4%	7	53.8%	6	40%	
Tic medication at T1 (n, %)	10	35.7%	3	23.1%	7	46.7%	0.25
Change in tic medication between T2 and T3 ^c	4	14.3%	1	7.7%	3	20%	0.60
Sig. life event(s) between T2 and T3 ^c	7	25%	4	30.8%	3	20%	0.67

*All two-tailed

^a Fisher's exact test conducted using pooled ethnicity data (White British vs other) in a 2 x 2 contingency table.

^b Fisher's exact test not conducted as frequencies too small.

^c Data collected at T3 assessment.

Table 3

Continuous descriptive data and group differences for participant characteristics at baseline

	Group			Independent-samples t-test
	All (n = 28)	Psych-Ed (n = 13)	CBIT (n = 15)	
	M (SD)	M (SD)	M (SD)	p-value*
Age (years)	10.80 (1.39)	10.67 (1.46)	10.91 (1.37)	0.66
Full-scale IQ	102.89 (12.86)	105.15 (13.63)	100.93 (12.29)	0.40
SES total score	41.56 (14.48)	46.42 (15.92)	37.35 (12.08)	0.10
YGTSS				
Motor tic severity	16.82 (4.00)	15.92 (3.23)	17.60 (4.53)	0.28
Phonic tic severity	12.61 (6.72)	12.92 (6.41)	12.33 (7.19)	0.82
Tic severity score	29.43 (9.29)	28.85 (8.70)	29.93 (10.05)	0.76
Total tic score	51.21 (15.59)	49.62 (16.08)	52.60 (15.57)	0.62
Tic observation (tics per minute)	7.29 (4.19)	8.21 (4.20)	6.50 (4.16)	0.29
Tic suppression (tics per minute)	6.22 (3.77)	5.58 (3.82)	6.77 (3.76)	0.42
Suppression ability	13.57 (44.59)	34.84 (36.78)	-6.17 (43.07)	0.01
Neuropsychological functioning ^a				
DCST	101.69 (12.76)	104.63 (11.42)	99.15 (13.69)	0.27
Flanker test	98.67 (11.36)	96.78 (8.99)	100.30 (13.17)	0.42
Motor dexterity	100.11 (13.97) ^b	103.04 (16.76) ^e	97.96 (11.67)	0.37
GTS-QoL total score	34.11 (15.74)	36.15 (14.37)	32.33 (17.14)	0.53

	Group			Independent-samples t-test
	All (n = 28)	Psych-Ed (n = 13)	CBIT (n = 15)	
	M (SD)	M (SD)	M (SD)	p-value*
GTS-QoL satisfaction score	74.50 (15.18)	72.23 (14.34)	76.47 (16.11)	0.47
School attendance (%)	93.08 (4.94) ^c	93.69 (4.11) ^d	92.60 (5.62)	0.58

* All two-tailed

^a Age-adjusted scaled scores

^b N = 26 due to missing data (CBIT = 15; Psych-Ed = 11)

^c N = 27 due to missing data (CBIT = 15; Psych-Ed = 12)

^d N = 12 due to missing data

^e N = 11 due to missing data

3.4 MAIN ANALYSIS

All analyses incorporated three time points (T1, T2 and T3) unless otherwise stated. Where significant effects are observed, a secondary, exploratory analysis was conducted to determine any continued changes occurring specifically during the follow-up period, between T2 and T3.

Hypothesis 1: Improvements in tic severity will be maintained at 12-month follow-up for both groups, with the CBIT group exhibiting greater improvements than the PE group.

A series of four 2 X 3 mixed model Repeated Measures Analysis of Variance (RM-ANOVA) tests were conducted to analyse the effects of time (T1, T2 and T3) and group condition (CBIT and PE) on tic severity, as well as any group-time interactions. The outcome variables that were analysed included subscales of the YGTSS (motor tic severity, phonic tic severity, total tic severity) as well as the YGTSS total score. Where the assumption of sphericity has not been met, Greenhouse-Geisser corrections are reported. Findings from four RM-ANOVA tests are presented in Appendix Q.

A significant main effect of time was observed for the motor tic severity score ($F(1.5,39) = 15.23, p < 0.001, \eta_p^2=0.37$, large effect size; see Figure 1). The assumption of sphericity was violated and the Greenhouse-Geisser correction is reported with adjusted degrees of freedom. There was no significant effect of group, however a significant polynomial linear contrast for the interaction was observed ($F(1,26) = 4.40, p = 0.046, \eta_p^2 = 0.15$, large effect size), suggesting an interaction effect between time and group. In this case, inspection of the plot indicates that there was greater reduction in motor tic severity over time in the CBIT group, however, this interaction is only just significant and should be interpreted conservatively.

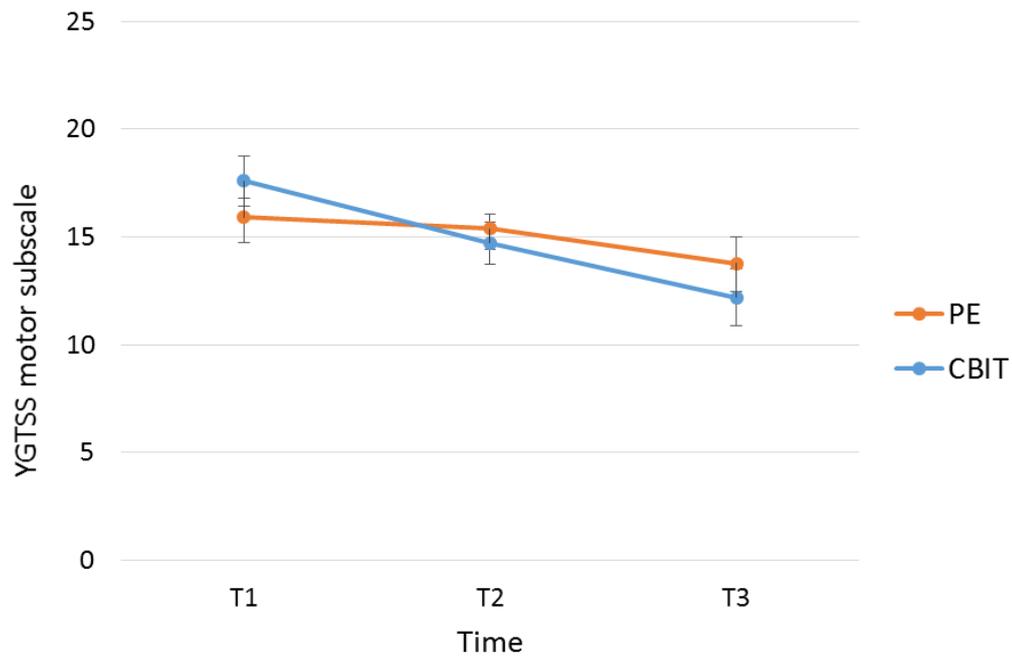


Figure 1: Main effect of time on the YGTSS motor tic severity subscale

A significant main effect of time was also observed for phonic tic severity scores ($F(2,52) = 4.76, p = 0.013, \eta_p^2=0.16$, large effect size), total tic severity scores ($F(2,52) = 12.25, p < 0.001, \eta_p^2=0.32$, large effect size) and YGTSS total scores ($F(2,52) = 7.38, p = 0.002, \eta_p^2=0.22$, large effect size; see Figure 2). All findings survived Bonferroni correction ($\underline{p} \leq 0.013$). The effect of group condition was not significant for any of these outcome measures and no significant group-time interactions were found, indicating that there were no significant differences in tic severity improvement between the two groups.

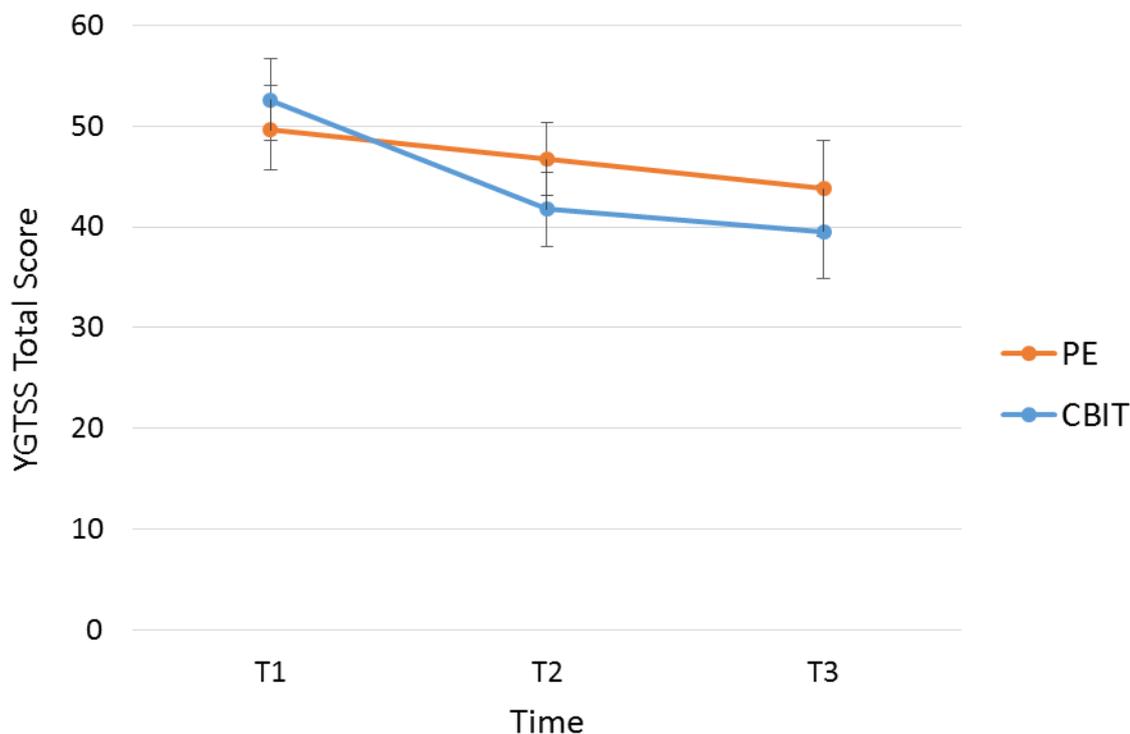


Figure 2: *Main effect of time on YGTSS total scores*

An average 8 point reduction on the YGTSS tic severity score was observed between T1 and T3 for the CBIT condition, compared to a 6 point reduction in the PE group. These findings suggest that both groups experienced significant symptom improvement in the period between pre-treatment and follow-up, as defined by Storch et al. (2011) who recommend a 6 point change on the YGTSS tic severity score as the best indicator of treatment response.

Jeon et al (2013) propose that a 25% reduction in an individual's tic severity score (the combination of the motor and phonic tic severity subscales) represents a clinically meaningful change or a 'responder'. In accordance with this proposed benchmark, 46.2% ($n = 6$; range of tic reduction = -12.5% to 63.0%) of participants in the PE group would be considered treatment "responders", whilst 53.3% ($n = 8$;

range of tic reduction = -23.8% to 70.6%) would be considered “responders” in the CBIT group, when measuring symptom change between T1 and T3.

Exploratory analysis 1:

Inspection of the line graphs indicated continued improvement on the YGTSS between T2 and T3 which was not specifically hypothesised, but nonetheless would be useful to determine.

A series of four RM-ANOVA tests were conducted to test for ongoing changes in outcome variables (YGTSS motor tic severity, phonic tic severity, total tic severity and total score) between T2 and T3. These analyses used a 2 X 2 mixed model design to observe the effects of time (T2 and T3) and group condition (CBIT and PE) as well as any group-time interactions.

A significant effect of time was observed for motor tic severity scores ($F(1,26) = 7.52, p = 0.011, \eta_p^2=0.22$, large effect size) and total tic severity scores ($F(1,26) = 7.25, p = 0.012, \eta_p^2=0.22$, large effect size) but no significant effects of group condition or group-time interactions were observed for either outcome measure. Complete results from the four RM-ANOVA tests are presented in Appendix R.

These results demonstrate continued improvements in tic severity in both group conditions over the follow-up period, with an observed reduction of four points and five points on the YGTSS tic severity scale for the PE and CBIT groups, respectively. There were no significant differences in improvement between groups across the follow-up period.

Hypothesis 2: Improvements in QOL will be maintained at 12 month follow-up for both the CBIT group and the PE group.

GTS-QOL total scores were used as a measure of self-reported QOL and were analysed using a 2 x 3 RM-ANOVA test. A mixed model design was implemented

with group condition (CBIT and PE) as the between-subjects factor and time (T1, T2 and T3) as the within-subjects factor. There were no main effects of time ($F(2,52) = 2.31, p = 0.109$), group condition ($F(2,52) = 1.27, p = 0.27$) or group-time interaction ($F(2,52) = 0.68, p = 0.511$).

A secondary analysis was conducted excluding cases that had reported significant life events during the follow-up period ($n = 7$). Results of this analysis showed a significant main effect of time on GTS-QOL total scores ($F(2,52) = 6.35, p = 0.004, \eta_p^2 = 0.25$, large effect size). Results from the RM-ANOVA test are presented in Table 4 and depicted in Figure 3.

Table 4

2 x 3 ANOVA test of GTS-QOL scores for hypothesis 2

	Psych-Ed (N = 9)			CBIT (N = 12)			Main effect of group	Main effect of time	Inter- action	All (N = 21)		
	T1	T2	T3	T1	T2	T3				T1	T2	T3
	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	<i>p</i>	<i>p</i>	<i>p</i>	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI
GTS-QOL total score	39.00 (16.15), 26.59 – 51.41	34.11 (7.62), 28.25 – 39.97	27.00 (13.90), 16.31 – 37.69	33.25 (18.83), 21.29 – 45.21	28.33 (16.89), 17.60 – 39.07	25.17 (16.93), 14.41 – 35.92	0.480	0.004	0.725	35.71 (17.54), 27.73 – 43.70	30.81 (13.74), 24.56 – 37.06	25.95 (15.35), 18.96 – 32.94

Note. N = 21 (participants reporting significant life events excluded from analysis)

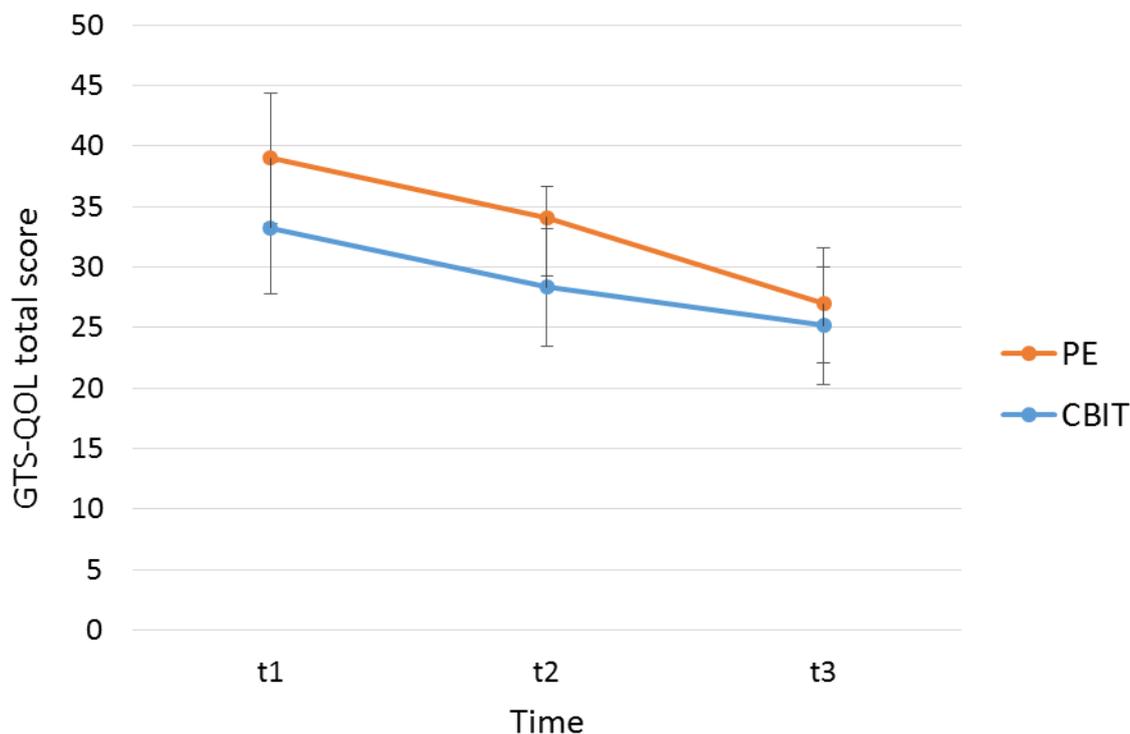


Figure 3: Main effect of time on GTS-QOL total scores

Exploratory Analysis 2:

Inspection of the line graph indicated continued improvement on the GTS-QOL between T2 and T3. This was not specifically hypothesised but would be useful to statistically determine.

A 2 x 2 mixed model RM-ANOVA excluding cases with significant life events (as above) was conducted to analyse changes in QOL during the follow-up period (T2 and T3) with time (T2 and T3) as the within-subjects factor and group (CBIT and PE) as the between-subjects factor). A significant main effect of time was observed ($F(1,19) = 5.73, p = 0.027, \eta_p^2 = 0.23$, large effect size). These findings indicate that both groups demonstrated continued improvement in QOL during the 12 months after completing group treatment, with a 7 point improvement observed in the PE condition whilst the CBIT group improved by an average of 3 points.

Hypothesis 3: Long-term quality of life (QOL) outcomes will be associated with tic suppression ability.

A one-tailed Pearson's correlational analysis was conducted to test for associations between the GTS-QOL total score and tic suppression ability (%) at T3 (follow-up). The GTS-QOL total score was significantly negatively correlated with tic suppression ability ($r = -.52$, large effect size, $p = 0.008$) indicating that a greater ability to suppress tics is associated with a better self-reported QOL (as measured by the GTS-QOL where smaller scores indicate better self-reported QOL). This association is depicted in Figure 4.

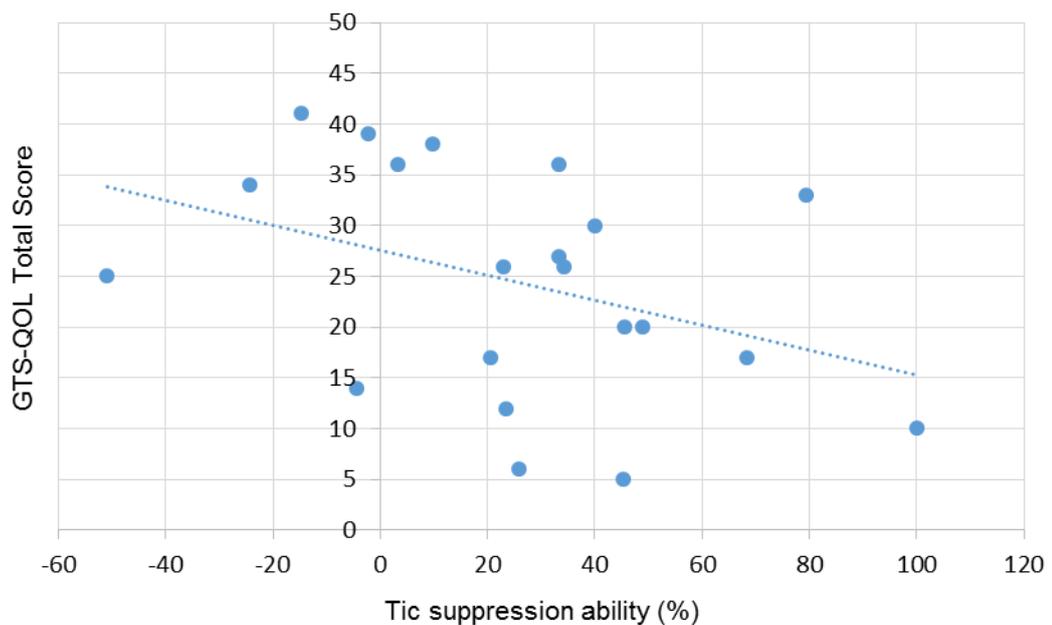


Figure 4: Correlational analysis of the association between tic suppression ability and quality of life at follow-up

Hypothesis 4: Improvements on the Flanker test of attention and inhibitory control will be maintained at 12-month follow-up in both groups.

A 2 x 3 RM-ANOVA test was used to analyse flanker age adjusted scaled scores. A mixed model design was used with group condition (CBIT and PE) as the between-subjects factor and time (T1, T2 and T3) as the within-subjects factor.

The assumption of sphericity was violated and the Greenhouse-Geisser correction is reported. There were no main effects of time ($F(1.4,33.4) = 0.81, p = 0.414$), group condition ($F(1,24) = 0.04, p = 0.836$) or group-time interaction ($F(1.4,33.4) = 0.48, p = 0.558$). These findings indicate that there were no observed long-term improvements in attention and inhibitory control in either group.

Hypothesis 5: Children in both groups will improve on school attendance in the 12 months post-treatment compared with the 12 months prior to group treatment.

School attendance data was analysed using a 2 X 2 mixed model RM-ANOVA with time (pre- and post-treatment) as the within-subjects factor and group (CBIT and PE) as the between-subjects factor. The CBIT group reported a change in attendance rates from 92.34% to 95.22%, whilst there was also an observed shift from 93.69% to 95.99% in the PE group.

A main effect of time was observed ($F(1,23) = 10.04, p = 0.004, \eta_p^2=0.30$, large effect size). There was no main effect of group ($F(1,23) = 0.13, p = 0.723$) or group-time interaction ($F(1,23) = 0.51, p = 0.484$). These results indicate that children in both group conditions demonstrated significantly higher school attendance rates at post-treatment when compared to pre-treatment school attendance. Findings support hypothesis 5 and are displayed in Figure 5.

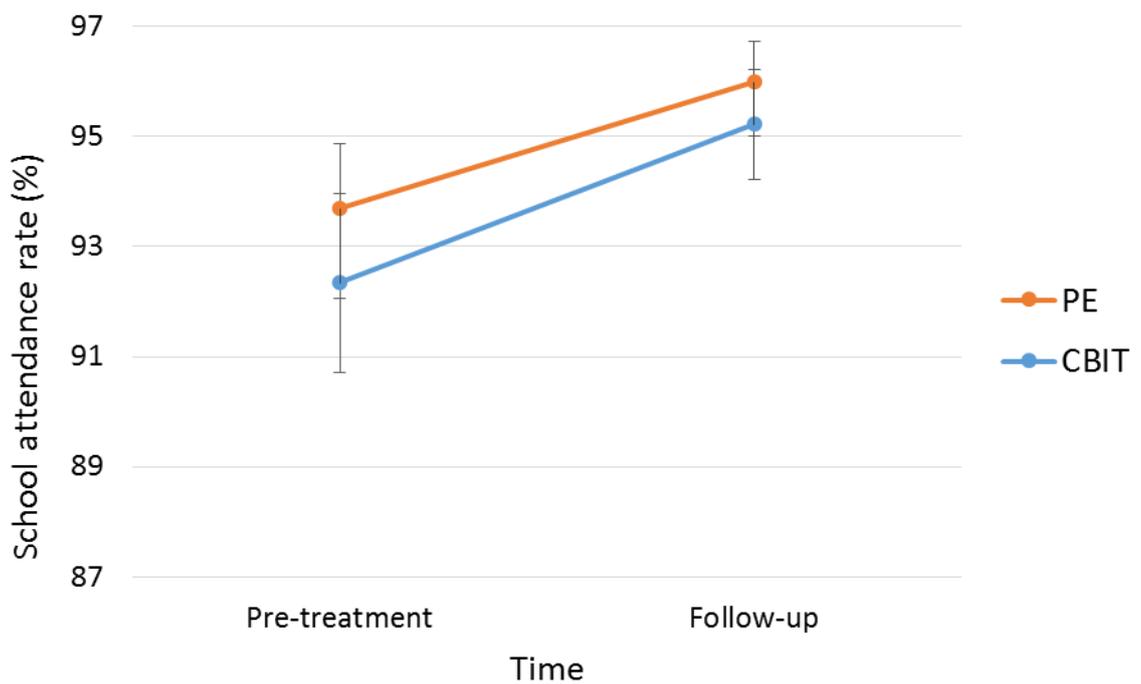


Figure 5: Main effect of time on school attendance rates⁸

4. DISCUSSION

4.1 MAIN FINDINGS

This study investigated 12-month follow-up outcomes of group interventions for children with TS. Overall, findings offer support for the long-term efficacy of group-based CBIT and PE treatments.

Results highlight continued improvements in tic severity in both CBIT and PE participants over the follow-up period, with indication of a slightly greater improvement in CBIT participants. Both group participants demonstrated continued improvement in QOL over the follow-up period and a greater ability to suppress tics was associated with greater QOL. Results also indicated that children in both group conditions improved in school attendance. Improvements in behavioural inhibition

⁸ Y-axis compressed to clarify findings.

observed at T2 for CBIT participants appear not to be maintained at the 12-month follow-up.

4.1.1 Tic severity

Twelve months after group treatment, children in both group conditions maintained the tic severity improvements observed at post-treatment assessment. In addition, both groups demonstrated continued tic severity improvements. These appear to be predominantly driven by ongoing improvements in motor tic severity, as observed on the motor subscale of the YGTSS. There is a tentative suggestion of greater motor tic improvement amongst the CBIT group compared to the PE group, with the CBIT condition demonstrating a 17.2% improvement in motor tic severity across the follow-up period, compared to an 11.4% improvement in the PE group. This is not surprising given that 73% of tics chosen to be treated in the CBIT group were motor tics and common motor tics (e.g. eye blinks and head jerks) have been found to be particularly responsive to behavioural treatment (McGuire et al., 2015). This potential group difference in improvement during the follow-up period is in line with group differences observed immediately following treatment (Yates et al., 2016).

Findings for the CBIT group in this study are comparable to previous trials, although on a more modest scale. In a trial comparing HRT to supportive psychotherapy in adults with TS, Deckersbach et al. (2006) reported a 10.9-point tic severity reduction between pre-treatment and six-month follow-up in the HRT condition. The present study found a slightly smaller reduction of 7.7 points in the behavioural treatment condition. It is possible that this study's more modest findings reflect a diluting effect of group-based behavioural treatments compared to individual treatment.

However, it should be noted that Deckersbach et al. offered 14 sessions of treatment, whilst the present study evaluated an 8-session intervention. This could explain the smaller reduction in tic severity. Studies by Verdellen et al. (2004) and

Woods et al. (2008) have also offered longer interventions, reporting treatment lengths of 12 and 10 sessions, respectively. Future studies aiming to replicate the findings of this study would benefit from increasing the number of treatment sessions. This would enable more confident comparisons to be made between group and individual interventions.

There are no existing long-term findings pertaining to psychoeducational treatment for TS, meaning that present outcomes cannot be contextualised in previous empirical evidence. Despite this, current findings demonstrate a 5.9-point reduction in tic severity in the PE group, which could be considered as an indication of long-term treatment response, in line with Storch et al. (2011)'s guideline of a 6-point reduction as indication of treatment response.

Continued improvement in tic severity was not anticipated or hypothesised. Of the follow-up data that exists, findings have predominantly shown a stabilisation of treatment effects, maintained between post-treatment and follow-up assessments (Deckersbach et al., 2006; Wilhelm et al., 2003).

There are several theoretical explanations for this observed effect. Firstly, it should be noted that thirteen participants engaged in further psychological treatment during the follow-up period (7 CBIT; 6 PE). Although in all cases on-going intervention was not directly focused on tic symptoms, it is possible that an improvement in related conditions, such as OCD or generalised anxiety, may positively influence tic symptoms. Indeed, anxiety has been found to exacerbate tic severity (Conelea & Woods, 2008), which suggests that alleviating anxiety may consequently contribute to tic severity improvement in the long-term.

It can be theorised that two distinct therapeutic working mechanisms were responsible for tic improvement in each of the two groups. Children randomised to the CBIT group may have continued to practice and master tic suppression

strategies following group completion, leading to ongoing improvements. Indeed, significant improvements in tic suppression ability were observed for the CBIT group between pre-treatment and follow-up but not the PE group.

Continued tic severity improvements observed for the PE group could be hypothesised as a secondary outcome of the long-term beneficial effects of psychoeducation on managing psychosocial symptoms such as anxiety and school functioning (Nussey, Pistrang and Murphy, 2014).

Another theory is the possibility of a mutual underlying mechanism present in both groups and hence influencing tic severity symptoms in both conditions. One example of this is exposure to peer support and social normalisation of symptoms. Again, this could lead to a reduction in overall anxiety that could positively influence symptoms. Additionally, the group format may have facilitated a sharing of coping strategies between participants leading to subsequent symptom improvement.

A change in evaluator between T2 and T3 does make the study vulnerable to a rater-effect which could have also contributed to the observed continued improvement in scores at T3. However, only the YGTSS (which is clinician-rated) was susceptible to a rater-effect. Steps were taken to minimise this by ensuring all three raters were trained by the same consultant clinical psychologist (TM) and inter-rater reliability was measured and considered acceptable.

4.1.2 Quality of life

Participants in CBIT and PE groups maintained QOL improvements at follow-up after excluding participants that had experienced a significant life event during the follow-up period. Furthermore, continued long-term improvements were observed for both groups of participants, with no significant differences between conditions. This continued improvement is consistent with previous research suggesting that psychosocial outcomes show greater improvement at six month follow-up than

directly following individual tic treatment, suggesting that participants may benefit from a consolidation period following intervention (Woods et al., 2011).

Quality of life outcomes were found to correlate with tic suppression ability across the whole sample of participants, indicating that children demonstrating greater tic suppression ability at follow-up also showed higher levels of self-reported QOL. This finding supports and builds upon recent research that demonstrated a relationship between participants' satisfaction with their ability to control tics and their self-reported QOL (Matsuda et al., 2016).

4.1.3 Neuropsychological outcomes

Post-treatment neuropsychological outcomes indicated an initial improvement in attention and inhibitory control for both CBIT and PE participants, as measured by the Flanker test at T2 (Yates et al., 2016). This effect was not observed at follow-up assessment and therefore it is possible that the group interventions may produce short-term changes in neuropsychological functioning that are not sustained in the long-term.

Improvements on neuropsychological measures have previously been demonstrated for both behavioural interventions and waitlist controls (Deckersbach et al., 2014) and it could therefore also be theorised that these observed improvements may be a consequence of practice effects given the short period of time between test and re-test (~10 weeks). This theory is consistent with the findings of this study, which showed that originally observed improvements in inhibitory control and attention at post-treatment assessment (T2), were not sustained at 12 months (T3). Test-retest reliability data for the flanker test indicates practice effects at 21 days ($ES = 0.27$, $p < 0.001$) when measured with an adult sample (Weintraub et al., 2014).

Unfortunately, reliability data from a child sample is not currently available for the flanker test. Currently, there are no recommended guidelines for acceptable retest

periods, however these practice effects could account for the apparent effects observed at T2.

4.1.4 School attendance

Participants in both conditions experienced a rise in school attendance to just above 95% following group treatment. These findings are significant given that medical illness accounts for 59% of school absences in the UK (Department of Education, 2016). Importantly, these findings also place both groups of participants in line with the national secondary school average of 95%, and marginally above the typical threshold for school attendance targets (Department of Education, 2016).

The observed improvement in school attendance is not surprising given that both groups of participants also demonstrated significant improvements in tic severity between T1 and T3 (follow-up). As previously reported, Leckman et al. (1998) identified that up to 20% of children with TS may experience school-interfering tic severity, affecting their ability to attend school. This suggests that an improvement in tic severity may directly reduce some of the tic-related practical difficulties experienced in the classroom which could subsequently improve school attendance. Alternatively, children may have indirectly benefited from an improvement in tic severity by experiencing a reduction in teasing and bullying and an improvement in peer relationships at school. This could in turn lead to an increase in the child's attendance.

The group format of the interventions may to some extent simulate a classroom setting, with children 'taught' in the presence of other children. The group format could therefore offer specific therapeutic gains that are more readily transferable to a school setting. Children in the CBIT group learnt to suppress their tics in the presence of other children, potentially strengthening their ability to utilise this strategy in a classroom setting. Psychoeducation participants on the other hand,

may have benefitted from a perceived social acceptance and normalisation of their symptoms by other children whilst attending the group. These psycho-social benefits could in turn have carry-over effects to the child's school environment. Future studies would need to directly compare school attendance outcomes of individual and group treatments in order to determine whether there is a unique benefit of group-based interventions.

4.2 CLINICAL IMPLICATIONS

These findings suggest that group treatment for TS can be considered a reasonable alternative to individual treatment where services are resource-limited. This study also offers specific support for the provision of group-based psychoeducation as an alternative to behavioural treatment, with comparable long-term outcomes.

These findings contribute to a wider evidence base that can support clinicians and families to make decisions about treatment. Results indicate that group treatments can contribute not only to reductions in tic severity, but can also positively impact on a child's school attendance and self-perceived quality of life in the long-term. These are important outcomes to consider when deciding on treatment and should be taken into consideration alongside the patient's identified needs and treatment goals.

4.3 STRENGTHS AND LIMITATIONS

A detailed description of the strengths and limitations of the original study design has been reported previously (Yates et al., 2016). In brief, the strengths of this study lay predominantly in the single-blinded, randomised, controlled design. This design allowed for the robust measurement of clinical change over time in two group conditions that were matched for frequency, duration and clinician-contact time. Treatment in both groups was structured and protocol-driven to maintain treatment fidelity and outcome measures were scored using the same detailed scoring

protocols across all three time points to maintain consistency. Treatment was conducted by highly experienced and specialised clinicians within a specialist clinic setting. A gold standard clinician-rated tic severity scale (YGTSS) was used as the main outcome measure, and evaluator blindness were accounted for and measured.

The study had an overall attrition rate of 15% between T1 and T3. The follow-up study benefitted from low attrition (3.4%) with only one participant lost between T2 and T3. This is significantly lower than in previously reported follow-ups (Verdellen et al., 2004; Wilhelm et al., 2012), and may have benefitted from the use of home-based assessments, increasing convenience for the family and reducing the burden of travelling to the clinic. Conducting assessments at the child's home rather than in the clinic also allowed for the measurement of symptoms in an environment familiar to the child, increasing the ecological validity of the measures.

The lack of an additional control group limits the conclusions that can be made from the findings. As previously discussed, natural remission of symptoms may have occurred over the course of the 12-month follow-up period. A waitlist control group could allow for this natural effect to be monitored and controlled for, enabling any treatment effects to be distinguished from natural symptom remission.

Encouragingly, existing literature reports peak tic severity as occurring between 10-12 years (Bloch et al., 2006; Leckman et al., 1998). It should be noted that the mean age at T1 and T3 assessments was 10.80 and 12.06 years, respectively, meaning that both time points fell within or very close to the peak severity period. This suggests that significant, naturally occurring tic severity reductions are unlikely to have occurred amongst the sample. This study did however use opportunity sampling as a recruitment method and it is possible that patients experiencing peak tic severity would be particularly inclined to participate in the study. Participants experiencing peak tic severity at initial assessment would be expected to experience some level of natural reduction in tic severity in line with the waxing and waning

nature of TS. Systematic consecutive sampling taken from the clinic's referral flow in place of opportunity sampling may have reduced this effect.

Follow-up assessments were conducted by a researcher not involved in the original study, and evaluators from the original study were not involved in any aspect of the administration or scoring of the follow-up assessment. The lack of evaluator crossover helped preserve blindness of the follow-up assessor. As previously reported, the assessment procedure was highly protocolled to reduce variation between evaluators. Furthermore, evaluators from the original study trained the follow-up evaluator in the assessment protocol and the same consultant clinical psychologist (TM) trained all three evaluators in the administration and scoring of the YGTSS. Inter-rater reliability data between the original study and the follow-up assessment would help account for any rater-bias, however it was not available for this study.

The relatively small sample size meant that the study was underpowered for the detection of smaller effects, and a larger RCT would be recommended in order to replicate these findings and explore further predictors of long-term treatment response that this study was not sufficiently powered to investigate.

4.4 FUTURE RESEARCH

Given the small sample size of the current study, a larger RCT would be needed to replicate findings. A multi-site, community-based study would also be informative. Future studies would benefit from a waitlist control in order to account for natural symptom change, or a 'minimal treatment' condition to account for the potential placebo effect of perceived support from a specialist clinic. It would be interesting to include an alternative control group consisting of individually administered treatment in order to directly measure the effect of a group-based format. This would help

determine whether there is in fact presiding long-term benefits of group treatment over individual treatment, as indicated in the findings from this study.

Given that both the CBIT and PE groups demonstrated significant symptom improvement in both the short-term and the long-term, further investigation into the precise mechanisms of change in these respective treatments (and to determine whether these therapeutic mechanisms are mutual or distinguishable between the two approaches) would be important for the future design and development of TS interventions.

4.5 CONCLUSION

In a sample of children with diagnosed TS, group-based interventions offered sustained benefits to tic severity, quality of life and school attendance. No long-term benefits were observed on neuropsychological measures. These results support the implementation of CBIT and PE group treatments for children with TS. Continued improvement over the follow-up period was observed in both group conditions suggesting that a mutual therapeutic mechanism may underlie long-term symptom improvements, although research is required to establish the specific treatment components offering the greatest long-term therapeutic benefit. Future studies would benefit from a larger sample and alternative control groups.

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PART 3: CRITICAL APPRAISAL

1. INTRODUCTION

This critical appraisal focuses on three key aspects of the research study. Firstly, it considers the process of conducting a follow-up study as part of a larger trial, appraising the unique advantages and disadvantages that this offered. Secondly, further strengths and limitations of the study's methodology are explored. Finally, the appraisal reflects on the experience of working with children with a neurodevelopmental disorder.

2. CONDUCTING A FOLLOW-UP STUDY AS PART OF A LARGER TRIAL

This follow-up study was part of a wider randomised controlled trial (RCT). My role was to assess participants at 12 months post-treatment in order to evaluate the long-term outcomes of the interventions that were trialled.

2.1 RECRUITMENT

Conducting a follow up study as part of a wider project had many unique advantages as well as some associated difficulties. One advantage was that the participant sample was pre-determined and therefore there was no need to identify new participants. This however also meant that the maximum follow-up study sample size was limited to the sample size of the original trial. All participants had previously agreed to follow-up participation, however, they were also free to drop out at any time during the follow-up period. Participants from the original study therefore needed to be 're-recruited'. Given that a significant amount of time had passed between the original recruitment phase and the follow-up assessment, there was potential for high levels of attrition. Previous studies of behavioural treatment for Tourette syndrome (TS) have reported attrition rates of 11%-28% across follow-up periods of shorter length (Himle et al., 2012; Piacentini et al., 2010; Wilhelm et al., 2003) therefore a dropout rate of at least 10% was anticipated for this study.

A small sample size had the potential to significantly under power the study and this was identified as a potential issue in the early stages of evaluating the study's feasibility. In order to help minimise attrition, it was decided that I would make contact with each of the families by letter a few months before recruitment began. A brief letter was sent out thanking the families for participating in the original trial, reminding them about the follow-up study, introducing myself and informing them that I would be in contact again in a couple of months' time. A second letter was then sent out a few months later followed by a telephone call. This multi-stage contact process aimed to facilitate recruitment and increase participant uptake.

The follow-up study did in fact suffer minimal attrition with only one participant considered a 'drop-out' between T2 and T3. The low attrition rate was a key success for the study, helping to not only power the study but also highlighting the feasibility of long-term follow-up research. On reflection, there are a number of reasons, aside from the potential impact of the frequent correspondence, which could help to explain the low dropout rate. Firstly, assessments were conducted at participants' homes, unlike previous follow up studies (Deckersbach, Rauch, Buhlmann, & Wilhelm, 2006; Wilhelm et al., 2012). Given that the clinic is a national centre, some of the participants lived relatively far away, meaning that travel time could be up to 3 hours when visiting a family to administer the assessment. Taking part in the follow-up therefore offered families an opportunity to make contact with the clinic whilst eliminating the burden of travel. Secondly, the reputation of the clinic may have influenced the rate of participant engagement. The clinic is renowned for its work with children with tics and many families had gone through a long referral process before being referred to the clinic, potentially increasing their appreciation for the support offered by the clinic and influencing their desire to maintain involvement. It also became evident that the group sessions had helped to facilitate links between the families, with some parents reporting that since taking part in the groups, their

children had maintained contact with other participants. It is possible that the group format of the interventions had helped develop a sense of unity and cohesion amongst some of the participants, which in turn could have positively influenced their continued willingness to participate in the research.

2.2 TIMING

Alongside the issue of attrition, the follow-up study also carried with it an element of time pressure. The assessment was planned for 12 months post-treatment, meaning that there was a significant amount of pressure resting on the completion of ethical approval amendments and the recruitment stage in order to ensure the appropriate timing of the assessments for each of the participants. On reflection, I felt that these added pressures were well balanced with advantages that the study held such as not having to go through the full process of gaining ethical approval. The study only required a major amendment to the original ethical approval and this substantially reduced the time spent on ethics, making it possible to begin recruitment in good time. All but one of the participants were assessed within 30 days of the 12-month mark.

2.3 STUDY DESIGN

Joining an existing research trial required me to quickly grasp the study's procedures and existing methodology whilst also ensuring that I understood the theoretical rationales underpinning the existing methodology.

The design of the follow-up assessment needed to be in line with the original assessment methodology in order to ensure consistency across the trial and both of the previous trainees devoted time to fully handing over the research. This support early on in the study was invaluable and without it, it would have been difficult to ensure the reliability of the assessment.

This need for consistency did however limit the flexibility of the follow-up study design. Measures used were largely limited to those that had previously been administered and for which there were previous sets of outcomes in order for comparisons to be made. This, to some extent, shaped the remit of the present study. An exception to this was the additional inclusion of school attendance data which was obtained post-hoc for the year prior to group involvement and for one full academic year post-treatment. This outcome measure contributed an additional, unique aspect to the study.

There were certain features of the study design that I would have liked to have adapted, such as including a third treatment condition consisting of individual treatment in order to directly compare outcomes between group and individual therapy. The results of the study demonstrated good outcomes for both group treatments, offering potential support for the theory that the psychosocial benefits of a group-format may have contributed to symptom improvement in participants. Including an individual treatment condition would further contribute to our theoretical understanding of these findings.

Despite the limitations of joining an established study, it is undoubtable that combining research efforts with two other trainees enabled the development of a larger, more robust research project. This enabled access to a relatively large amount of data, affording me a good amount of flexibility in hypothesis development and outcome analysis. It also offered the opportunity to contribute to a high quality, longitudinal, RCT: a study design that would have been unrealistic to develop and execute as an individual project.

3. FURTHER STRENGTHS AND LIMITATIONS OF THE STUDY

3.1 DESIGN

A randomised controlled design facilitated the experimental comparison of two interventions matched for treatment length and clinician contact time. However, the lack of a waiting list or individual treatment control group limited the conclusions that could be made from this study. A waiting list control group would have accounted for natural symptom fluctuation or remission over the course of the follow-up period, enabling natural fluctuation in symptoms to be distinguished from treatment effects over time. This is particularly important when evaluating long-term effects of treatment as longer follow-up periods are more likely to capture some element of symptom fluctuation. These adaptations would be useful to consider in future studies.

The distinguishable nature of the therapeutic components of each intervention meant that it was not possible to blind participants to group allocation. Both groups were however described as active treatments for TS with neither pitched as more effective than the other when recruiting participants. Despite this, participants may have been susceptible to expectancy effects that could have influenced findings.

Occasionally, during home visits, participants would unintentionally discuss their tics in such a way that indicated their group allocation to the assessor. An example of this is when a child would use the word 'suppress' when describing tic management. This would suggest that they had taken part in the CBIT group, and therefore potentially compromise assessor blindness. This may also explain the larger proportion of assessor unblinding detected in the CBIT condition.

3.2 OUTCOME MEASURES

The study included both subjective and objective measures of tic severity. The primary outcome measure consisted of the Yale Global Tic Severity Scale (YGTSS): a clinician-administered, gold standard outcome measure. This scale enabled both children and their parents to be interviewed together, offering multiple perspectives

and information on the variety and frequency of the child's tics. This was particularly important given that on multiple occasions parents were able to identify tics that the child did not seem aware of and therefore would not have reported if interviewed alone. Indeed, self-report assessments of tic severity have been shown to be inaccurate, with most individuals underestimating the severity of their symptoms (Pappert, Goetz, Louis, Blasucci & Leurgans, 2003).

Video observations of tic expression and tic suppression were also conducted for each participant, however the setup of the video recording meant that observation was limited to the head and upper torso area and lower body motor tics were therefore not recorded. This was a significant limitation of the measure that affected its reliability. Furthermore, despite efforts made to match the emotional content of the T3 Simpsons episode to the content of the episodes used at T1 and T2, episodes will have inherently varied from one another. Contextual factors such as stressful and anxiety-inducing events have been found to worsen tics (Conelea & Woods, 2008) and therefore the varying emotional content of the episodes at each time point may have confounded tic frequency outcomes. For this reason, it was decided that video recordings would be used to calculate a measure of tic suppression ability only, computed by comparing tic frequency during a period of free ticcing, against tic frequency during a period of active tic suppression. This approach enabled episode content to be controlled for and provided a suppression ability measure whilst controlling for any tics that were unobservable.

3.3 SETTING

Home-based follow-up assessments reduced burden on families and contributed to the ecological validity of the study, enabling the assessment of tic severity and tic-associated symptoms to take place in an environment familiar to the child.

Nonetheless, conducting outcome measurement in family homes meant that the testing environment was not strictly controlled for. All families were informed in

advance that the assessment would need to take place in a quiet room with a table and chair in order to enable the participant to concentrate on the various tasks and questionnaires. It is of course difficult to eliminate all distraction and disruption in a naturalistic setting. The neuropsychological measures, which were timed to the accuracy of a centisecond, were most vulnerable to disruption. This variable partially obviated by the fact that participants acted as their own controls across time points, therefore controlling for the testing environment to some extent. Despite this, the presence of siblings and other distractions will have influenced concentration levels and the child's ability to focus. Efforts were made to manage these distractions through the use of regular breaks and pauses in testing where necessary and possible.

4. WORKING WITH CHILDREN WITH TOURETTE SYNDROME

An interest in developmental neuropsychology and an affinity for working with children drew me to this study. However, prior to undertaking this research I had little direct experience of tic disorders and TS and much of my knowledge about this condition was influenced by popular media's portrayal of the condition. Tourette syndrome is a disorder that garners a relatively large amount of media attention relative to other conditions. This is predominantly due to the syndrome's often conspicuous symptoms which can mimic intentional behaviours. There is a common misconception that TS is primarily characterised by vocal tics, and more specifically, coprolalia. In fact, I quickly grew to understand the nature of the disorder and the significance of motor tics. It was primarily motor tics that children cited as bothersome, often interrupting everyday tasks such as handwriting or sports activities, and therefore becoming a significant source of frustration.

I witnessed a broad range of family approaches, coping strategies and attitudes to the condition, ranging from humour, to those that were experiencing a significant family-wide emotional struggle with the disorder. It was of course upsetting to hear

of the many struggles that families had experienced and to witness clear frustration and dismay at times, however this range of responses also served an important reminder of the different ways that a disorder can impact the wider family and the importance of not making assumptions or generalisations about coping and resilience.

Whilst conducting follow-up assessments, I was in the privileged position to be able to witness many inspiring accounts of recovery. The evident gratitude from families, alongside the first-hand experience that I gained from home visits, instilled a sense of hope and optimism for clinical effectiveness in the area of TS. On the whole, this was hugely encouraging and became a motivating factor for my research, having seen the benefits attributed to the approaches that I was investigating.

I occasionally came across children who appeared to be experiencing a peak in their tic severity. With so many stories of recovery and symptom improvement, these sporadic cases were particularly conspicuous in their severity. One child stood out in particular due to the high frequency and complexity of their tics which presented not unlike a seizure. This seizure-like presentation was particularly difficult to witness throughout the video observation, during which the intensity of the bodily tics made it difficult for the child to remain in his seat, and most of his attention was focused on trying to stabilise himself rather than being able to utilise the 'break' in assessment to watch the Simpsons episode. Moments like these were upsetting and made me question the usefulness of the assessment. These moments demonstrated the tension in research ethics between deontological and utilitarian factors and made me wonder whether in this case, the assessment process was adding unnecessary pressure to a child already experiencing significant burden from his symptoms.

Conducting home-based assessments offered an opportunity to gain a broader picture of what it is like for a child and their family living with the symptoms of TS.

This experience contributed to a richer understanding of the wide-reaching impact of TS and the systemic impact that it can have.

5. SUMMARY

Conducting a follow-up study as part of a wider RCT presented both specific difficulties as well as unique advantages, which overall I believe were adequately balanced. Reflecting on the limitations of the current study has helped to identify potential changes that could be made to future studies.

Working with children with TS and their families offered a unique insight into the daily highs and lows of living with TS and it was a privilege to witness the admirable resilience of these families. Reflecting on this research journey as a whole has highlighted not only the extent of the knowledge that I have gained in this research area, but also how my understanding of both the research topic and the empirical process has developed and evolved over time. This study has given me an appreciation for the practice of conducting high quality empirical research and has strengthened my interest in conducting research in the future.

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Appendix A: Outline of trainee contributions to the wider project

The original study was designed and carried out by two trainee clinical psychologists (KE and RY) as a joint research project. Ethical approval was at that time submitted for a follow-up study to be conducted 12 months post-treatment.

The clinical team at the tic clinic adapted the treatment protocols and ran the groups. KE and RY recruited the participants, designed the assessment protocol which was adapted for use in the present study, and carried out assessments at T1 (pre-treatment) and T2 (post-treatment). Data from these two time points contributed to the present study's longitudinal data set.

The follow-up study required a major amendment to ethical approval and adaptations to the assessment protocol. Additional outcome measures (tic suppression ability and school attendance rates) were also added to the study's design. Separate documents (consent forms, questionnaires, letters and information sheets) were developed for the follow-up study although these were adapted from and in line with the original study's documentation in order to maintain consistency.

KE and RY'S involvement in the current study was limited to the provision of assessment protocol training. The author conducted all follow-up assessments, video coding, scoring, data entry, analysis and write up, independently. The external supervisor re-coded 10% of YGTSS interviews to test for inter-rater reliability.

Appendix B: Further details of ethical considerations

Home-based assessments were conducted in accordance with the hospital's Lone Working Policy and parents were asked to remain at home at all times during the assessment. The author made contact with the principal investigator upon completion of each assessment.

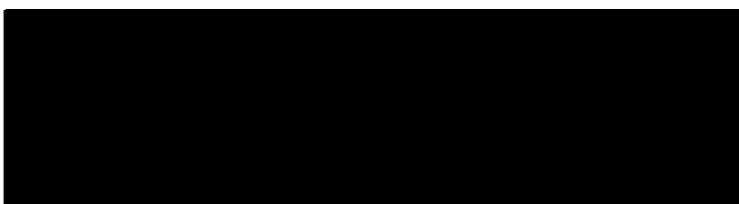
All confidential data was securely stored in accordance with the NHS Code of Confidentiality. Each participant was allocated a study ID number that was used on all paper-based documentation and electronic databases. Electronic databases were password protected and confidential paper-based documentation was stored in a locked office at the hospital. Electronic data collected during the home assessment was stored on the laptop within an encrypted hard-drive and transferred to the main secure electronic database and encrypted hard-drive at the hospital following the assessment.

Appendix C: Ethical approval letter from London Queen Square Research Ethics Committee



NRES Committee London - Queen Square
HRA NRES Centre Manchester
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

01 October 2014



Dear

Study title: **Group work for children with Tourette Syndrome (TS): A randomised pilot study to evaluate the efficacy of a tic-specific behavioural intervention versus psycho-education in improving tic severity, quality of life and neuropsychological functioning (v1)**

REC reference: 13/LO/0511
Protocol number: 13BS04_1
Amendment number: 1
Amendment date: 18 September 2014
IRAS project ID: 126154

The above amendment was reviewed on 01 October 2014 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Letters of invitation to participant	1	18 September 2014
Notice of Substantial Amendment (non-CTIMP) [NOSA]		18 September 2014
Participant consent form [Consent: Parents and carers]	2	18 September 2014

A Research Ethics Committee established by the Health Research Authority

Participant consent form [Child Assent]	1	18 September 2014
Participant information sheet (PIS) [PIS Parents and carers]	2	18 September 2014
Participant information sheet (PIS) [PIS Child]	1	18 September 2014
Research protocol or project proposal	1	19 September 2014

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

13/LO/0511:	Please quote this number on all correspondence
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Yours sincerely



**On behalf of
Dr Yogi Amin
Chair**

E-mail:



Enclosures:

List of names and professions of members who took part in the review

Copy to:

Ms Emma Pendleton, Division of Research and Innovation

NRES Committee London - Queen Square

Attendance at Sub-Committee of the REC meeting on 01 October 2014

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Dr Yogi Amin	Consultant in Neuroanaesthesia & Neurocritical Care	Yes	
Dr Eamonn Walsh	Postdoctoral Researcher	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Ms Rachel Heron	REC Manager

Appendix D: Ethical approval email from the hospital's research and development department

Dear Dr [REDACTED]

PROJECT TITLE	Randomised Pilot Study Evaluating Two Group Therapies for TS - Group work for children with Tourette Syndrome (TS): A randomised pilot study to evaluate the efficacy of a tic-specific behavioural intervention versus psycho-education in improving tic severity, quality of life and neuropsychological functioning
REC Reference	13/LO/0511
R&D Reference	13BS04
Amendment Number	1
Amendment Date	18 th September 2014
Date of REC approval	1 st October 2014

Notification of host site amendment approval

Thank you for your correspondence with regards to the amendment(s) for the above named study. The Joint Research & Development Office can confirm that this/these amendment(s) do not affect current local approval for the study.

Thank you for keeping us informed.

Yours Sincerely

Dr [REDACTED]

Research Management and Governance Officer

Joint Research and Development Office

[REDACTED]

[REDACTED]

Tel: [REDACTED]

Fax: [REDACTED]

Email: [REDACTED]

Appendix E: Additional details of the group interventions

Session	Key elements	
	Psycho-education	CBIT
1	<ul style="list-style-type: none"> ■ Introduction to aims and content of the group ■ Establish and agree 'rules' for the group ■ Define the condition 	<ul style="list-style-type: none"> ■ Introduction to aims and content of the group ■ Establish and agree 'rules' for the group ■ Define the condition ■ Introduce HRT
2	<ul style="list-style-type: none"> ■ Self esteem ■ Personal strengths ■ 6 month goals 	<ul style="list-style-type: none"> ■ Tic awareness ■ Identifying triggers for tic onset
3	<ul style="list-style-type: none"> ■ TS and school ■ Bullying 	<ul style="list-style-type: none"> ■ Tic awareness ■ Moving on to treatment ■ Selecting the first tic
4	<ul style="list-style-type: none"> ■ Noticing everyday emotions ■ Noticing anger ■ Relaxation exercise 	<ul style="list-style-type: none"> ■ Tic awareness ■ Tic detection ■ Choosing competing response for tic 1 ■ Relaxation exercise
5	<ul style="list-style-type: none"> ■ Anxiety ■ OCD (identifying obsessional thoughts and compulsions) ■ Relaxation exercise ■ Introduction to ERP and habituation 	<ul style="list-style-type: none"> ■ Using competing response on tic 1
6	<ul style="list-style-type: none"> ■ ADHD (the see-saw) 	<ul style="list-style-type: none"> ■ Selecting tic 2 ■ Recognising tic 2 ■ Practicing competing response on tic 2
7	<ul style="list-style-type: none"> ■ Problem solving situations at home ■ Improving attention 	<ul style="list-style-type: none"> ■ Using competing response on tic 3

8	<ul style="list-style-type: none">■ Quiz■ Certificates	<ul style="list-style-type: none">■ Practicing competing response on tics 1, 2 and 3■ Identifying potential future situations that may trigger tics■ Getting help in the future■ Certificates
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Appendix F: Assessment protocol

Beforehand

- Tell TM where you will be and time of visit.
- Take contact details for TM
- Agree a time after which you will speak.
- Copy demographic information into new empty Excel spreadsheet. Save on F drive under ppt number.
- Make sure you know if they've had a WISC in the last 6 months and input data if so.
- **Set up new login for that child on the assessment centre and add password and login to the spreadsheet**
- Book travel. Bring address and contact details and give this information to TM

If contacting families from own phone change settings to hide phone number:

Either dial 141 before the number or (if this doesn't work) change mobile phone settings (Menu – Settings-Call-Additional settings-Caller ID)

Equipment List (bold = things to replace each time)

- ID badge**
- Tickets and travel information**
- Address of family; name, date of birth and age of child**
- Participant number for child**
- Laptop + power cable**
- Demographic info sheet**
- Three-way plug adaptor
- Monitor, connector cable + power cable
- Keyboard, mouse, speakers
- Pegboard, pegs and spares
- Stopwatch
- Pencil without rubber x 2
- Little reward**
- Bluetak**
- Internet dongle
- DVD for watching during obs
- Full assessment protocol
- Questionnaire pack for right age range (i.e. 13/ under 13 based on age they were at first assessment):**
 - *YGTSS form*
 - *Tourette Syndrome Questionnaire*
 - *PUTs*
 - *PEDs-QL (version different if aged 13)*
 - *GTS-QOL (version different if aged 13)*
- Parent questionnaire pack:**
 - *Rage attacks questionnaire*
 - *SNAP-IV 26*
 - *SDQ*

Equipment for Scoring

- Ruler, Clicker counter

Introduction

Introductions

Outline of assessment – show visual timetable

Reminder not to disclose group allocation if possible

Collect parent consent forms

Give parent questionnaires

Request internet password (2 mins)

Go over T3 questions from demographic sheet:

- Since the end of the group treatment have there been any changes in medication?
- Since the end of the group treatment have there been any significant or stressful life events?
- Contact details still correct?
- Would they like to be contacted with regards to the findings of the FU study?

Initial questionnaires

1. GTS-QLS (NB: different questionnaire if age 13)(5 mins)

2. TS Visual Analogue Scale (5 mins)

Allow them to complete these on paper during the set up the computer equipment etc.

Neuropsychological Measures

3. Dimensional Card Sort (4 mins)

Only index finger

4. Flanker Inhibitory Control (3 mins)

Only index finger

5. Motor Dexterity task (Pegboard) (4 mins)

Test dominant hand first.

Position board horizontally with round container next to hand being tested, use bluetak to pin down

Demonstrate task

Practice and test trials for each hand

Other hand to be kept by side

Lay hand on table until told to go. 3-2-1 go...

Start the stop-watch as soon as the person touches the first peg

Stop the stopwatch as soon as the last peg hits the container.

[Record time with milliseconds for dominant and non-dominant hand]

Reposition the unit so round container is next to non-dominant hand. Repeat test.

6. PEDs-QL (NB: different questionnaire if age 13) (5 mins)

Enter data directly onto computer as they complete the paper form

Can put equipment away at this stage if necessary or convenient

7. PUTS (5 mins)

Enter data directly onto computer as they complete the paper form

8. Direct Obs while watching video (20 mins)

Set up video and camera

“Now I’m going to film you, just to get a bit of a sense of what you’re like. I’ll put this video on so you can have something to watch and don’t worry about the camera. It can be a bit of a break for you as well.”

Say **“Simpsons 1”**.

Start stop watch.

At 15 minute, say **“stop”**.

Label video Ppt number and assessment date and NS (non-supp) or TS (tic suppression)

“Now I’d like you to watch for another 5 minutes, but this time try your best to hold your tics in as much as you can for 5 minutes. After that I’m going to give you this toy as a reward.”

Then say **“Simpsons 2”**. Start stopwatch.

Say **“stop”** after 5 minutes and stop video.

Label second video (see above)

Give small reward.

While child watches the video, check their questionnaire filled in on paper for any missing items or unclear responses. Score Visual Analogue scale.

9. YGTSS (30 mins)

Video this (parent and child) if this is one of the first 10% for inter-rater reliability.

“Now I’d like to ask you both a bit more about the tics X has had in the last week.”

Make sure they understand about:

- Sound tics
- Movement tics (can affect any part of the body, can give e.g.s if necessary)
- Sometimes might have several that happen in a sequence

- Tic signal – urge and feeling better afterwards (like the urge to scratch an itch)

“I’ll start by asking you about your movement tics.”

Ask intro questions about age of onset etc

“In the last week have you, or have other people noticed any eye blinking tics?”

Then go through e.g.s

Point out things you think are tics and check if they are (do they get tic signal? Is it unpleasant? How do you feel after the tic? Does it happen in different places?)

Make sure to differentiate between hyperactivity and tics

“Now let’s move on to your sound tics. Again, just thinking about the last week, have you, or have other people noticed any coughing tics?”

All specific e.g.s

“Now I’ve just got some more general questions about your tics”.

FREQUENCY

- **“How often did your tics happen during the last week?”**

Follow-up questions

- Do you have at least one motor tic every day?
- How about every hour, when awake on average?
- How about every five minutes?
- Do they occur in different places?
- What’s the longest time you’ve gone without ticcing in the last week?

Look out for

If the reported frequency varies from what you observe ask about the discrepancy
It is not uncommon to tic more/less during discussion of tics

INTENSITY

“How forceful or strong are your tics?”

- Do they feel like they are bursting out of you really powerfully?
- How noticeable are your tics because of their intensity?
- You can ask how much others notice the tics (aside from family members and adults who know the child well)
- Use your own observation
- How exaggerated are the tics? Do they turn heads in public?
- Does it lead to pain/ wounds?
- Do you get scared of the tics? Would you turn your head? Higher scores then! If you doubt if someone coughs because of tics or because of having a cold, score lower.

COMPLEXITY

How involved or orchestrated are the tics? – for us to code but ask more questions if necessary to clarify.

Follow-up questions:

If necessary ask about how hard they are to camouflage/how much they stand out due to:

- Duration
- Bizarre or obscene character
- Inappropriateness
- Unusual nature

INTERFERENCE

“How do tics get in the way when you’re trying to do things? Like speaking or playing or doing things at school or at home?”

IMPAIRMENT

“How much do tics affect your life? Are the tics stopping you from doing anything? Are you still able to feel good about all the great things you do?”

Queries

How do tic affect your:

- Self-esteem/mood
- Enjoyment of things
- School, grades
- Relationships with friends, family
- Social acceptance, involvement, avoidance

10. Check over any items which were missing from the child questionnaires completed on paper

11. Collect and check parent questionnaires (check over any missing items)

Save spreadsheet

Dismount the F drive

After visit

Enter data for:

- GTS-QoL
- Tourette Syndrome Questionnaire
- Parent questionnaires (SNAP-IV; Rage attacks questionnaire; SDQ)
- Score video – non-suppression and suppression. Enter data into spreadsheet.
- Get NIH data and add to Excel

- Contact participant’s school to request school attendance for last two years
- Double check all data entered and no remaining red cells anywhere
- If there are any red cells, make a note of why and delete the cell in the final entry data so that the cell is empty and will therefore register as “system missing” in SPSS

When next at GOSH -

Make sure participant number is correct. Then copy final data line from last tab of excel spreadsheet into the main SPSS file.

Copy the video onto hard-drive which is kept in office (DS has password)

Put questionnaires in TM's office.

Appendix G: Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989)

[REMOVED FOR COPYRIGHT REASONS]

Appendix H: Further details of 'The Simpsons' episode selection process

Episodes were carefully reviewed by researchers from the original study (KE and RY) to ensure that their content was age-appropriate. Four age-appropriate episodes were then rated for emotional factors that have been found to influence tic expression (Conelea and Woods, 2008). Ratings were provided by a 14-year old girl not otherwise involved in the study. Ratings for each video were then totalled. Video 1 was selected for use at T1. Ratings for the remaining 3 videos were then compared to video 1. Differences in ratings were calculated to establish similarity of videos. Video 2 was used at T2 and video 3 was selected for use at T3 based on similarity of ratings.

Video	Episode name	Rating						Total difference in ratings compared to video 1
		Anxiety-provoking	Boring	Relaxing	Stimulating	Upsetting	Frightening	
1	"Homer Simpson, This is your Wife" Season 17, Episode 15	1	4	7	5	0	0	0
2	"Mr Lisa Goes to Washington" Season 3, episode 2	2	4	6	7	2	0	6
3	"Lemon of Troy" Season 6. Episode 24	3	6	4	6	0	2	10
4	"Bart Vs Australia" Season 6, Episode 16	5	3	3	4	2	4	16

Appendix I: The English translation of the Gilles de la Tourette Syndrome-Quality of Life Scale for children and adolescents (C&A-GTS-QOL; Cavanna et al., 2013)

[REMOVED FOR COPYRIGHT REASONS]

Appendix J: Additional information questionnaire



Identification Number _____



ADDITIONAL INFORMATION

1. Since our last visit (1 year ago), have there been any changes in medication? If yes, please state what the change is and please include any information about increases or decreases in dosage.

2. Since our last visit (1 year ago), have there been any significant or stressful life events?

3. Since our last visit (1 year ago), has your child had any further psychological treatment (either from Great Ormond Street Hospital or another service)? If yes, please elaborate on type of treatment and number of sessions.

Thank you for completing this questionnaire.

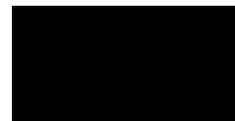
Appendix K: Invitation letter



NHS Foundation Trust

[Name]

[Address]



[Date]

Dear [Name],

Earlier this summer you will have received a letter from us providing you with an update about the research study that you took part in at the Tourette Syndrome Clinic at [redacted]. The letter was also hopefully a reminder about the planned 12-month follow-up to this research that was mentioned to you and discussed at your last home visit. I am now writing again to formally invite you and your child to the 12-month follow-up assessment.

Alongside this letter you will find an information sheet that outlines our reasons for conducting a follow-up assessment as well as information about what the follow-up assessment involves and what to expect if you agree to participate. There is also a children's version of the information sheet included which we would be grateful if you can discuss with your child.

If you and your child are happy with the information provided and would like to continue participating in this study, or would like to know more, please contact Dr [redacted] on [redacted]. Further details are also provided on the enclosed information sheets.

If we do not hear from you, we will contact you by telephone in the next few weeks to check you have received this information and to discuss any queries you may have.

If you agree to participate in the follow-up, we will aim to arrange a suitable time to visit your home for the follow-up assessment.

Many thanks for taking the time to read the enclosed information.

Yours sincerely,

Signature

Dr [redacted]

Consultant Clinical Psychologist



Appendix L: Parent information sheet



NHS Foundation Trust



Information about the project

Project title: Follow-up to a Randomised pilot study evaluating two group therapies for Tourette Syndrome

We work at the Tourette syndrome Clinic at [REDACTED]. We would like to invite you and your child to take part in the follow-up of a research study that you have been involved in. Before you decide if you would like to take part, it is important for you to understand why the follow-up research is being done and what it will involve. Please read through the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. Participation would involve a member of the research team visiting your home at your convenience to carry out an assessment to evaluate whether the group therapy that your child attended at [REDACTED] has been effective in the long-term (1 year on).

What is the purpose of the study?

This follow-up study is interested in the long-term effects of group based psychological therapy for Tourette Syndrome and other chronic tic disorders. As you probably know, the symptoms of these disorders, including tics themselves, can impact greatly on the quality of life of those who experience them. This can be either directly, in terms of physical discomfort associated with the tics themselves, or indirectly, as a result of factors such as the reactions of other people or by making it difficult to concentrate on school work. It is therefore very important that we find effective means of treating the symptoms.

Why have my child and I been asked to help?

We are inviting all families who initially consented to taking part in this research study and attended group treatment at [REDACTED] as part of the study, to take part in a follow-up assessment which aims to identify any long-term effects of group treatment, one year on.

Do I have to take part?

No. Taking part in this follow-up study is entirely voluntary. If you decide not to take part, you do not have to give a reason, no one will be upset and the standard

of care your child receives will not be affected. If you do decide to take part, you can still withdraw at any time, without giving a reason.

What will my child and I be asked to do if we take part?

We will telephone you to arrange a home visit to carry out the reassessment.

The follow-up assessment would be very similar to the initial assessment your child took part in shortly before the group treatment started. During the visit, we would complete some puzzles, tasks and questionnaires with your child. We expect that the tasks would take about 2 hours and 50 minutes, including rest breaks. During this time, your child would also spend 20 minutes watching a DVD while we video them. For the final five minutes of this section, we would ask your child to reduce their tics as much as they are able. We would also ask you as parents and carers to complete some additional questionnaires prior to this assessment.

As part of this study we would also like to consider how your child's school attendance might have been affected by their symptoms in order to help us get a fuller picture of the effects of their tic disorder. In order to do so, with your consent we would speak to your child's school to obtain a % attendance rate during the past two years. If you have any questions about this, please do not hesitate to call us to discuss or alternatively we can answer any questions when we contact you in the next few weeks.

Is there anything to be worried about if my child and I take part?

There are no specific risks from taking part in the follow-up study. If your child gets tired when we are doing the tasks and puzzles then they will be able to take breaks.

It is possible that thinking about their life and the effect of having a chronic tic disorder could be upsetting for your child. If the questionnaires do cause any distress, I would ask that you let us know so that we can offer support and think about what further help is needed.

How will the information help people?

When the follow-up study has finished we will write to you to let you know what we found out about the long-term effects of the groups. We hope this study will help us find out if and how group therapies are useful for children with tic disorders.

Will my child's usual treatment be affected by taking part?

If your child is currently receiving treatment at [REDACTED], they would continue to be seen as usual. Any school liaison work, or medication, would continue as normal and be unaffected by participation in the follow-up assessment.

Who will know that my child and I are taking part in the study?

All information that is collected about your child during the course of the study will be kept strictly confidential. We would keep your and your child's name, address and results from the puzzles and questionnaires secret. We would also keep all

paperwork in a safe place. After we have watched the videos of your child, in order to count their tics, the videos will be permanently deleted. We would write about the study but no names would be used or any information that would show it was your child. If you agreed then we would write to your GP to let them know you are taking part in the follow-up study. We would also liaise with your child's school to obtain a school attendance record.

What will happen to the results of the study?

The results will not be known until the 12-month follow-up data is collected for everyone taking part in the study. We hope to complete data collection and outcome analysis by mid-2015. The results may appear in professional publications and meetings and as part of a doctoral university assignment, but neither you, nor your child, would be recognisable from any transcription. We will also write to you at the end of the study with a brief summary of what we found out. We hope to hold a general feedback session once the study is complete, which you will be invited to.

Who has organised and approved the research?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the London Queen Square Research Ethics Committee. Their contact details are provided below. The research is being sponsored by [REDACTED].

Who is funding the research?

Funding for the study has been provided from two sources. These are, University College London and the Tourette Action, UK (the National Charity for Tourette syndrome).

What if something goes wrong?

This study is indemnified under the Clinical Negligence Scheme for NHS Trusts, which provides cover for negligent harm. If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this via the Patient Advice and Liaison Service at [REDACTED]:

[REDACTED] Patient Advice and Liaison Service (PALS):

PALS will help and advise on any issue related to your hospital experience.
Email: [REDACTED] – Telephone: [REDACTED]

What do I do now?

Thank you for reading this information. If you and your child are interested in taking part in the follow-up study, please contact Dr [REDACTED] (Tel: [REDACTED]) to hear more. If we do not hear from you, we will contact you by phone during October 2014 to answer any questions you may have and to see if you are interested in taking part.

Who do I speak to if I have further questions or worries?

Contact: [REDACTED]

Address: [REDACTED]
[REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]

Email: [REDACTED]

Tel: [REDACTED]



NHS Foundation Trust



Information about the project

Project title: Follow-up to a Randomised pilot study evaluating two group therapies for Tourette Syndrome

We work at [REDACTED]. We are asking you and your parents to take part in the follow-up to a project you were involved in just under a year ago. This leaflet will remind you about the project you took part in, and tell you about the follow-up. We hope you can read about the project with someone in your family. Please ask us if you have any questions. Take your time to decide whether or not you want to take part.

What is this project and why are we doing it?

This study is interested in whether new therapies can have long-term effects for children with tic disorders. We would like to find out if the group treatment you attended just under a year ago has helped you in your life or made your difficulties easier to cope with over the past 12 months.

We would also like to find out whether you have found it easier to attend school since completing the group treatment. We would get this information by contacting your school directly.

Why have I been asked to take part?

We are asking all children and young people who attended group treatment at [REDACTED] and were involved in the original study, to take part in this follow-up study.

After you finished the group treatment you were visited by one of our research team members when you would have completed some puzzles, tasks and questionnaires. We would now like to visit you at home once more, to see if there have been any changes over the past 12 months.

Do I have to take part?

No, you do not have to take part. If you decide not to take part in this follow-up study, you do not have to give a reason and no one will be upset. You

can change your mind at any time. You can stop being in the study even if you said yes at the beginning.

Will taking part help me?

We will evaluate whether it has helped you to reduce your tics over the past 12 months or whether it has helped you in other areas such as your satisfaction with your life or your ability on certain thinking tasks as well as your attendance at school. Afterwards, we would let you know if the groups helped you in terms of any of the areas we have evaluated.

Once the study is finished we will invite you and your family to a feedback session where we will explain the results of the study and what we have learnt.

What will I be asked to do if I take part?



- We will arrange a meeting with you and your parents at your home, which should last about 3 hours.
- We'll spend this time doing puzzles and asking you some questions.



- We will ask you to do a selection of different things and hope you will find them interesting.
- During the visit we would ask you to watch a DVD for 20 minutes and make a film of you as you watch it. For five minutes we would



- also ask you to try to tic as little as you can.
- You would be able to have short breaks if you feel tired or to stop if you want to.
- We would also ask your parents or carers some questions.

Is there anything to be worried about if I take part?

When we do the games and puzzles you can take breaks if you get tired. If you are upset by taking part in the study, please speak to your parents about it. If you would like to speak to someone else, your parents know how to contact us and our address and phone number are at the end of this sheet. Your treatment at [REDACTED] will not be changed by taking part or not taking part in the study.

Who will know I am taking part in the study?

We would keep your name, address and your results from the games and puzzles secret. We will write about the study but no names will be used. If you agreed then we would write to your doctor to let them know you are taking part.

What will happen to the results of the study?

The results of the 12-month follow-up visit will not be known until about September 2015. We hope to organise a time to tell everyone about the study soon after that, which you would be invited to.

Who do I speak to if I have further questions or worries?

Your parents also have information about this study. You can ask them questions. You can contact [REDACTED] if you have any other questions.

Contact: [REDACTED], Consultant Clinical Psychologist

Address: [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Email: [REDACTED]

Tel: [REDACTED]

Supervised by: [REDACTED], Consultant Clinical Psychologist, [REDACTED]
[REDACTED]

PLAN FOR TODAY

- 3 forms



- Computer games x 2



- Peg game



- 2 forms



- Games and puzzles

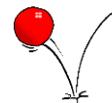


- Watching a Simpsons episode



- Trying to hold in your tics for 5mins →

bouncy ball REWARD!



- Talking together with your

parents/carers about your tics this week

- 1 form



THE END

THANK YOU! 😊

Appendix O: Parent consent form



NHS Foundation Trust

Identification Number _____



CONSENT FORM FOR PARENTS/ GUARDIANS

Title of Project: Follow-up to a Randomised pilot study evaluating two group therapies for Tourette Syndrome

Names of Researchers: Julia Dabrowski, Trainee Clinical Psychologist

, Consultant Clinical Psychologist

, Consultant Child Psychiatrist

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily.

2. I understand that my child's participation is voluntary and that I am free to withdraw at any time, without giving any reason, without medical care or legal rights being affected.

3. I agree to my child being videoed for the purpose of the study.

4. I understand that relevant sections of my child's medical notes and data collected during the study may be looked at by responsible individuals from regulatory authorities or the NHS trust, where it is relevant to their taking part in this research. I give permission for these individuals to have access to my child's records.

5. I agree to a researcher contacting my child's school in order to obtain their school attendance rate.

- 6. I understand that the videos will be encrypted and stored on password protected computers. They will be permanently erased once they have been viewed by the researchers, in line with data information governance and the law.

- 7. I understand that while participating in the study my child will be unable to receive any individual psychological treatment, but that should they require this, we will be able to withdraw from the study at any time.

- 8. I understand that sections of my child's medical notes may be looked at by the researchers where it is relevant to my taking part in the study. I give permission for these individuals to have access to my child's records.

- 9. I agree to my child's GP being informed of their participation in the study.

- 10. I agree to participate in the above follow-up study.

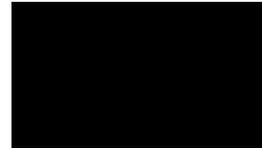
Version and date of the participant information sheet that the parent/carer has read: _____

Please initial the box after each statement.

Name of Child _____

Name of Parent or Guardian	Date	Signature
_____	_____	_____
Researcher		
_____	_____	_____

Appendix P: Child assent form



Identification Number _____

PARTICIPANT ASSENT FORM

Title of Project: Follow-up to a Randomised pilot study evaluating two group therapies for Tourette Syndrome

Names of Researchers: Julia Dabrowski, Trainee Clinical Psychologist

, Consultant Clinical Psychologist

, Consultant Child Psychiatrist

Please circle YES or NO

Have you understood the information you were given? YES NO

Have you understood that we would video you as part of the study? The videos would be deleted once we have used them and will not be viewed by anyone except the researchers. YES NO

Have you understood that we would contact your school to obtain a school attendance record? YES NO

Have you been able to ask questions and had them answered? YES NO

Would you like to take part? YES NO

Do you understand that you can stop being involved
in the study at any time you like? YES NO

Name Date Signature

Researcher Date Signature

Appendix Q: Mixed model Repeated Measures Analysis of Variance (RM-ANOVA) tests analysing the effects of time (T1, T2, T3) and group condition (PE and CBIT) on tic severity

	PE (N = 13)			CBIT (N = 15)			Main effect of group	Main effect of time	Interaction	All (N = 28)		
	T1	T2	T3	T1	T2	T3	<i>p</i>	<i>p</i>	<i>p</i>	T1	T2	T3
	M (SD), 95% CI	M (SD), 95% CI				M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI				
YGTSS												
Motor	15.92 (3.23), 13.97 – 17.87	15.54 (2.33), 14.13 – 16.95	13.77 (4.46), 11.08 – 16.46	17.60 (4.53), 15.09 – 20.11	14.73 (3.83), 12.61 – 16.85	12.20 (5.07), 9.39 – 15.01	0.86	<0.001**	0.07	16.82 (4.00), 15.27 – 18.37	15.11 (3.19), 13.87 – 16.34	12.93 (4.78), 11.08 – 14.78
Phonic	12.92 (6.41), 9.05 – 16.80	11.15 (6.35), 7.32 – 14.99	9.23 (7.28), 4.83 – 13.63	12.33 (7.19), 8.35 – 16.31	12.33 (5.64), 9.21 – 15.46	10.00 (7.10), 6.07 – 13.93	0.84	0.013**	0.66	12.61 (6.72), 10.00 – 15.21	11.79 (5.90), 9.50 – 14.07	9.64 (7.06), 6.90 – 12.38

	PE (N = 13)			CBIT (N = 15)			Main effect of group	Main effect of time	Interaction	All (N = 28)		
	T1	T2	T3	T1	T2	T3	<i>p</i>	<i>p</i>	<i>p</i>	T1	T2	T3
	M (SD), 95% CI				M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI					
Tic Severity	28.85 (8.70), 23.59 – 34.10	26.69 (7.50), 22.16 – 31.22	23.00 (10.83), 16.45 – 29.55	29.93 (10.05), 24.37 – 35.50	27.07 (8.44), 22.39 – 31.74	22.20 (10.84), 16.20 – 28.20	0.946	>0.001**	0.791	29.43 (9.29), 25.83 – 33.03	26.89 (7.87), 23.84 – 29.94	22.57 (10.64), 18.45 – 26.70
Total tic score	49.62 (16.08), 39.90 – 59.33	46.69 (13.15), 38.75 – 54.64	43.77 (17.27), 33.33 – 54.21	52.60 (15.57), 43.98 – 61.22	41.73 (14.04), 33.96 – 49.51	39.53 (18.04), 29.55 – 49.52	0.695	0.002**	0.235	51.21 (15.59), 45.17 – 57.26	44.04 (13.62), 38.76 – 49.32	41.50 (17.49), 34.72 – 48.28

** Significant result that survives Bonferroni correction ($0.05/4 = 0.013$).

Appendix R: Results from a series of 2 X 2 RM-ANOVA tests analysing the effects time (T2 and T3) and group condition (PE and CBIT) on tic severity

	Psych-Ed (N = 13)		CBIT (N = 15)		Main effect of group	Main effect of time	Interaction
	T2	T3	T2	T3			
YGTS	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	M (SD), 95% CI	<i>p</i>	<i>p</i>	<i>p</i>
Motor tic severity	15.54 (2.33), 14.13 – 16.95	13.77 (4.46), 11.08 – 16.46	14.73 (3.83), 12.61 – 16.85	12.20 (5.07), 9.39 – 15.01	0.382	0.011**	0.630
Phonic tic severity	11.15 (6.35), 7.32 – 14.99	9.23 (7.28), 4.83 – 13.63	12.33 (5.64), 9.21 – 15.46	10.00 (7.10), 6.07 – 13.93	0.670	0.059	0.851
Total tic severity	26.69 (7.50), 22.16 – 31.22	23.00 (10.83), 16.45 – 29.55	27.07 (8.44), 22.39 – 31.74	22.20 (10.84), 16.20 – 28.20	0.715	0.012**	0.948
YGTS total score	46.69 (13.15), 38.75 – 54.64	43.77 (17.27), 33.33 – 54.21	41.73 (14.04), 33.96 – 49.51	39.53 (18.04), 29.55 – 49.52	0.394	0.364	0.897

** Significant result that survives Bonferroni correction ($0.05/4 = 0.013$).