A randomised trial comparing Habit Reversal and psycho-education treatment groups for children with Tourette Syndrome

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Abstract

The quality of life of children with Tourette Syndrome, a neurodevelopmental condition characterised by chronic tics, is impacted greatly by both the symptoms themselves and their social consequences. Habit Reversal Therapy, a behavioural therapy for tic management, has substantial empirical support in its individual form, but this approach has never been investigated in a group format. Group based delivery of Habit Reversal Therapy could increase access to therapy, improve the cost-effectiveness of treatments and potentially offer additional therapeutic benefits.

This randomised controlled pilot study evaluated the feasibility and preliminary efficacy of Habit Reversal Therapy compared to psycho-educational groups for 33 children aged 9 to13 years with Tourette Syndrome and Chronic Tic Disorders. Outcomes of the groups were evaluated in terms of reductions in tic severity and improvements in quality of life.

Good attendance rates in both groups suggested feasibility and acceptability of the interventions. Improvements in tic severity and quality of life were found in both groups, although to a lesser extent compared to previous studies of individual behavioural therapy for tics. Motor tic severity showed greater improvements in the Habit Reversal Therapy group on the main outcome measure (Yale Global Tic Severity Scale) but not on a direct observational measure of tic frequency.

Given the potential for such groups to provide additional treatment options for families, further research is warranted. Clinical implications and suggestions for improvements to the current design for a larger study are outlined as well as indications for wider reaching future research.

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Chapter 1. Introduction

Tourette Syndrome (TS) and Chronic Tic Disorders (CTDs) are characterised by frequent vocal or motor tics, aversive premonitory urges (PU) to tic and high rates of comorbidity. The quality of life (QoL) of children with the condition is impacted greatly by both the symptoms themselves and their social consequences (Cutler, Murphy, Gilmour, & Heyman, 2009). Individual Habit Reversal Therapy (HRT) has substantial empirical support (McGuire et al., 2014) but HRT has never been investigated in a group format. Group based delivery of HRT has the potential to increase access to therapy and cost-effectiveness of treatments, as well as potentially offering additional therapeutic benefits. There is also preliminary evidence that psycho-educational groups may be of benefit to children with TS.

The present study was a randomised controlled pilot study, investigating the feasibility and preliminary efficacy of HRT and psycho-educational groups for children aged 9 to13 years with TS. The groups were evaluated in terms of their ability to reduce tic severity and improve QoL. This chapter introduces the rationale for the study, describing TS and its impact in terms of psycho-social functioning and quality of life (QoL). Current therapeutic approaches based on neuro-behavioural models of TS are discussed. The rationale for the study is then outlined in the context of the research described.

1.1 Tic Disorders

A tic is "*an involuntary, rapid, recurrent, non-rhythmic motor movement…or vocal production that is of sudden onset and that serves no apparent purpose*" (World Health Organisation, 1990). Simple tics include movements like eye-blinking or

shrugging and vocal tics such as hissing or throat-clearing. Complex tics involve co-ordinated muscle movements. Examples are hopping or hitting oneself or vocal tics, such as saying words or phrases.

The most widely recognised tic disorder is Tourette Disorder, or Tourette Syndrome (TS), a developmental neuropsychiatric disorder first described by Gilles de la Tourette in 1885. Tourette Disorder is defined as involving multiple motor tics and at least one vocal tic that have been present for over a year (American Psychiatric Association, 2013). Onset must occur before age 18 and the condition should not directly result from another medical condition or substance. TS is one of a spectrum of tic disorders, including chronic motor and chronic vocal tic disorders. Shorter tic episodes may be given a diagnosis of provisional tic disorder.

Media presentations of TS tend to highlight coprolalia and copropraxia (i.e. obscene words and gestures respectively). In clinical populations, coprolalia only occurs in 19.3% of males and 14.6% of females with TS, and copropraxia in 5.9% of males and 4.9% of females (Freeman et al., 2009). Such tics are associated with severer forms of TS and the presence of comorbidity (Kobierska, Sitek, Gocyła, & Janik, 2014).

Scharf, Miller, Mathews and Ben-Shlomo (2012) have reported that, at age 13, TS prevalence rates are about 1% among UK population based samples. Prevalence rates in international community samples are similar among children aged 5 to 18 years (Robertson, 2008). TS is documented in all cultures and seems to present in a similar way globally, perhaps indicating its biological roots (Robertson, 2008). TS is about four times as common in males as females (Freeman et al., 2000). In contrast to the full TS diagnosis, tics alone are very common, with a point prevalence of between 7 and 28% (Robertson, 2008).

Tics tend to present in a fluctuating pattern, occurring in bouts over days, weeks and months (Leckman et al., 1998). The mean age of tic onset is about 6.4 years (Freeman et al., 2000) and symptoms peak between 10 and 12 years (Bloch & Leckman, 2009). Tics then tend to reduce in frequency towards later adolescence, by which point prevalence drops to about 4 in 10,000 (Apter et al., 1993). However such changes are not seen in all cases. Pappert, Goetz, Louis, Blasucci and Leurgans (2003) followed 31 children with TS into early adulthood. They found that, despite reporting significant improvements, 90% of the sample still displayed tics on objective video based assessment.

TS is associated with high comorbidity. In clinical samples, only an estimated 12% of children with TS have no reported comorbid diagnosis and most have an average of two additional diagnoses (Freeman et al., 2000). The most common comorbidities are Attention Deficit Hyperactivity Disorder (ADHD; 60%) and Obsessive Compulsive Disorder (OCD; 27%). Mood disorders, anxiety and learning disability are also common (Freeman et al., 2000). Interestingly, rates of comorbidity are reportedly considerably lower in community samples. Scharf et al. (2012) reported OCD in 20% of children with TS and ADHD in 18%. The data suggest the presence of additional diagnoses causes an additional functional impact and increased likelihood of presentation to specialist clinics. These community sample rates among children with TS remain about 10 times higher than rates for OCD and ADHD in the population as a whole. In contrast to tics themselves, symptoms of comorbid conditions more often continue into adulthood (Bloch & Leckman, 2009).

1.2 Aetiology

Historically tics were considered completely involuntary movements and TS purely biological in origin. The neurobiological processes involved are not yet clearly defined but are thought to involve disruption of cortico-striatal-thalamo-cortical pathways in the brain, probably via dysfunction of the dopaminergic system (Felling & Singer, 2011). Genetics plays an important role but the pattern of inheritance is complex and poorly understood (Deng, Gao, & Jankovic, 2012).

It is now recognised that, while tics are usually experienced as involuntary, they are in fact subject to a degree of control and affected individuals can suppress their tics for varying lengths of time (M. Himle & Woods, 2005; Woods, Himle, et al., 2008). In addition, tic frequency is influenced by environmental antecedent factors such as stress levels, excitement, fatigue and social events, or consequent factors such as the reactions of other people (Conelea & Woods, 2008b). Many people with TS report that their tics often reduce when they are concentrating on an absorbing activity and can be provoked by suggestion, such as somebody mentioning a particular tic or seeing another person's tic (Jankovic, 2001).

The evidence suggests that, while TS has biological origins, its symptoms are influenced by environmental factors. Further information regarding tic suppression and psychological elements of tic expression has arisen through investigation of the premonitory urge (PU). The PU is an aversive sensation experienced prior to a tic by 92% of those with TS (Kwak et al., 2003). The strength of this sensation varies. Tic suppression is reported to lead to an increasing sense of inner tension or pressure which is relieved when the tic occurs (Leckman, Walker, & Cohen, 1993). Kane (1994, p. 806) described the experience of attempting to suppress a tic, saying "*The intensity rises until it becomes so unpleasant and distracting that tics must be*

executed (with a compulsion that rivals the scratching of a severe itch)". Rather than simply preceding tics, it seems therefore that the PU directly precipitates them. Such descriptions support the suggestion that tics are voluntary responses to involuntary urges (Bliss, Cohen, & Freedman, 1980). This characterisation is condoned by 67% of individuals with TS (Kwak et al., 2003).

Conelea and Woods (2008b) have questioned whether the tics themselves are directly influenced by these antecedent and consequent factors, or whether only the ability or motivation to suppress them changes. Support for this suggestion comes from experimental paradigms in which children believed rewards were contingent on tic suppression (M. Himle & Woods, 2005; Capriotti, Brandt, Turkel, Lee & Woods, 2014). In such circumstances, children can suppress their tics, suggesting that voluntary suppression is possible for many children given sufficient motivation.

Piacentini, Pearlman and Peris (2007) suggest that the aversive nature of the PU and its relief when the tic occurs may contribute to a process of negative reinforcement which serves to maintain tics. Capriotti et al. (2014) found evidence for this in a controlled experiment with 8 to 17 year olds. Participants were rewarded for tic suppression across several different conditions and were also given the option to press a button to initiate breaks in the experiment when they were free to tic. They also asked children to give periodic reports of the strength of their urges to tic throughout the experiment. In support of the negative reinforcement hypothesis, children reported increased urges during the tic suppression intervals and especially just prior to moments when they opted to take a break. Reported urges then decreased progressively during break periods, during which the children displayed more tics. In addition, as the experiment progressed, the longer the children had spent suppressing their tics during the reinforcement phases, the smaller the urge strength they reported

each time. According to the negative reinforcement hypothesis, this suggests that they began to habituate to the PU. As this happened, they also began to take fewer breaks from the paradigm, suggesting the act of tic suppression was becoming more tolerable.

The negative reinforcement model described suggests a parallel with models of OCD in which suppression of intrusive thoughts leads to temporary relief and subsequent reinforcement of the aversive thoughts (Purdon, 1999). This is consistent with reports that Exposure and Response Prevention (ERP) has demonstrated effectiveness in reducing tics (Verdellen et al., 2008).

1.3 Neuro-Behavioural Models

Findings such as those described above have led to the development of new theoretical models for TS and opened the door to psychological treatments. The neuro-behavioural model which is currently most influential is the Comprehensive, Integrated model of TS (CIM; Woods, Piacentini, & Walkup, 2007). According to the CI model, tics emerge as the result of genetic and neurological factors which provide a neurobiological substrate for tics and associated features, such as the PU. The tics then influence the individual's internal and external environment. The context in which tics appear, in turn, influences the neurobiology and hence shapes tic expression. The behavioural element to the model considers environmental factors to act as antecedents or consequences to tics. For example, external antecedents might include particular places, such as the cinema or the classroom; activities, such as watching television or taking exercise; or the presence of particular stimuli, such as the mention of a particular tic. Internal antecedents include the PU or particular mood

states or thoughts. External consequences include other people's reactions to tics, such as teasing, being stared at in the street or being asked to leave the room at school. Internal consequences include the relief of the PU. The exact profile of antecedents and consequences is suggested to be idiosyncratic to each individual, based on their experiences.

A recent extension to the behavioural model is the suggestion that the PU itself develops through behavioural processes (Capriotti, Espil, Conelea, & Woods, 2013). This suggestion developed from evidence that younger children's experience of the PU differs from that of older children (Banaschewski, Woerner, & Rothenberger, 2003). Early reports suggested that the PU may develop a few years later than tics themselves (Leckman et al., 1993), raising the question of why younger children might not experience the urge. Woods, Piacentini, Himle, & Chang (2005) compared older children to children aged 10 and younger on responses to the Premonitory Urge for Tics Scale and found that mean scores did not differ. This suggests both younger and older children do experience an urge. Interestingly, the measure showed reduced internal consistency in the younger sample, leading the authors to argue that rather than lacking the urge itself, younger children lack the ability to consistently identify and report on the experience, perhaps based on limited language function.

While limited verbal ability could explain the finding, another suggestion is that the nature of the PU changes over time through behavioural processes. Capriotti et al. (2013) suggest that the PU itself develops through a behavioural process. The authors suggest that mild and relatively benign pre-tic sensations become aversive and increasingly salient over time as the child experiences negative consequences to their tics. Experiencing repeated pain or social consequences, such as bullying, may

gradually cause pre-tic sensations to be associated with negative emotions. It is hypothesised that pre-tic sensations are present in all children but that these take on their highly aversive nature over time, through interaction with the environment. Consistent with this theory, Wang et al. (2011) have reported that when the PU is active, the neural structures activated in the brain are those consistent with punishment based learning and negative emotions.

Another study by Zinner et al (2012) examined reports of PUs, comparing children who reported regularly experiencing bullying to those who did not. The victims of bullying reported significantly greater PU scores compared to non-victims. While this finding is consistent with the behavioural hypothesis, the data are cross-sectional and correlational and could alternatively be explained by the fact that children with greater urges have more frequent and noticeable tics making them more vulnerable to bullying. Additionally, the data did not report whether bullying was directed at the tic behaviour.

Capriotti et al. (2013) examined the behavioural theory of PU development in a survey of youths with TS. They directly examined relationships between tic severity, PU severity and perceived impact in relation to tics by asking about negative consequences experienced as a result of tics. The authors reported that while tic severity was predictive of PU severity, this relationship was no longer significant once tic related impact was controlled for. Although the data are again correlational and, therefore, cannot be used to infer cause and effect, this does suggest the relationship between tic related impact and PU is primary. This is consistent with the proposed theory of a behavioural link between negative tic consequences and negative experience of the PU.

The CI Model of TS is emphasised here as it has been used in the development of the treatments for TS discussed below. Full discussion of alternative models is not within the scope of the current thesis. However, it is worth mentioning a possible criticism of the CI Model which is that it does not adequately incorporate potential cognitive factors which may be involved in maintaining tics. While thought processes are suggested as possible internal antecedents or consequences, these are not emphasised and have not been explicitly addressed in treatment approaches based on the model. O'Connor, Gareau and Blowers (1994) have suggested that expectations of judgement by others and feelings of obligation to constrain tics may be associated with tic exacerbation. Alternative models have been offered which place additional emphasis on such features and may offer avenues for the development of interventions in the future (O'Connor, 2002).

1.4 The Impact of TS

Symptoms of TS and comorbid conditions significantly impact many areas of children's lives and psychosocial functioning, such that, for more than one child in five, symptoms at their peak affect school attendance (Leckman et al., 1998). Tics can result in physical pain, such as muscle aches from repeated tics (Riley & Lang, 1989) and, in extreme cases, stress fractures (Fusco, Bertani, Caricati, & Della Giustina, 2006). Children often have to manage tics at their most severe while also coping with the complex developmental challenges of adolescence (Happich, 2012). Self-abusive behaviour is reported in 22% of children with TS (Wand, Matazow, Shady, Furer, & Staley, 1993). The impact can continue into adulthood (Lewin et al., 2012).

Sleep difficulties, such as nightmares and tiredness on waking, are reported in 80% of children with TS (Storch et al., 2009). Educational difficulties such as attention problems and performance on time-limited tasks are also commonly reported (e.g. Shady, Fulton, & Champion, 1989; Storch, Lack, et al., 2007) .

Aggressive outbursts or explosive rage attacks are common and can be very disabling (Budman, Rockmore, Stokes, & Sossin, 2003). Frank, Piedad, Rickards and Cavanna (2011) found that 74% of children with TS, compared with about 9% of healthy children, met criteria for an impulse control disorder. Parents report that, when present, explosive outbursts are their child's most impairing symptom (Dooley, Brna, & Gordon, 1999). Family dysfunction has been reported in affected families (Conelea et al., 2011; Eddy, Rizzo, et al., 2011) and stress among parents and caregivers is often high, with carers at increased risk of psychiatric comorbidity (Cooper, Robertson, & Livingston, 2003).

Difficulties in socialisation and peer relationships are also common among children with TS (Meucci, Leonardi, Zibordi, & Nardocci, 2009; Packer, 2005; Stefl & Rubin, 1985; Storch, Lack, et al., 2007). Wand et al. (1993) reported that 42% described social isolation and embarrassment as the most disabling element of their disorder. Children displaying tics tend to be rated as less socially acceptable by peers (Boudjouk, Woods, Miltenberger, & Long, 2000; Woods, Fuqua, & Outman, 1999). Zinner, Conelea, Glew, Woods and Budman (2012) found that 26% of children with TS reported victimisation by peers and this was associated with lower reported QoL.

While tics frequently reduce in later adolescence or early adulthood, the impact of TS at a key stage of development may have lasting consequences. Pappert et al. (2003) followed children with TS into early adulthood. They reported that while

many were functioning well, over 25% experienced significant problems such as unemployment, alcohol abuse or criminal activity.

1.5 Quality of Life

Given evidence that children with TS are adversely impacted by their condition, interventions should aim to reduce this impact. One means of measuring the overall impact of an illness or chronic condition is by assessing quality of life (QoL). There are many definitions of QoL and debate over the best way to measure it (Cummins, 2000). The World Health Organisation defines QoL as being "*an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns*" (The WHOQOL Group, 1995, p. 1405). This is a multi-dimensional construct encompassing physical, psychological, social and spiritual QoL, our level of independence and the quality of the environment in which we live.

The related concept of Health Related QoL is used frequently in health research to evaluate the impact of health conditions and the value of interventions (Varni, Seid, & Kurtin, 2001; Zekovic & Renwick, 2003). Improving QoL of those with chronic health conditions is now an explicit aim of the National Health Service (Department of Health, 2012). The focus has moved from objective measures of physical changes to subjective individual experience. Within child mental health research, QoL is usually measured in relation to physical, psychological and social functioning domains with the frequent addition of a cognitive domain (Danckaerts et al., 2010). Both generic health related QoL scales (Upton et al., 2005) and disease specific measures (Cavanna et al., 2008) have been used in TS research. Single point

measures have also shown reliability in producing a global impression of perceived QoL (de Boer et al., 2004).

1.6 TS and Quality of Life

Given the impact described, it is unsurprising many studies demonstrate that both adults (Elstner, Selai, Trimble, & Robertson, 2001) and children (Cutler et al., 2009; Elstner et al., 2001; Meucci et al., 2009; Storch, Merlo, et al., 2007) with TS report diminished QoL compared to those without the condition. A qualitative investigation of factors influencing QoL in children with TS (Cutler et al., 2009), identified "fitting in with peers" and "attempts to control tics" as important factors. Other important factors were emotional well-being, bullying and physical pain from tics.

In adulthood, OCD is reported to be the main psychiatric comorbidity but high rates of depression are reported to have a greater impact on QoL (Jalenques et al., 2012). Conelea, Busch, Catanzaro and Budman (2014) found that adults with TS who restrict their activities because of tics are more likely to report poor emotional functioning and reduced QoL than those who continue to participate in their usual activities despite tic severity. It is, therefore, possible that interventions aimed at reducing embarrassment about tics, improving self-concept and promoting continued activities may be as important as reducing tics themselves.

Symptoms of ADHD are also found to impact considerably on QoL (Limbers, Ripperger-Suhler, Heffer, & Varni, 2011; Marques et al., 2013; Remschmidt & Mattejat, 2010) and these effects can continue into adulthood (Agarwal, Goldenberg, Perry, & Ishak, 2012). Graetz et al. (2001) found that those with inattention problems showed higher levels of social and school-related difficulties as well as lower self-esteem but they showed fewer externalising problems compared to those with greater

impulsivity or hyperactivity symptoms. Children with both inattention and impulsive difficulties were the most impaired. Gjervan, Torgersen, Rasmussen and Nordahl (2012) looked at the QoL domains affected by the various symptoms and reported that while inattentiveness was related to impaired emotional outcomes, hyperactivity and impulsivity were more closely related to social function and mental health.

In order to develop effective interventions to improve QoL in children with TS, it is relevant to consider which features of the condition impact most directly. Candidates for the most debilitating feature of TS include the severity of tics, the severity of the PU and comorbid symptoms. Whether tic severity independently impacts QoL has been debated. Many studies report that tic severity is not correlated with QoL measures (Bernard et al., 2009; Carter et al., 2000; Eddy, Cavanna, et al., 2011) and argue that comorbidities are more important (Carter et al., 2000; Eddy et al., 2012; Eddy, Cavanna, et al., 2011; Pringsheim, Lang, Kurlan, Pearce, & Sandor, 2009; Rizzo, Gulisano, Calì, & Curatolo, 2012). However, individuals with "pure" TS and no comorbidities are reported to experience reduced QoL compared to healthy controls (Rizzo et al., 2012), particularly in areas of social functioning and relationships (Eddy, Rizzo, et al., 2011). Some studies have also demonstrated a direct relationship between tic severity and QoL even in those without comorbidities (Eddy, Rizzo, et al., 2011).

One explanation for these different findings may be that an association between tics and QoL is harder to detect in individuals with mild to moderate tics (Bernard et al., 2009). Another is that factors which have been shown to impact the strength of the association, such as anxiety and depression (Lewin et al., 2011), may not have been taken into account. In addition, many studies used generic measures of QoL which were not disease specific for TS.

A recent case report of a man treated for tics using deep brain stimulation indicated that, while his tics improved considerably, he reported an ongoing sense of inner tension and no subjective improvement in QoL (Foltynie et al., 2009). This suggests the intervention may have reduced tics but the ongoing PU continued to affect QoL. Some have suggested the PU may be more debilitating than tics themselves (Leckman et al., 1993). It is, therefore, another candidate for the symptom that impacts QoL most directly. This would be consistent with the notion that the PU develops its aversive quality through negative feedback in relation to tics and the finding that there is a stronger relationship between negative tic consequences and the PU than between negative consequences and tic severity (Capriotti et al., 2013). Despite this, many studies of QoL in TS have not included measures of the PU (see Cavanna, David, Orth, & Robertson, 2012).

Ganos et al. (2012) did not find an association between QoL and PU intensity however their sample consisted of only 15 adults. Larger studies have reported such a relationship (Crossley & Cavanna, 2013) and the relationship is stronger in those without additional comorbid conditions (Eddy & Cavanna, 2013). Cavanna et al. (2012) found that tic severity was the childhood symptom which best predicted QoL in adulthood, followed by the presence of the PU and finally a family history of TS. Neither ADHD nor OCD symptoms were found to be predictive. The authors argue that their finding differs from others as they used TS specific QoL measure (Cavanna et al., 2008) better able to detect the aspects most relevant to people with TS. While this is true, the measure of PU used can be questioned, as the authors included only the presence or absence of the PU in their model, rather than urge severity. The hypothesis outlined above would suggest that, if PU strength were included in the

model, it might have shown a stronger relationship to QoL than the tic severity variable.

While the precise relationships between these variables remain somewhat unclear, there is preliminary evidence that both the PU and tic severity can independently affect QoL and considerable evidence that this impact is increased by comorbid conditions. The debate may be somewhat academic, as rates of comorbidity are high (Freeman et al., 2000) and phenotypes change over time. The validity of current diagnostic categories has also been debated (Cavanna, Servo, Monaco, & Robertson, 2009; Rizzo et al., 2012). What is clear is that those with TS experience reduced QoL as a result of their disorder and associated comorbidities. There is, therefore, a clear need for effective treatment to address both tics themselves and other impairments.

1.7 Therapeutic Approaches

The biological framework led most early treatment research to focus on pharmacotherapy, particularly dopamine antagonists, such as typical antipsychotics like Haloperidol, or atypical antipsychotics like Risperidone (Thomas & Cavanna, 2013). Such medications have shown reductions in tic severity of between 13 and 54% (Scahill et al., 2013) with effect sizes of up to $d = 1.05$ against placebo. Medicines are not without drawbacks, however. Some affected individuals refuse drugs or discontinue treatment due to side effects while others find their tics do not respond or only respond partially to medication (Deckersbach, Rauch, Buhlmann, & Wilhelm, 2006). Concern about side effects is a commonly cited reason for avoiding medication (Woods, Conelea, & Himle, 2010).

Another medical treatment for which there is preliminary evidence of effective tic reduction is deep brain stimulation, involving surgical placement of electrodes over particular brain areas and continuous electrical stimulation from a subcutaneously implanted pulse generator (Piedad, Carlo, Rickards, & Cavanna, 2012). Preliminary research has shown improvement in 59 of 63 patients studied; however, extensive randomised trials have not been conducted (Müller-Vahl et al., 2011). Although the procedure is reversible, it is an invasive and radical treatment option and, in the absence of further research, is recommended only for adults with severe treatment resistant tics (Müller-Vahl et al., 2011).

Evidence that tics are partially voluntary in nature and affected by environmental factors, combined with the limitations of medical treatments, has led to a demand for alternative therapeutic approaches and precipitated research into behavioural therapies. Various approaches have been suggested and trialled but few have received empirical support (Verdellen, van de Griendt, Hartmann, & Murphy, 2011). The therapy with the strongest empirical support following recent meta-analyses is Habit Reversal Training (McGuire et al., 2014; Wile & Pringsheim, 2013). This approach and its evidence base are discussed in more detail below.

1.8 Habit Reversal Training

Habit Reversal Training (HRT) was initially developed in the 1970s as a method of reducing habits and tics (Azrin & Nunn, 1973). The treatment involves five main elements. Firstly, awareness training encourages the child to notice details of tic occurrences, associated sensations and environmental factors that influence them.

Given that tics can be suppressed, it may be assumed that, as with other habits, awareness of impending tics is a precursor to successful tic suppression. Single case studies, such as Billings (1978), have reported success of the approach in reducing both tic frequency and intensity. However, systematic evaluation of this approach individually has not been conducted so it cannot be considered to have an independent evidence base (Cook & Blacher, 2007).

The next stage of HRT involves development of an incompatible competing response for each tic. This is carefully designed as something socially inconspicuous to be conducted alongside other activities for about a minute each time the urge to tic arises or a tic occurs. This was originally thought to work by strengthening muscles antagonistic to tics. However, this theory was discredited when it was shown that competing responses remain effective when they involve unrelated muscle groups (Woods, Murray, et al., 1999). Given that the neuro-behavioural model suggests negative reinforcement is involved in tic maintenance, habituation has been suggested as a possible mechanism (Verdellen, Keijsers, Cath, & Hoogduin, 2004) and this theory is currently popular. The competing response is thought to interrupt the tic sequence so the child is exposed to the aversive PU and may then habituate to it, breaking the negative reinforcement cycle. This may explain why ERP techniques have also received some empirical support in the treatment of TS, as they may share underlying mechanisms (Verdellen et al., 2008). A subsequent and compatible theory is that the new behaviour comes to replace the original tic through social reinforcement whereby children receive praise and encouragement for using competing responses (Miltenberger, Fuqua, & McKinley, 1985). This relates to the third element of the HRT protocol – contingency management.

Contingency management is used to aid implementation of the competing response at home. Parents are asked to praise their child for noticing tics and attempting to use the competing response, regardless of success at controlling tics. This is based on evidence that tics are influenced by antecedent and consequent factors (Conelea & Woods, 2008b). The idea is to reinforce use of the strategies learnt while ignoring tics themselves, so as not to provide negative feedback which could lead to tic exacerbation. Studies using single case experimental designs have assessed the use of operant conditioning approaches in an attempt to modify tic expression, producing inconsistent results (Roane, Piazza, Cercone, & Grados, 2002; Wagaman, Miltenberger, & Williams, 1995).

The fourth element of HRT is generalisation training which is designed to help transfer strategies to a variety of situations in which tics are problematic. This is based on evidence that tics are extremely context specific and children may therefore need support to generalise skills to new contexts (Conelea & Woods, 2008b).

Finally, relaxation training is included in the HRT protocol because stress and anxiety are reported to increase tics in up to 98% of affected individuals (Bornstein, Stefl, & Hammond, 1990). It is, therefore, thought that reducing muscular tension may be helpful in reducing tic frequency and severity. Relaxation training involves coaching in techniques such as deep breathing, progressive muscle relaxation and imagery. This approach has tended to be included as one element of a broader intervention but some studies have examined its independent effect. Peterson and Azrin (1992) found that this approach produced short-tem reductions in tics under controlled laboratory conditions. However, the study had limited ecological validity as interventions were delivered in a single session in which training was given for three different techniques in 30 minute slots and then participants were assessed while

they were asked to implement different strategies. The inclusion of only six participants also limits the generalisability of these results. Bergin, Waranch, Brown, Carson and Singer (1998) conducted a randomised trial comparing relaxation training to minimal control therapy in children. They found no significant differences between conditions after six training sessions. Nonetheless, this element has tended to be included in HRT programmes and research is necessary to determine whether this is a key element of the therapy.

HRT has more recently been developed into a Comprehensive Behavioural Intervention for Tics (CBIT; Woods, Piacentini, et al., 2008), based on the CI model of TS, described earlier. This variation is eight sessions long and includes an element of functional analysis, the purpose of which is to minimise environmental triggers which exacerbate tics. This is a more sophisticated contingency management approach in which functional analysis is used to identify factors which may be reinforcing tic expression for a particular child. These can then be manipulated to reduce tics. Elements of this approach are often combined with other intervention strategies, such as those described above, making evaluation of its independent contribution difficult (Verdellen, van de Griendt, Hartmann, et al., 2011). Watson and Sterling (1998) have reported the success of functional analysis in a single case in which reduction of social reinforcement reduced tics in a four-year-old girl.

Efficacy. Early controlled studies demonstrated that HRT was successful at reducing tics. In adults, fourteen sessions of HRT were found to reduce tics more than supportive psychotherapy, although both treatments improved life satisfaction and psychosocial functioning (Deckersbach et al., 2006). These results were maintained six months later. Evaluation mid-way through therapy in this study

showed that most symptomatic improvement was achieved after eight sessions. As a result, many subsequent therapies have used eight sessions.

CBIT has now been evaluated for use with children and adolescents in a large scale randomised controlled trial (Piacentini et al., 2010) and showed greater tic reduction compared to supportive psychotherapy and education. The mean tic reduction on the YGTSS Tic Severity Scale was 7.6 compared to an average reduction of 3.5 in the supportive therapy control group. This represented a reduction in tics in the HRT group of 31% and a medium effect size of $d = 0.68$ compared to the control group. A reported 53% of children showed clinically significant improvement in functioning as measured by the Children's Global Impressions – Improvement Scale (Shaffer et al., 1983). Participants classed as having responded to treatment were followed up six months later and 87% showed continued benefit, although between-group comparisons on the tic measure were not made at follow-up. The study showed high acceptability to families with low attrition (9.5%) and tic worsening reported in only 4% of cases. The control condition consisted of providing parents and children with information about tic disorders and allowing them a space to discuss their difficulties, however no direct advice about tic management was provided.

A related study (Woods et al., 2011), looked at the impact of the intervention on the same children in relation to psychosocial functioning and other variables considered secondary to the tics themselves. The two groups did not differ on these variables immediately following treatment but six month later "responders" from the CBIT group demonstrated reductions in anxiety, disruptive behaviour and family strain as well as better social functioning. The study did not include a measure of QoL.

Similar results have been found in adults (Wilhelm et al., 2012). Recent systematic literature reviews (Verdellen, van de Griendt, Hartmann, et al., 2011) and meta-analyses (McGuire et al., 2014; Wile & Pringsheim, 2013) have outlined considerable support for HRT and it is considered as effective as medication (Hwang, Tillberg, & Scahill, 2012), with arguably fewer side-effects. Overall, HRT and its variants are reported to show tic reductions of 30 to 100% (Verdellen, van de Griendt, Hartmann, et al., 2011) and medium to large effect sizes relative to control groups (McGuire et al., 2014). HRT is now considered the gold standard intervention for TS as it is the only treatment recommended as "well established" (Cook & Blacher, 2007).

It is worth noting that despite broad empirical support for the complete intervention package there has been some debate over which are active elements of HRT with preliminary evidence suggesting awareness and competing response training alone may be as effective as the complete package (Miltenberger et al., 1985).

Comparison to alternative therapies. Some studies have investigated the addition of a cognitive element to behavioural interventions which consist of restructuring of expectations in situations where the risk of tics is high. All studies evaluating this approach have combined cognitive strategies with HRT. The effectiveness of the combined intervention has been demonstrated in both medicated and non-medicated samples (O'Connor et al., 2009) and has been shown to be superior to a waiting list control group (O'Connor, 2001). As cognitive interventions have not been evaluated independently we cannot conclude whether the addition of a cognitive element provides additional benefit. O'Connor, Gareau and Borgeat (1997) compared Cognitive Behavioural Therapy (CBT) to traditional HRT and found the

interventions to produce comparable results. The finding was limited however by the small sample size and the fact that there were significant overlapping intervention components as both contained an awareness training element. Further research is needed to determine whether cognitive strategies provide independent benefit.

Another arguably related behavioural therapy which has empirical support, is Exposure and Response Prevention (ERP). One trial found ERP to be as effective as HRT for the treatment of tics (Verdellen et al., 2004), although the ERP sessions were longer, so it is unclear whether, with equal length sessions, ERP would have been as effective. Although this approach has not been as widely researched, recent meta-analyses have recommended it as probably efficacious (Cook & Blacher, 2007; Wile & Pringsheim, 2013), particularly as the proposed underlying mechanism between HRT and ERP appear similar.

Concerns about HRT. When asked about their expectations regarding HRT (Woods et al., 2010), many young people reported concern about possible onset of new tics and about a possible rebound effect, whereby tic suppression might cause tics to subsequently return more strongly. While families and children report 'outbursts' on arrival home from school, the evidence does not suggest this is due to a rebound effect. Experimental paradigms in which children receive rewards for tic suppression (M. Himle & Woods, 2005; Woods, Himle, et al., 2008) and diary record studies (Verdellen, Hoogduin, & Keijsers, 2007) have both shown that, while tics increase following tic suppression, they do not exceed baseline levels. Instead, the experience families report is likely to represent a return to baseline following suppression of tics at school. Similar evidence has not supported the presence of a rebound effect in adults (Müller-Vahl, Riemann, & Bokemeyer, 2014).

Children report concerns that suppressing tics may make it harder to concentrate on school work (Woods et al., 2010). Although there is some evidence that deliberate tic suppression can distract from other tasks (Conelea & Woods, 2008a), overall HRT has not been found to have secondary negative consequences in terms of attention, behaviour, mood, anxiety or family conflict (Woods et al., 2011). Neither is the ability to suppress tics affected by the requirement to simultaneously engage in another task (Conelea & Woods, 2008a). Initial tic suppression possibly does distract attention but, with practice through HRT, this becomes more automatic and eventually does not require additional attention (Conelea & Woods, 2008a).

Factors affecting treatment response. Research into the factors which affect response to HRT treatment has been limited. In their meta-analysis, McGuire et al. (2014) found some factors which moderated treatment effects. A small positive relationship was found between effect size and number of therapy sessions offered. Some other areas which might be expected to influence response to treatment were also assessed. These were age, medication status and presence of a comorbid diagnosis of ADHD.

Studies have found that children can benefit from HRT from the age of nine, but there is as yet no firm evidence for use of behaviour therapy in younger children (Wile & Pringsheim, 2013). McGuire et al. (2014) found a positive relationship between mean age of sample and effect size in studies of HRT, which might be explained by inclusion of children under the age of ten. Woods et al. (2005) have found that younger children may be less able to identify and describe the PU, which may make it harder for them to benefit from the awareness training element of HRT.

Further research is needed to clarify the nature of and reason for any relationship between age and treatment response.

Given the frequent use of medication in treatment of TS it is important to consider the effect medication may have on treatment response. O'Connor et al. (2009) studied the response of adults with TS to CBT including an HRT component. Comparison between medicated and unmedicated individuals found similar degrees of positive response between groups. Medication has also not been shown to moderate treatment outcome in children receiving HRT for TS (Piacentini et al., 2010). McGuire et al. (2014) found no significant relationship between the proportion of participants on tic-influencing medications and effect sizes reported in studies of HRT.

A third area which might be expected to influence outcomes would be comorbid symptoms of ADHD. Indeed, McGuire et al. (2014) did find a small negative relationship between the proportion of children with a diagnosis of ADHD and the effect size reported by a study. This relationship was not found for comorbid OCD diagnoses. Impairment in response inhibition, as might be expected in children with comorbid ADHD, has been shown to affect response to HRT treatment (Deckersbach et al., 2006). It is possible this may affect children's ability to suppress tics and therefore interfere with HRT. Another explanation could simply be that children with ADHD have more difficulty attending in therapy sessions and therefore reap less benefit. Several elements have been included in the current HRT intervention with a view to increasing access of children with ADHD as recommended by Döpfner and Rothenberger (2007). These include promoting adherence using reward strategies and increasing motivation using a habit inconvenience review and tic hierarchy, as described by Piacentini and Chang (2005).

Despite inclusion of these elements, children with comorbid ADHD may benefit from the intervention to a reduced extent compared to those without. This was assessed in the current study.

1.9 Group HRT

Despite the strong evidence base described, implementation of HRT has proven difficult in practice. A recent study in the United States found that only 6% of families seeking treatment for children with CTDs had received either HRT or CBIT (Woods et al., 2010). Where talking therapies had been offered, most had instead received CBT, relaxation training alone or psychotherapy without a behavioural basis. The authors suggest two possible reasons for this as being limited awareness of available treatment and insufficient training of health professionals.

In order to increase access to HRT, additional approaches may be required, such as therapy by videoconference or in group formats. M. B. Himle et al. (2012) have shown that CBIT via videoconference is equally effective and acceptable to families as face-to-face therapy. Group based HRT may be an additional means of delivering HRT to larger numbers of children, yet this has not been previously investigated.

Preliminary evidence from case studies of non-HRT groups appears to suggest that group therapy could be beneficial. These are described below. Further research in this area has been recommended (Verdellen, van de Griendt, Hartmann, et al., 2011). HRT group therapy has never been empirically evaluated. A Google Scholar search for “Tourette Syndrome” AND “Group Therapy” AND “Habit Reversal” reveals no studies in this area since Verdellen, van de Griendt, Hartmann, et al.'s, 2011 review.

Investigation of the efficacy and feasibility of group based HRT and psycho-education is worthwhile because such groups could offer an additional treatment option to children and families with TS. Group-based delivery may also be more cost-effective and has the potential to reduce waiting times in stretched services. In addition to practical considerations, group based delivery may provide additional and independent benefits. Group-based delivery of therapeutic interventions has long been a feature of psycho-therapeutic work for a wide range of conditions and more recently as a means of delivery of more structured interventions such as psycho-education and CBT (see Burlingame, MacKenzie, & Strauss, 2004). Such groups are based on the idea that, in addition to benefit children may gain from the core group material, they may benefit from interactions with other group members and the sharing of stories. It is felt that, through social learning and cooperative support within the group, the effects of the intervention may be strengthened both during and after treatment, as families may form support networks (Lukens & McFarlane, 2004). It is hoped that the normalising effect of meeting others with similar difficulties may reduce feelings of isolation.

Burlingame et al. (2004) review evidence suggesting that group therapies may be preferable to individual treatment in a range of conditions including mood disorder, panic disorder, social phobia and bulimia nervosa. Groups have also been reported beneficial for anxiety (Avny & McLeod, 2010; Muris, Meesters, & van Melick, 2002; Silverman et al., 1999), OCD (J. A. Himle, Fischer, Van Etten, Janeck, & Hanna, 2003), ADHD (Waxmonsky et al., 2013) and behavioural difficulties (Yeo & Choi, 2011).

Although no HRT groups for children with TS are reported in the literature, there have been case studies of groups aimed at supporting children to cope with

secondary consequences and comorbid symptoms. Lambert and Christie (1998) evaluated a group for boys with TS aged between 8 and 15, which aimed to teach social skills and improve self-esteem. The group was established in response to parental requests and observations by clinicians that many children attending the TS clinic had social skills deficits that were impacting on their wellbeing. Topics covered in seven fortnightly sessions included conversational skills; recognition of the feelings of others; skills in entering a social group; skills in taking another person's perspective and skills in positive assertiveness. No attempt was made to address or evaluate core TS symptoms. Small changes in self-esteem were reported and qualitative feedback was positive. Meeting others with TS was felt to be important and parents were reported to have commented that a parent group would be valuable, having appreciated the opportunity to meet informally during the children's sessions.

J. A. Himle et al. (2003) reported on a group for 12 to 17 year old children with OCD. This included children with and without tics. The group did not aim to treat tics, but rather to treat OCD symptoms using ERP principals. Both children with tics and those without reported fewer obsessions and compulsions following therapy. No measures of tic severity were taken.

One reason for this lack of group treatments for TS might be the suggestibility of tic expression described earlier. Families may be concerned about their child being exposed to other affected individuals in case they adopt new tics or their symptoms worsen. This has yet to be evaluated formally but clinical experience has shown that, while it is possible in the short-term, it is unlikely to be a lasting effect. Following their group, Lambert and Christie (1998) reported anecdotally that "*by the end of the group several of the boys were so involved that….their tics had stopped*". The current

study provided the opportunity to assess for this possibility more formally by assessing pre- and post-measures of tic severity.

1.10 Group Psycho-education

The studies described above seem to provide preliminary evidence that group therapies may be an acceptable form of intervention for families. Psycho-education also has the potential to be delivered in group format. This intervention combines psychotherapeutic elements with education. It is a strengths-based, present-focussed approach, aiming to empower the individual through the collaborative development of coping strategies and family members are often involved (Lukens & McFarlane, 2004). While psycho-education has rarely been empirically evaluated as an intervention in its own right, it is widely offered and generally considered to be a starting point for intervention and a necessary adjunct to other therapies (Verdellen, van de Griendt, Hartmann, et al., 2011). Verdellen, van de Griendt, Hartmann, et al. (2011) argue that psycho-educational approaches could help reduce uncertainty and stigma in TS by providing information about the nature and course of symptoms. Having information about their condition can improve children's self-efficacy and may help them in explaining symptoms to peers (Nussey, Pistrang & Murphy, 2014).

Psycho-educational groups have been reported to be beneficial for a range of conditions from mood disorders (Fristad, Goldberg-Arnold & Gavazzi, 2003) to schizophrenia and coping with cancer (Lukens & McFarlane, 2004). Murphy and Heyman (2007) described a psycho-educational group for adolescents with TS. The group did not aim to directly reduce tics but instead to manage some of the secondary consequences, such as bullying, self-esteem, coping with anger and managing OCD

symptoms. The group was considered a supportive context in which children and families could meet others experiencing similar difficulties. Attendance was consistently good and the children gave good qualitative feedback, but no quantitative data were collected.

1.11 Summary of Literature Reviewed

In summary, the QoL of children with TS is impacted greatly by a combination of the tics, the associated PU, comorbid conditions and social consequences of the symptoms. Further research into effective therapeutic approaches is clearly needed. Individual HRT and CBIT have substantial empirical support as evidence-based behavioural therapies for TS but have never been investigated in a group format. Group based delivery of HRT is worthy of investigation as it has the potential to increase access to therapy and the cost-effectiveness of treatments as well as potentially offering additional benefits of reduced stigma and social support. Case reports provide preliminary evidence suggesting that group based interventions are acceptable to children with TS and their families. There is also preliminary evidence that psycho-educational groups may be of benefit and this is therefore an appropriate comparison group.

1.12 The Current Study

The present study was a randomised controlled pilot study which investigated the feasibility and preliminary efficacy of HRT and psycho-educational groups for children aged 9 to13 years with CTDs. The groups were evaluated in terms of their ability to reduce tic severity and improve QoL. While this study alone will not be

sufficient to draw firm conclusions about a group based approach to therapy for TS, it could pave the way for further research in this area to confirm any findings and answer additional questions this study has been unable to address.

As the aim of HRT is specifically to reduce tics, it is expected that this will lead to a reduction in tic severity and an associated improvement in QoL. The psycho-educational group does not address tics directly but focuses on broader topics of commonly co-occurring difficulties such as bullying, self-esteem and dealing with anger, anxiety and attention problems. It is therefore expected that children attending this group will benefit from improved QoL. It is possible tics may also reduce due to the indirect effect of reduced stress and anxiety but this is expected to be a smaller effect compared to the HRT group.

In addition to these main questions, some secondary research hypotheses were also tested. Given reported findings regarding the aversive nature of the PU, its potentially primary relationship with tic related impact and its key role in the theoretical basis of HRT, it is hypothesised that improvement in QoL following intervention will be better predicted by changes in PU than changes in tic severity. Secondly, given previous findings in relation to the impact of ADHD symptoms on treatment outcome, it is expected that children with more comorbid symptoms of inattention and hyperactivity and impulsivity will benefit less from the group than those without. Specifically, the current study set out to test the following hypotheses:

- The HRT group will experience greater reductions in tic severity compared to the psycho-education group.
- Children in both the HRT and psycho-educational groups will show significant post-treatment improvements in QoL.

- Reduction in the PU will be a better predictor of improved QoL than reduction in tics.
- Post-treatment improvements in QoL will be predicted by participants' lower inattention, hyperactivity and impulsivity symptoms.

Chapter 2. Method

2.1 Wider Project

The project took place at Great Ormond Street Hospital (GOSH) in London. This thesis reports one element of a wider study. Data were collected both for the current study and also for another doctoral thesis relating to neuropsychological outcomes following the treatment groups. The two trainee clinical psychologists collected the data together. Each assessed half of the children involved in the study and collected data for both projects during the assessment visits. In addition, ethical approval was obtained for the principal investigator to follow up all participants one year after treatment and results will be incorporated in a future journal article.

2.2 Design

This study was a pilot for a future, larger scale, randomised controlled trial (RCT). The CONSORT guidelines for RCTs have therefore been considered in design and reporting of the trial (Moher et al., 2010; Schulz, Altman, & Moher, 2011). The study used a longitudinal design, with two parallel conditions. Each child participated in only one treatment, which was either an HRT therapy group or a psycho-educational therapy group. Allocation to condition was random and used an equal allocation ratio. Further details of this process follow.

Pre-treatment assessments were conducted in the month prior to the start of treatment (Time 1) and follow-up assessments within a month of the end of the group sessions (Time 2). This was the shortest time frame practicable in order to maximise consistency in assessment times relative to the groups. Only one child was assessed a few weeks later at Time 2 due to the family's availability. Data were collected by two

trainee clinical psychologists unaware of treatment condition, making the study single-blind. Figure 2.1 shows the sequence of events as a participant progressed through the study.

2.3 Affiliations, Approvals and Funding

The study was sponsored by GOSH. It was reviewed and approved by the London Queen Square Research Ethics Committee (see Appendix A) and also by ethics committees at Royal Holloway, University of London and University College London. Funding was provided by Tourette Action, UK (the National Charity for Tourette Syndrome), Royal Holloway and University College London. This contributed towards study administration, postage costs and travel costs for the researchers conducting assessments at participants' homes.

The study is registered for an International Standard Randomised Controlled Trial Number (ISRCTN) via the National Institute for Health Research (NIHR) Portfolio Database. This is recommended by the World Health Organisation (WHO, 2012).

2.4 Participants

Children aged 9 to 13 years old with a chronic tic disorder (Chronic Vocal Tic Disorder, CVTD; Chronic Motor Tic Disorder, CMTD or Tourette Syndrome, TS) were invited to take part in the study. Participants were recruited from the specialist TS Clinic at GOSH. The children had received a diagnosis at the clinic, which is a national specialist service run by highly experienced clinicians.

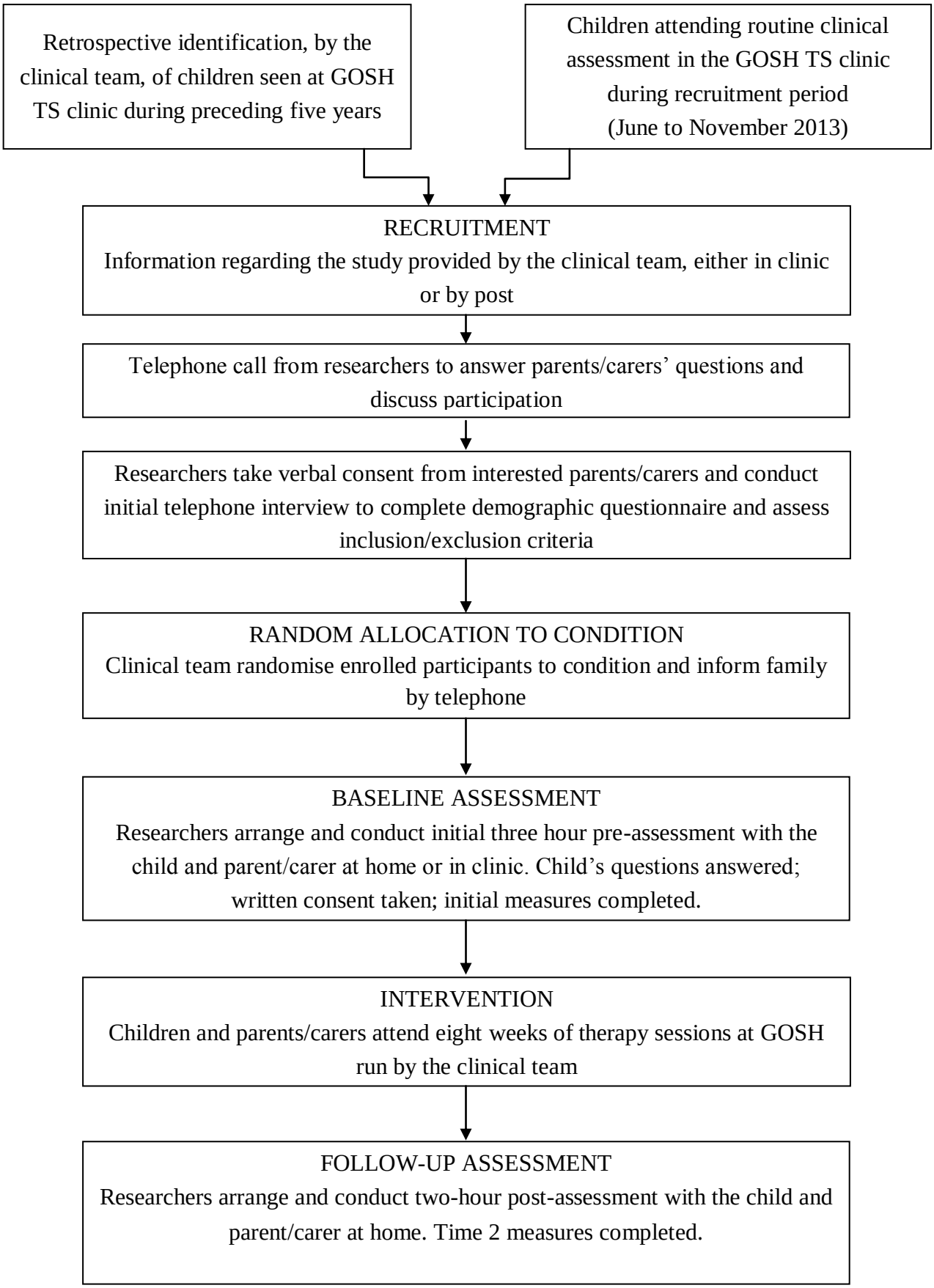

Figure 2.1. Flow chart showing sequence of events for study participants.

All children aged 9 to 13 during the study period, who had been seen at the clinic within the preceding five years were invited to participate. In addition, children assessed at the clinic during the recruitment phase of the study were invited if they met criteria.

Several factors were considered in selecting the age range. Piacentini et al. (2010) found that children aged 9 to 17 benefitted from the HRT intervention delivered individually. For this study it was desirable to choose a sufficiently narrow age range that the group intervention could be targeted to the benefit of all children. The chosen range is similar to those used in other reports of treatment groups for children with anxiety (Barrett, 1998; Flannery-Schroeder & Kendall, 2000; Silverman et al., 1999) and was therefore considered sufficiently narrow. The period chosen is also the time when children with TS tend to experience the most debilitating symptoms, which peak around the age of 10 to 12 years (Bloch & Leckman, 2009; Leckman et al., 1998). The average age of children referred to the GOSH clinic is 11.2 years (ranging from 6 to 16 years) so the age range selected is best suited to a group therapy which requires high numbers of attendees and it is likely to reflect the ages of children seeking treatment.

2.5 Exclusion Criteria

Children with a Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) total tic severity score below 13 (range 0 to 50) were excluded to ensure a sufficient level of symptoms at Time 1, with room for improvement following treatment. This is consistent with previous studies (Piacentini et al., 2010). Children were also excluded from the group and the study if TS was not their primary presenting problem.

Children with a history of psychosis or current substance abuse or dependence were also excluded as these were considered factors which might compromise the child's ability to engage in treatment.

Participants with a Full Scale IQ (FSIQ) below 80 were excluded, again consistent with previous studies (Piacentini et al., 2010). Not having a sufficient level of English to be able to complete questionnaires and participate in the group treatment was also an exclusion criterion. This allowed participants to perform optimally and benefit maximally from the groups.

Previous treatment was also considered, as it was desirable to minimise recent experiences of therapy which might influence the experience of the current treatment. As many children who attend the clinic are offered either the psycho-educational group or a limited number of sessions of HRT, it was considered impractical to exclude all those who had received any previous therapy. Therefore, those who had attended a psycho-educational group at the clinic within the previous two years were excluded as were those who had previously attended more than four sessions of individual HRT or CBIT treatment at any time. This criterion was also used by Piacentini et al. (2010).

2.6 Sample Size

A power calculation was used to determine an informative sample size. No previous study of this kind has been conducted but previous studies of individual HRT treatment for TS have reported medium to large effects on tic severity outcomes (Piacentini et al., 2010; Verdellen et al., 2004). Therefore, the analysis was based on a conventional medium effect size (Clark-Carter, 1997; Cohen, 1992), as smaller effect

sizes would likely be of limited clinical interest. The analysis was conducted using G*Power 3 (Faul, Erdfelder, Lang, & Buchner, 2007) based on using an Analysis of Variance (ANOVA) for repeated measures (mixed design) with power of 0.8, a medium effect size (f = 0.25) and alpha = 0.05. This was based on the one main outcome measure (YGTSS tic severity), taken at two time-points, with correlation among repeated measures of 0.5 and a non-sphericity correction of 1. This analysis indicted a minimum recommended total sample size of 34. Based on dropout rates reported in previous studies of group therapy of between 5 and 27% (J. A. Himle et al., 2003; Silverman et al., 1999), a conservative target of 48 participants was set for this study (24 participants to each condition).

2.7 Recruitment Procedure

Recruitment took place from June to November 2013. Figure 2.2 shows the progress of participants through the study. Participants recruited retrospectively were sent an invitation letter (see Appendix B) from Dr Tara Murphy, principal investigator and Consultant Clinical Psychologist in the clinic. The letter was accompanied by both parent and child information sheets (see Appendices C and D respectively) explaining the study. These outlined exactly what would be involved in the study and explained how children would be randomised to one of two treatment groups. It also explained that the researchers would contact the family two weeks later to ensure they had received the information, answer any questions and discuss whether they were interested in participating.

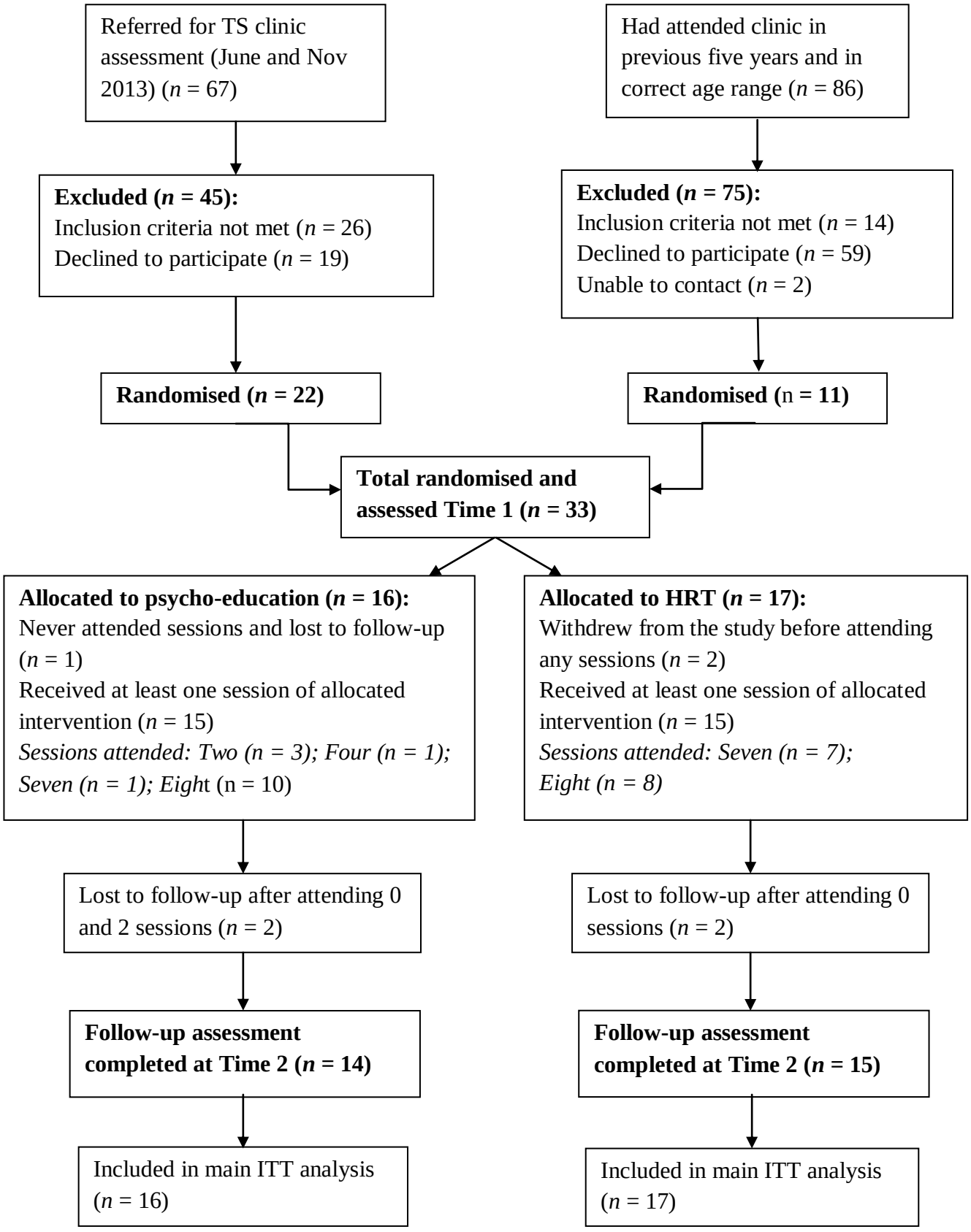

Figure 2.2. Flow chart of participants through the study. Based on CONSORT guidelines.

Recruitment of participants from the clinic was conducted through the clinicians. If children assessed in the clinic met inclusion criteria for the group, clinicians discussed the study with families at assessment and gave them the invitation letter and information sheets. If interested, these families were then contacted by the researchers a few days later to answer any questions and discuss their participation.

2.8 Ethical Considerations and Consent

Families were initially contacted by letter and advised to expect a follow-up phone call. They could opt out of this phone call by contacting the research or clinical team. The information families received emphasised that they were under no obligation to participate and that the care they received would be unaffected by their decision. This was reiterated by the researchers on the telephone. Both researchers had honorary contracts at GOSH and clinical roles at GOSH during the study. This recruitment procedure was agreed by the NHS ethics committee.

Families were given the opportunity to ask any questions they wanted. If they chose to participate, verbal parental consent was collected by the researchers in the initial telephone conversation. Written parental consent was then obtained at the first assessment appointment along with written assent from the children themselves. Before completing the assent form the researcher read the information sheet with the child, discussed it with them to ensure their understanding, gave them a chance to ask questions and reminded them that they were free to withdraw at any time. Once children were enrolled in the study, their GP was informed of their participation which was made clear to the participants (see GP letter, Appendix E).

Patient confidentiality was maintained throughout the study in accordance with the NHS Code of Confidentiality and GOSH confidentiality policies. Personal contact details were used by the researchers for contacting participants and arranging and attending assessment appointments. These details were stored securely at GOSH. Participants were assigned a confidential participant number which was used as an identifier on all assessment materials. Participant names and numbers were stored in a separate spreadsheet on the secure electronic system at GOSH. Only consent and assent forms included both names and participant numbers. These were stored securely at GOSH and only accessible to members of the research and clinical teams. All electronic data were stored in password protected databases and anonymised using participant numbers. Data and video recorded on laptops during assessment visits was stored on encrypted drives and identified only by participant number. These were then transferred to encrypted hard-drives stored securely at GOSH at the earliest opportunity. All paper records, such as questionnaires, were stored securely at GOSH.

When conducting home visits, the researchers followed GOSH lone working policies. Researchers carried separate mobile phones for the purposes of the research. This was the only number available to participants and the phone used to contact families where necessary prior to visits. Parents were at home at all times during the assessments. Both researchers were trainee clinical psychologists with experience of working with children and families.

Any clinical situations or disclosures that arose were dealt with following NHS protocols and frameworks at the GOSH clinic. Dr Murphy provided supervision to both researchers and was the point of reference for any risk situation arising. She shared information with the clinical team as appropriate.

2.9 Generalisability of Sample

When families declined to participate, their reason for declining was recorded, along with the child's age and gender. This procedure was agreed with the ethics committee in order to allow assessment of the generalisability of the final sample. Of the total 86 potential participants identified retrospectively 81% were male and their mean age was 11.03. Of the 67 children who attended the clinic during the recruitment phase, 73% were male and their mean age was 11.18. This broadly reflects the sample of those recruited of whom 76% were male and the mean age was 10.96. Reasons for exclusion or declining participation are given in Table 2.1.

2.10 Randomisation

Once enrolled, participants were sequentially randomised to treatment group using web-based minimisation software called QMinim (see Saghaei, 2011). Minimisation is a randomisation procedure which allows the researcher to balance certain characteristics between groups (Treasure & MacRae, 1998). In this case minimisation was used to balance age and gender as much as possible across conditions. The program randomises each new participant sequentially based on previous allocations.

2.11 Blinding

The researchers involved in data collection and video coding were blind to group allocation in order to maximise the internal validity of the data. It was not considered feasible to blind participants themselves to group allocation given the nature of the interventions. In line with previous studies (Piacentini et al., 2010), the clinicians involved in running the groups were not blind to group allocation and those analysing the data were no longer blind at the analysis stage in the study.

Table 2.1

Reasons for Exclusion or Declining Participation

Reasons for Exclusion	Retrospective	New referral
Tics not primary problem[a]	4	6
Distance - Lived outside England	2	–
FSIQ below 80	2	5
Previous therapy met exclusion criteria	6	–
Above age cut-off	–	6
Below age cut-off	–	7
Tics absent or minimal at assessment	–	2
Reasons for Declining Participation	**Retrospective**	**New referral**
Distance/travel difficulties	23	10
Improvement in symptoms/not wanting treatment	13	2
Child themselves declined	12	2
Missing school	8	4
Financial	7	3
Child or family busy/too big a commitment	7	1
Child care for other children	4	–
Parental work commitments	4	–
Child had not been given a diagnosis or family disagreed with diagnosis	4	–
Family did not like the idea of group therapy	3	–
Time of group inconvenient	2	–
Practicalities (non-specified)	2	–
Family felt child had different primary difficulty	1	–
Not wanting to miss extracurricular activities	1	–
Concerns about picking up new tics	1	1
Not happy to be randomised	1	–
Reason not specified	1	1

Note. FSIQ = Full Scale IQ.

[a] Such as anxiety, OCD, anger and aggression, behaviour difficulties or complex multiple difficulties

Several measures were taken to maintain the blinding of the researchers during the assessment phase. Randomisation was carried out by a clinician who was uninvolved in conducting assessments. The clinician was given the instructions shown in Appendix F. Another member of the team, also uninvolved in assessments, contacted families to inform them of their group allocation and the day of the week they would be attending the clinic. The spreadsheet in which group allocations were recorded was stored in a password protected file on the team shared drive. Those conducting the assessments were not told this password and members of the clinical team were made aware not to disclose group allocations or passwords to the researchers.

Families were reminded not to mention their group allocation to the researchers at the initial telephone call and also before each assessment. The researchers were careful not to be in the vicinity during the hours of the group, to avoid seeing children they knew from Time 1 assessment.

As recommended by Kolahi, Bang and Park (2009), the success of blinding of the researchers was assessed following completion of the follow-up assessments and scoring of all measures. The researchers recorded their predictions as to the condition allocation of each participant they had assessed as HRT, psycho-education or 'don't know'. These predictions are shown in Table 2.2 along with the true allocations.

Predictions were then used to calculate Bang's blinding indices (Bang, Ni, & Davis, 2004) which are scores of blinding success representing the proportion of unblinding which has occurred in each study arm separately. Scores range from -1 to 1. Zero is the middle value which represents complete blinding success. A score of 1 represents complete unblinding while -1 represents complete negative unblinding, in which all predictions are the reverse of the true treatment allocation.

Table 2.2

Researcher Predictions Regarding Condition Assignment and Actual Assignment

	Condition prediction			
Actual condition	HRT	Psych-Ed.	Don't know	Total
HRT	7	1	9	17
Psych-Ed.	3	1	12	16
Total	10	2	21	33

Note. HRT = Habit Reversal Therapy; Psych-Ed. = Psycho-education

This score was calculated for each study arm following Williamson, Harvill and Stamey (2013). In the HRT condition Bang's blinding index was 0.35, representing 35% of condition assignments that were correctly guessed, beyond chance, in that condition. In the psycho-education condition this score was -0.125 representing that in this condition there was a slight tendency for the researchers to guess that participants had been assigned to the HRT condition. Overall, these scores demonstrate that in the majority of cases blinding was successfully achieved. However there were a proportion of cases in the HRT group for whom blinding was compromised.

2.12 Retention and Attendance

Measures were taken to maximise retention of participants in the group. An administrator telephoned families in advance of the first four weekly sessions to remind parents about the group and encourage attendance. Feedback from families then showed this was unnecessary so it was ceased. Additionally, children who attended six or more intervention sessions were given the chance to win a £50 Amazon gift voucher, which was also contingent on positive child behaviour in the group, as judged by the lead clinical psychologist facilitating the groups.

2.13 Interventions

Two HRT groups and two psycho-educational groups were run during this study. Both groups were highly structured manualised interventions. The core therapeutic content differed between the groups, but other practical elements of the treatments were kept as similar as possible in order to minimise potential alternative explanations for any findings. All groups consisted of a total of eight sessions, which took place weekly except during school holidays. The first HRT and psycho-educational groups were run from September to October, including a one-week break for half-term. The second HRT and psycho-education groups were run from November to January, with a three-week break over Christmas. In both groups the initial two sessions were 90 minutes long and remaining sessions an hour in length. All groups were run at GOSH on a week day afternoon, beginning at 4:30pm. All were run by Dr Murphy (Consultant Clinical Psychologist) and two or three facilitators from a variety of professions (Clinical Psychologist, Trainee Clinical Psychologist, Assistant Psychologist, Specialist Nurse, Research Assistant, Assistant Speech Therapist). The researchers themselves were not involved in group delivery.

Sessions were structurally similar in both conditions. Each week children were welcomed to the session and an initial warm-up game was played. They were then reminded of the ground rules they had generated in the first session and a star-based reward system that was in place to reward listening skills, sharing of ideas, helping others and completion of tasks. The session plan was then outlined and homework from previous sessions reviewed. The main content of the session was then delivered consisting of a mixture of group discussion, didactic teaching and small group activities specific to condition. More details are given below. The groups were designed so that the material was varied and each individual task was brief. In the

middle of each session there was a break for drinks and snacks. Before the end of each session children were given a small task to complete at home with support from parents. The children were then each asked to share with the group one thing they had learnt that session. Finally, stars on the reward chart were reviewed before the end of the session.

The last ten minutes of the final session in both groups consisted of a fun activity, as a way of celebrating the children's achievements and finishing the therapy on a strong positive note. In the psycho-education group this consisted of a quiz about the material learnt across sessions and in the HRT group it consisted of a brief talent show. All children were given a certificate in recognition of their achievements.

There were some similarities in content between the groups. Specifically, both groups started with the same first session of psycho-education about tics. Both groups also included a relaxation element in which children were taught to use progressive muscle relaxation techniques. Thirdly, both groups included the use of reward strategies intended to increase the implementation of strategies learnt both in-session and at home.

HRT group. The broad structure of the HRT intervention was as described in the Introduction. The group sessions were based on individual HRT treatment for children and adolescents with TS (Woods, Piacentini, et al., 2008), as well as an HRT therapy manual and workbook for children developed by Verdellen, van de Griendt, Kriens and van Oostrum (2011). These approaches were converted into a group therapy protocol by Dr Murphy.

Throughout the sessions the children were taught to increase their awareness of their three most troublesome tics. This was achieved through describing each tic in

detail in terms of its appearance and accompanying physical and premonitory sensations. Tics were treated one at a time. In addition, the children were assisted in playing games in which they tried to guess when their own tics were coming before another child, a process which serves to heighten their awareness of the premonitory urge (PU). Children were encouraged to keep track of when and where tics occurred during the week to encourage awareness and support a functional analysis element to the intervention.

The children then developed a suitable competing response (an action they carried out which made the tic impossible to perform, was less socially notable than the tic and required no props) to each tic and were supported to practice using the techniques in-session and at home. Time in session was dedicated to developing and practicing appropriate competing responses and then using these while engaging in other activities, such as playing games. The children chose up to three tics to work on during the intervention. 73% of the tics chosen were motor tics. Nine of the fifteen children who attended HRT group sessions chose only motor tics.

In the final session, the children were encouraged to think about relapse prevention such as situations in which their tics might come back or increase and consider what they would do and where they could get help if this occurred.

During each weekly HRT group, all children recorded subjective units of distress in relation to their top five tics over the preceding week. This was not done in the psycho-educational group to avoid focus on tics. Group facilitators recorded the children's ratings on a Likert scale from 0 to 10. This process was considered part of the therapeutic content of the group aimed at increasing awareness of the tics and motivation to focus on use of competing responses.

Psycho-educational group. The protocol for the psycho-educational group sessions was adapted from a six-session protocol for psycho-educational groups that have been routinely run at GOSH over recent years (Murphy & Heyman, 2007). Adaptations were made by Dr Murphy to increase similarity to the structure of the HRT intervention, which included adding an additional two sessions. The content of each of the eight sessions were: Psycho-education about TS; Self-esteem and Independence; School and Bullying; Anger; Anxiety and OCD; Attention; Planning and Organising; Review, Quiz and Certificates. The session themes were chosen based on common areas of difficulty for children with TS, as described in the Introduction. Brief details of each of these sessions are given below.

Psycho-education about TS. As well as an introduction to the group itself, this session consisted of a discussion of what the children would like to gain from attending and a basic introduction to tics, tic disorders and common comorbidities. This session was exactly the same as the first HRT session, except that children in the HRT groups were introduced to the HRT model at the end of the groups, instead of discussing comorbidities.

Self-esteem and independence. In this session children were encouraged to think about their lives, hopes, dreams and the challenges they face. Through thinking about challenges faced in the past, they were supported to think about their personal strengths and then discussed why awareness of personal strengths is important. They discussed the relationships between thoughts, feelings and behaviours and how this relates to self-esteem. Finally they thought together about activities they enjoy and are good at and goals they would like to achieve in the future.

School and bullying. This session covered types of bullying; the reasons why children may bully and things children can do to stop bullying. In particular they were

encouraged not to smile and join in but rather to tell others to leave the scene, tell the pupil who is bullying to stop, to go with the child being bullied to a teacher and tell them what they have seen.

Anger. In this session the children discussed what anger is, its positives and negatives and the changes that occur in the body when we feel angry. The children were taught that anger can rise gradually, before exploding like a volcano and helped to think about how to notice when their anger is rising. They were encouraged to think together about how to tackle anger before it rises too high, such as by counting to ten; getting a drink of water; leaving the room; doing something active or using relaxation strategies.

Anxiety and OCD. This session focussed on understanding what anxiety is and the nature of the fight or flight response. Obsessions and compulsions were discussed and how obsessions can be reinforced by trying to avoid them. To illustrate this, the children were encouraged to follow a behavioural experiment such as not thinking about a pink elephant when being reminded to do so and then reflected on how difficult this was. They were taught basic principles of Exposure and Response Prevention (ERP) in confronting feared scenarios without conducting compulsions. They were encouraged to try confronting particular fears at home.

Attention. This session focussed on the nature of attention and distractibility. The children were introduced to the concept of Attention Deficit Hyperactivity Disorder (ADHD) and discussed the role of fidgeting in maintaining focus in ADHD. They were encouraged to think creatively about different ways to fidget and the situations in which they might be appropriate.

Planning and organising. This session was designed to develop children's executive functions. Specifically the session focussed on planning and organisation.

The children were introduced to the concept of executive function and the role of the frontal lobes in skills such as planning, organising and problem solving. They were encouraged to think about areas in their lives when they use these skills and what strategies they use to help. They were taught strategies to help plan, organise and problem solve and then given a chance to practice implementing these while playing some games together.

Review, quiz and certificates. The final session consisted of a review of the material covered in the groups and then a quiz in teams about what had been learnt.

Parent groups. Alongside the children's groups, parents were invited to attend four parent sessions, run by two clinical psychologists. The protocols were different for HRT and psycho-education groups. Both parent groups were based on use of reward strategies and psycho-education which linked to the content of their children's group. These sessions overlapped with the first four children's sessions. During sessions five to eight parents were able to meet together in a room with tea and coffee made available, but there was no structured, facilitated group session led by a clinician. One clinician was available to greet parents at the beginning of these meetings, answer any questions that had arisen during the week and collect completed homework.

Parents of children from both groups were asked to observe their child for 15 minutes each day of the week in the same situation (e.g. while watching TV in the evening), and count the frequency of a specific tic. This is part of the individual HRT protocol by Verdellen, van de Griendt, Kriens, et al. (2011). Parents were given mechanical tally counters to facilitate tic counting and forms on which to record daily totals.

Additional treatment. For the duration of the study participants were able to attend only the treatment group to which they were randomised and received no individual TS related sessions in the clinic. They did continue to receive treatment as usual in terms of school liaison work and medication, regardless of group assignment. A small number of children received ongoing sessions for other conditions during the study. These are listed in the Results section and analyses were conducted both including and excluding these children.

2.14 Treatment Fidelity

Manualisation of the groups was intended to maximise the consistency of treatment delivery and fidelity to the treatment protocols. Fidelity was monitored by an undergraduate psychology student or a trainee clinical psychologist responsible for reading the protocols while observing the groups and ticking off elements of the protocol as they were delivered. This volunteer was asked to bring any deviations from the protocol to the attention of the clinicians delivering the group at the moment they occurred, by raising a hand and catching the facilitator's eye. This is similar to fidelity checklist approaches used to monitor treatment fidelity in other similar studies (e.g. Sukhodolsky et al., 2009).

The approach resulted in complete fidelity to the protocol with the only exception being that several of the groups ran out of time just at the end. The scheduled space at the end of sessions for each child to say something they had learnt was missed on these occasions due to time constraints. This was consistent across both HRT and psycho-educational groups.

2.15 Measures

Demographic information. If families chose to participate, and provided verbal consent, the investigator completed a demographic information sheet with them by telephone (Appendix G). As well as information relating to the exclusion criteria for the study, information was gathered regarding ethnicity, additional diagnoses received, previous treatment, medications and parental occupation and education to calculate socioeconomic status (SES; Hollingshead, 1975). Ethnicity was recorded according to the 2011 Census codes as recommended by the Office of National Statistics (2011).

Measures only taken at Time 1. Some measures were used to characterise the groups, rather than to detect outcomes and therefore were only completed once. These included a measure of IQ and a measure of ADHD symptoms.

Short form of the Wechsler Intelligence Scales for Children (WISC-IV-SF; Crawford, Anderson, Rankin, & MacDonald, 2010). This test was used as a measure of Full Scale IQ (FSIQ). This includes seven subtests of the full ten-subtest version, namely Block Design, Similarities, Digit Span, Coding, Vocabulary, Matrix Reasoning and Symbol Search. This measure is reported to have good reliability and criterion validity with the FSIQ score showing a correlation of .99 with the index score based on the full length version of the test (Crawford et al., 2010).

If children had completed this assessment in the clinic during the preceding year, the test was not repeated and scores from that assessment used instead. This was the case for four children. This was to avoid practice effects and unnecessary additional testing. Such tests show good temporal stability when used with children

over age four (Braaten & Norman, 2006; Wahlstrom, Breaux, Zhu, & Weiss, 2012) so scores were not expected to have changed over a one-year period.

The MTA version of Swanson, Nolan, and Pelham–IV (SNAP-IV; Swanson et al., 2001). ADHD symptoms were measured using this 26-item parent-report scale of symptoms, a copy of which is included in Appendix H. Parents rated each item on a Likert scale from zero to three. The measure provides two subscales relating to elements of ADHD, namely inattention and hyperactivity or impulsivity. In addition, a subscale reflecting symptoms of oppositional defiant disorder is included. Scores on each subscale reflect the average of ratings given for items on that subscale.

In a sample of school children, this measure has been shown to have high internal consistency ($\alpha = .94$). In addition, scores are highly predictive of children who would meet criteria for an ADHD diagnosis (Bussing et al., 2008). Within the current sample the measure showed internal consistency with Chronbach's α of .94.

Tic measures.

Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989). The YGTSS is a semi-structured clinical interview conducted with the child and their parents, which is used to rate tic severity over the preceding week. This widely used measure is considered the gold standard measure of tic severity (Storch et al., 2011). It is therefore the primary outcome measure in this study. The interview takes about 30 minutes to complete. A list of motor and phonic tics which have been present over the week is generated first, followed by ratings reflecting the number, frequency, intensity and complexity of tics and degree of interference they cause. The clinician rates each variable on a 6-point Likert scale for motor and phonic tics separately, using

descriptors for each scale point as a guide. On all items, higher scores reflect greater severity of symptoms. A copy of this interview is included in Appendix I. An overall rating of the impairment caused by tics is also given, rating both vocal and motor tics together on a 6-point Likert scale. This subscale was not used in the current study, however, as a more comprehensive QoL measure was used instead (see below).

The YGTSS also provides four composite scores which represent total motor tic severity (rated from 0 to 25), total phonic tic severity (rated from 0 to 25) and an overall total tic severity score (rated from 0 to 50). A total YGTSS score (rated from 0 to 100) can be obtained by adding the total tic severity and impairment scores. The clinician uses the self-report of parent and child as well as their own clinical observation during the assessment in scoring the measure. Items such as frequency and impairment ratings are based more strongly on the parent and child self-report as they relate to the course of symptoms and their subjective experience over the whole week and therefore there is less scope for clinical judgement.

For participants aged 5 to 51 years, the YGTSS has been shown to have 'good' to 'excellent' inter-rater reliability across trained raters, good convergent validity with other measures of tic severity and divergent validity when compared to measures of ADHD symptoms (Leckman et al., 1989). Among children aged 6 to 17 years with TS, the measure showed high internal consistency with Chronbach's alpha of between .93 and .94 for the global tic severity score (Storch et al., 2005). The same study also demonstrated that the measure shows stability over time, finding Intraclass Correlation Coefficients (ICCs) of .89 for the global tic severity score on measures taken seven weeks apart. Within the current sample the measure shows internal consistency with Chronbach's α of .80, .89 and .87 for the motor, phonic and total tic severity scores respectively. Research has suggested that the most appropriate way to

classify clinically meaningful treatment response using this measure is as a reduction in score of 25% on the tic severity scale (Jeon et al., 2013).

In this study the measure was administered by the two main researchers who are trainee clinical psychologists. They were trained by Dr Murphy, who has ten years experience working in the National Specialist TS Clinic at GOSH. The training involved studying and discussing the measure and related materials carefully, watching and co-rating example videos and matching scores with Dr Murphy. Dr Murphy was also available during the study for discussions when uncertainty arose around coding.

YGTSS inter-rater reliability coding. Reliability of YGTSS scores was established by double coding of 20% of the videos. The repeat coding was completed by a clinical psychologist who had also been trained in administration of the measure by Dr Murphy. The videos to be double scored were chosen using an online random number generating tool (http://www.random.org/). ICCs were calculated comparing these scores with the researchers' scores. Good inter-rater reliability was shown for the total tic severity score (ICC = .85) with a 95% confidence interval (CI) of .54 to .96. For the motor tic severity ICC = .88 (95% CI: .62, .97) and for phonic tic severity ICC = .95 (95% CI: .83, .99).

Direct tic observation. A secondary observational measure was included to provide a convergent direct measure of tic frequency, less dependent on the memory of the parent and child and with the potential to be more objective. Some research has shown low correlations between direct tic measures and YGTSS scores, and recommend supplementation with additional direct measures of tic frequency (M. Himle et al., 2006). Similar studies have found that segments as short as five minutes

are sufficient to gain reliable results and such measurements also show stability over time (Chappell et al., 1994).

Children were filmed for 15 minutes while watching an episode of The Simpsons. During filming children sat on a chair in front of a laptop and were recorded using the in-built webcam and video-capture software (Debut Video Capture, NCH Software - http://www.nchsoftware.com/capture/). The laptop was positioned so that their head and upper torso could clearly be seen. The children were asked simply to watch the 15 minute video. The researcher remained in the room but engaged herself in another activity such as reading a book or packing away test equipment.

The protocol aimed to follow that used by Himle et al. (2006). The physical set-up of the observation was similar, in that the camera was in view of the child as they watched the DVD and the child was aware they were being filmed. In contrast to the Himle et al. (2006) protocol, it was not possible to leave the child alone in the room due to the fact that they were watching the film on the researcher's laptop which could not be locked while the DVD was playing.

Choice of video. It was desirable to find an episode of something participants were likely to find engaging. The researchers liaised with a parent of a child who had been seen at the clinic about what she felt would be popular among children her son's age. After discussion with her son they recommended The Simpsons. A range of episodes were screened for age inappropriate content by the researchers. The episode "Homer Simpson, This is Your Wife" (Nastuk, 2006) was chosen for use at Time 1. It was then necessary to identify a sufficiently similar episode for the children to watch at Time 2. Although this contrasts with the protocol used by Himle et al. (2006), in which the same programme was shown at each observation, it was felt that using the

same episode again would potentially create a bias in the number of tics displayed due to reduced engagement on seeing the same episode again only three months later.

A potential three episodes were chosen by the researchers and screened for appropriateness. These episodes were then rated on a range of variables that have been shown to exacerbate or attenuate tics (Conelea & Woods, 2008b) and might realistically vary between episodes. The six questions developed were:

1. How stressful/ anxiety provoking was this episode?
2. How boring was this episode?
3. How relaxing was this episode?
4. How stimulating was this episode? (i.e. funny/exciting?)
5. How upsetting or sad was this episode?
6. How frightening was this episode?

These questions were rated on the following zero to ten scale:

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely

A 14-year-old volunteer (a cousin of one of the researchers) watched the Time 1 episode and answered the above questions. She then watched the additional three possible episodes and rated each on the same variables. The absolute difference between her score on the original episode and each other episode was calculated for each question. The sum of these differences represented the degree of difference between the episodes based on her ratings. The episode with the lowest total difference score to the Time 1 episode was chosen. This was "Mr Lisa Goes to Washington" (Archer, 1991). The scores she gave for each episode are shown in Appendix J.

Video coding. Videos of participants were coded by a clinical psychologist and a trainee clinical psychologist blind to condition allocation and time point. Each coder

scored half the videos. The coding procedure followed an event frequency method similar to M. Himle et al. (2006). The complete protocol followed is included in Appendix K. The coders were trained in tic counting by the researchers (trainee clinical psychologists who had themselves been trained by Dr Murphy). Training involved discussion of the protocol and answering of any questions the coders had. Example tic videos were then watched and coded together and ratings discussed and compared.

The tics to count were operationalised using information gathered from the YGTSS. For each participant the researchers generated a single list of phonic and motor tics by combining the two tic lists generated at Time 1 and Time 2 assessments. The coders were asked to review the list before counting participants' tics and only to count tics which appeared on the list. The objective was to reduce potential subjectivity in judgements of which movements were and were not tics, while maintaining consistency in what was counted at each time point.

The coders counted tics observed on each video using a hand held tally counter. They also recorded the total number of seconds during which the child was not visible. For example, if the child bent down and was out of shot or turned around and could not be observed. A tics-per-minute score was then calculated by dividing the number of tics by the total number of minutes the child was observable. The coders always coded all videos for one child together in a single block, taking 40 minutes. The coding sequence was counterbalanced, such that they coded half the Time 1 videos first and half the Time 2 videos first. The videos were labelled using a code to maintain blinding to time point.

Inter-rater reliability of video coding. As there were two coders involved in counting the tics, it was desirable to calculate the inter-rater reliability between them.

In order to establish this, they each coded 20% of the videos coded by the other. As above, the videos to be double scored were chosen using an online random number generating tool (http://www.random.org/). Inter-rater reliability between tics-per-minute scores was ICC = .63 (95% CI: .30, .82). This is slightly lower than the .70 usually considered to represent good reliability (Dancey & Reidy, 2011).

Additional outcome measures.

Premonitory urge. The Premonitory Urge for Tics Scale (PUTS; Woods et al., 2005) is a self-report measure of the PU. Nine items on a four-point Likert scale are completed with scores ranging from one to four. A higher total score indicates more intense and more frequent PUs. This total ranges from 9 to 36. A copy of this questionnaire is included in Appendix L.

The measure has been shown to have high internal consistency (α = .81) and to show stability over time (Woods et al., 2005). The PUTS has not been shown to have strong psychometric properties when used with children under ten years old, however, which may relate to findings that young children often do not report awareness of a PU. Nonetheless, there is no other such measure available and the PUTS has often been used clinically by the principal investigator with children from eight years old. It is possible that the HRT treatment would increase children's perception of the PU and hence change the consistency of their response on the measure. It was, therefore, included despite this caveat. Within the current sample the measure shows internal consistency with Chronbach's α of .87.

Quality of life. The Gilles de la Tourette Syndrome – Quality of Life Scale (GTS-QOL; Cavanna et al., 2013) is a measure of QoL specifically developed for use

in children with TS. It is a 27-item self-report measure in which responses are summed to provide four subscales relating to psychological, physical and cognitive elements of QoL as well as obsessional symptoms. In addition, the measure provides a total QoL score and a single visual analogue item which asks the respondent how satisfied they feel overall with their life from 0 (extremely dissatisfied) to 100 (extremely satisfied). A copy of this questionnaire is included in Appendix M.

The Italian children's version of this measure was adapted from a measure originally developed in English for use with adults (Cavanna et al., 2008). This study used an English translation of the Italian children's version. The measure has shown good psychometric properties with Italian children (Cavanna et al., 2013), with Chronbach's alpha scores of .70 or greater on all subscales. Among adults, Cavanna et al. (2008) report high internal consistency and stability over time (α = .80 and ICC = .80 respectively). This measure is the only condition-specific measure of health related QoL available for children with TS. Its psychometric properties have not yet been formally studied in English children, but it is routinely used clinically with children at GOSH and is currently in the validation process. Within the current sample the measure shows internal consistency with Chronbach's α of .89.

Additional measures collected for separate studies. A series of additional measures were collected during the visit. These did not form part of the current study but were required for the thesis of the other trainee clinical psychologist involved and another research project planned by the principal investigator.

The children completed three additional questionnaires. The Tourette Syndrome Questionnaire is a brief five-item measure developed by Dr Murphy to

assess children's confidence in relation to their tics and their acceptance of the condition. The Children's Obsessive Compulsive Inventory Revised (ChOCI-R; Uher, Heyman, Turner, & Shafran, 2008) is a 32-item child-report measure of OCD symptoms. The Paediatric Quality of Life Inventory Version 4.0 (Varni et al., 2001) is a general measure of QoL, non-specific to condition.

Three neuropsychological measures from the NIH Toolbox were also included (Weintraub et al., 2013). These were two computer based tasks looking at cognitive flexibility and executive function, namely the Dimensional Change Card Sort Test and the Flanker Inhibitory Control and Attention Test. Each task required about four minutes for administration. The Motor Dexterity Test was also completed as a measure of fine motor skills. This is a peg test which took just a few minutes to complete.

The direct tic count observation included an additional five minutes, after the 15 minutes described above, during which the child was asked to suppress their tics as much as possible. They were told that after this they would receive a small reward. At Time 1 this reward was a small yellow rubber person that could be stretched and played with. At Time 2 this was a small plastic slinky toy.

Finally, parents were asked to complete the following questionnaires: a parent-report version of the ChOCI-R scale; a brief 4-item screening questionnaire assessing the presence or absence of anger outbursts which is included at the beginning of the Rage Attacks Questionnaire (used in Budman et al., 2003) and the Strengths and Difficulties Questionnaire (Goodman, 1997). An additional copy of the SNAP-IV parent-report scale was collected at follow-up which was not used in the present study.

2.16 Assessment Procedure

Testing took place either at the family's home or at the clinic, depending on the family's convenience and practical constraints. Four families were assessed at the clinic at Time 1 and all families were assessed at home at Time 2. This was because post-assessments took place during the school term so it was not possible to conduct assessments during the week. It is worth noting that observational measures of tic severity in the clinic have been found to show good correspondence with those taken in the home (M. Himle et al., 2006).

Parents were sent questionnaires and consent forms ahead of the visits to allow them to read them and save time on the day of the assessment. If this was inconvenient, questionnaires were completed on the day. At the assessment, the researcher collected questionnaires, answered any questions parents had and checked all items had been completed. At the beginning of the initial assessment, after offering an opportunity for questions, consent forms were collected from parents or carers (see Appendix N) and assent forms completed by the children to show their agreement to participate (Appendix O). Children were shown a visual plan of the timetable (Appendix P) and the researcher explained to them what would happen and discussed when they would like to have breaks.

Where possible, a quiet room in the house was used with a table on which equipment could be arranged. The same researcher conducted assessments at each time point to maintain consistency. The sequence of assessments completed at Time 1 and Time 2 are shown in Table 2.3. The researchers followed the complete assessment protocols shown in Appendices Q (Time 1) and R (Time 2).

Table 2.3

Sequence of Measures at Time 1 and Time 2 Assessments

Measure	Time 1	Time 2
Gilles de la Tourette Syndrome – Quality of Life Scale*	1	1
Tourette Syndrome Questionnaire	2	2
Dimensional Change Card Sort Test	3	3
Flanker Inhibitory Control and Attention Test	4	4
Motor Dexterity Test	5	5
Paediatric Quality of Life Inventory Version 4.0	6	6
Premonitory Urge for Tics Scale*	7	7
Wechsler Intelligence Scales for Children (WISC-IV-SF)*	8	–
15 minutes tic observation without tic suppression*	9	8
5 minutes tic observation with suppression	10	9
Yale Global Tic Severity Scale*	11	10
ChOCI-R child self-report measure	12	–

* Measures included in the current study

The assessment battery at Time 1 took a total of just under three hours, on average, allowing for breaks. The Time 2 protocol took about half that time. The length of the assessment is not dissimilar to test batteries completed with children clinically or in previous studies (Channon, Pratt, & Robertson, 2003; Schuerholz, Baumgardner, Singer, Reiss, & Denckla, 1996; Schuerholz, Singer, & Denckla, 1998). The assessment was designed to be maximally engaging for the children. This was achieved through inclusion of brief computer games, puzzles and table-top games, watching of a video and interview measures in addition to questionnaires. The order of the items was carefully considered and breaks were provided so as to maintain variety and interest. Children's attention and the constructs measured were taken into account. Questionnaires were spread out amongst more engaging activities.

The majority of the children said they enjoyed completing the tasks and the investigators felt that most children maintained engagement throughout.

At the end of the follow-up visit, the family were asked whether there had been any changes to medication during the study and whether their child had experienced any significant or stressful life events. Responses to these questions were included on the demographic information sheet (Appendix G).

2.17 Service User Involvement

Service users were involved at several stages of this project. In order to predict the families' experience of participation in the study and to improve this where possible, a parent of a child with TS provided feedback on the study design and paperwork in advance, including the adult and child information sheets, consent form and invitation letter. The service user said that the information sheet answered comprehensively all the questions of which she could think and also provided clear and understandable answers. She was able to provide some useful suggestions for improvements to the wording of the information sheets to make them more accessible for younger children. In addition, she was consulted about which DVD children in this age group would like to watch during the tic observation.

After the groups, parents and children were asked for feedback about their experience of attending the groups via a short satisfaction questionnaire (Appendices S and T). Following completion of the wider study, the intention is to invite families to a feedback session where the study results will be presented and they will be thanked for their participation. In addition, it is intended to send all families a short report describing the study findings.

Chapter 3. Results

This chapter outlines the study results. The analytic strategy is described first and then an outline of preliminary analyses, data screening and test selection is provided. A description of the sample and differences between groups at Time 1 is then given followed by a full outline of the results in relation to each hypothesis.

3.1 Analytic Strategy

The analysis was conducted using IBM SPSS Statistics software, version 21. All participants remained in the groups to which they had been assigned and there was no cross-over between study arms. An intention to treat (ITT) model was used in which all participants who had been randomised and assessed at Time 1 (n = 33) were included in the analysis, using last observation scores carried forward for those lost to follow-up (n = 4). This approach is recommended as more likely to retain balance in prognostic factors achieved through the randomisation process (Abraha & Montedori, 2010; Heritier, Gebski, & Keech, 2003). This is likely to produce a more conservative estimate of treatment effect than analyses including only those who completed the full protocol. This approach is arguably more ecologically valid. A subsequent secondary analysis was conducted including only participants who attended five or more group sessions (n = 26) in order to provide a measure of the strength of effects when the protocol was fully adhered to.

To maximise power and reduce the chance of Type II error, parametric tests were used throughout, having established that the data met the necessary test assumptions. Two-tailed probability values are given in all cases.

Bonferroni corrections were considered as a means of controlling for family-wise error. While widely used, Bonferroni is considered a conservative correction and Perneger (1998) argue that it can be unclear how to define a "family" and whether it should therefore be applied to all comparisons under a single hypothesis, all those presented in a paper or those categorised in another way. Perneger suggests that describing the tests conducted and interpreting results conservatively is preferable. No corrections were therefore made for family-wise error rates in these analyses, so this is important to bare in mind in reading the results.

Given the small sample size examined, findings are highly tentative and would need to be replicated in future studies with larger samples. Exact *p* values, effect sizes and confidence intervals are provided where appropriate in order to provide as complete a description of the data as possible. Approximate 95% confidence intervals are calculated using formulae recommended by Nakagawa and Cuthill (2007). Full formulae used in calculation of Cohen's *d*, adjusted Cohen's *d* and related confidence intervals can be found in Appendix U.

Age, Full Scale IQ (FSIQ), socioeconomic status (SES) and gender were considered as control variables in all cases. As there were no Time 1 group differences on these variables (see below) they were not included on group based analyses (Hypotheses 1 and 2). Similarly, for whole sample analyses (Hypotheses 3 and 4), correlations were examined between outcome variables and age, SES and FSIQ. As no significant associations were found, these were not included as controls. Similarly, outcome variables were not found to vary by gender on *t*-tests, so this was excluded as well.

3.2 Preliminary Analysis

The data were checked to identify missing values. It was not possible to obtain WISC-IV-SF scores for one participant who declined to complete the measure. Direct tic count data was also missing for the three children who did not attend a single group session. The dataset otherwise contained no missing values.

The main variables were then screened for univariate and multivariate outliers and for normality assumptions. Screening was completed separately both for the complete sample and then for the two groups (HRT and psycho-education). The variables assessed included change variables which were computed as Time 1 scores minus Time 2 scores on each relevant variable.

Univariate outliers were classed as any data point more than three standard deviations from the variable mean. Multivariate outliers were taken as any data point for which Cook's distance was greater than 1.00 (Tabachnick & Fidell, 2013, p. 109). The skewness and kurtosis of each continuous variable were assessed to ensure the data met normality assumptions. The test statistics for both skewness and kurtosis were converted into z scores for all variables. Z score values between -2.58 and 2.58 on either measure were considered to be within acceptable limits (Field, 2000, p. 41).

Only one univariate outlier was found in the whole data set. This was the direct tic observation (tics per minute) score for one participant in the psycho-education group at Time 2. In order to reduce its influence on the mean, the score was winsorised, whereby the data point was changed to a score one greater than the next highest score within that group and a similar transformation was made at the opposite end of the distribution in order to balance the effect (Tabachnick & Fidell., 2013, p. 111). Following this adjustment, no multivariate outliers were detected and all variables fell within acceptable limits for both skewness and kurtosis, both for the

sample as a whole and for separate groups. It was therefore considered appropriate to use parametric tests.

3.3 Assumptions of Tests

Assumptions of tests were checked before proceeding with analyses. The hypotheses were tested using a combination of Analysis of Variance (ANOVA) tests, Multivariate Analyses of Variance (MANOVA) tests and hierarchical linear regression analyses. For ANOVA tests, equality of variances and of the variance-covariance matrices were checked using Levene's test and the more conservative Box's test respectively. For MANOVA, the additional assumptions of linearity and lack of multicollinearity were assessed through inspection of scatter plots and correlations between variables. Multivariate normality was assumed given normality of all variables individually. In two cases Box's test of equality of covariance matrices was non-significant, however Levene's test for equality of variances showed significant differences in variance between groups. In these situations Tabachnick and Fidell, (2013) recommend calculating the F_{max} statistic (F_{max} = larger variance/smaller variance). Unequal variances present greater risk to alpha levels when sample sizes are more unequal and for sample size difference ratios of four to one or smaller, as was the case in this study, F_{max} values below 10 are considered acceptable (Tabachnick & Fidell, 2013). In addition, inflated Type I error rates are possible if the larger variance is associated with the smaller cell size (Tabachnick & Fidell, 2013), but here the reverse was true in both cases. It was therefore considered acceptable to use the MANOVA analyses without implementing more stringent alpha levels.

For linear regression analyses, assumptions of independence of residuals, linearity, homoscedasticity, absence of multicollinearity, normality and absence of outliers in the regression solution were assessed following Tabachnick and Fidell (2013). The data met these assumptions in all cases.

3.4 Description of the Sample and Group Differences at Time 1

Descriptive data for the full sample are provided in Table 3.1 (continuous variables) and Table 3.2 (categorical variables), together with data for each group separately. Independent samples *t*-tests were conducted to check for group differences at Time 1 on continuous variables. Results are displayed in Table 3.1. Chi-squared tests were not possible in testing for group differences on categorical variables because of low expected cell counts. Fisher's Exact Tests were used instead. Results of these tests are displayed in Table 3.2. No significant differences were found between groups on any variables.

Formal diagnoses reported by parents at telephone interview are given in Table 3.2. It is worth noting that three parents (two psycho-education and one HRT) reported spontaneously that their child had possible Autism Spectrum Disorder (ASD) but had not yet been formally investigated. Therefore the counts of formal diagnoses may not fully reflect social communication difficulties of all participants.

Table 3.1

Descriptive Data for Continuous Variables and Group Differences at Time 1

	Group			Independent samples *t*-test for Time 1 group differences		
	All (*n* = 33)	Psych-Ed (*n* = 16)	HRT (*n* = 17)			
	M (SD)	*M (SD)*	*M (SD)*	*t*	*p*	*df*
Age in years	10.96 (1.45)	11.05 (1.62)	10.87 (1.31)	0.35	.73	31
SES score	41.93 (14.60)	45.91 (14.76)	38.19 (13.82)	1.55	.13	31
FSIQ score	101.81 (12.48)	103.13 (13.75)	100.65 (11.55)	0.56	.58	30
SNAP ADHD-Inattention	1.66 (0.69)	1.62 (0.56)	1.69 (0.81)	0.31	.76	31
SNAP ADHD - Hyperactivity/ Impulsivity	1.49 (0.88)	1.63 (0.82)	1.35 (0.94)	0.88	.38	31
SNAP ODD	1.30 (0.88)	1.50 (0.93)	1.12 (0.81)	1.26	.22	31
YGTSS Motor Severity[a]	17.00 (4.00)	16.31 (3.03)	17.65 (4.74)	-0.97	.34	27
YGTSS Phonic Severity	12.67 (6.40)	12.63 (5.93)	12.71 (6.99)	-0.04	.97	31
YGTSS Impairment	22.73 (8.76)	21.25 (8.06)	24.12 (9.39)	-0.94	.36	31
Tic count (tics per minute)	7.09 (4.12)	7.68 (4.14)	6.50 (4.16)	0.78	.44	28
PUTs Total Score	18.73 (6.79)	20.31 (7.44)	17.24 (5.95)	1.32	.20	31
GTS-QoL Total Score	34.61 (15.78)	34.38 (13.76)	34.82 (17.90)	-0.08	.94	31
GTS-QoL Satisfaction	73.64 (16.15)	73.06 (14.10)	74.18 (18.30)	-0.20	.85	31

Note. Psych-Ed = Psycho-educational; HRT = Habit Reversal Therapy; SES = Socioeconomic Status; FSIQ = Full Scale IQ Score; SNAP = Swanson, Nolan, and Pelham–IV Scale; ADHD = Attention Deficit Hyperactivity Disorder; ODD = Oppositional Defiant Disorder; YGTSS = Yale Global Tic Severity Scale; PUTs = Premonitory Urge for Tics Scale; GTS-QoL = Gilles de la Tourette Syndrome Quality of Life Scale.

[a] Levene's test for equality of variance significant ($F = 6.65$, $p = .015$) so equality of variance not assumed.

Table 3.2

Descriptive Data for Categorical Variables and Group Differences at Time 1

		Group			Fisher's Exact Test for Time 1 group differences
		All (*n* = 33)	Psych-Ed (*n* = 16)	HRT (*n* = 17)	*p*
Gender	Male	25	12	13	1.00
	Female	8	4	4	
Ethnicity	White British	23	12	11	0.71[a]
	Other White	7	3	4	
	British Indian	1	1	0	
	Black British	1	0	1	
	Mixed/ multiple ethnic	1	0	1	
Tic Disorder	TS	30	15	15	1.00
	CMTD	3	1	2	
Any comorbidity[b]	Yes	18	10	8	0.49
	No	15	6	9	
ADHD diagnosis	Yes	7	5	2	0.23
	No	26	11	15	
OCD diagnosis	Yes	9	5	4	0.71
	No	24	11	13	
ASD diagnosis	Yes	2	1	1	1.00
	No	31	15	16	
Other diagnoses[c]	Anxiety/Panic	2	0	2	
	Dyspraxia	2	1	1	
	Dyscalculia	1	1	0	
	Epilepsy	1	0	1	
	PTSD	1	0	1	
	ODD	1	1	0	
Medication at Time 1[d]	Yes	11	4	7	0.47
	No	22	12	10	
Recruitment source	New referral	22	10	12	0.72
	Retrospective	11	6	5	
Month group began	September	16	6	10	0.30
	November	17	10	7	

Note. Psych-Ed = Psycho-educational; HRT = Habit Reversal Therapy; TS = Tourette Syndrome; CMTD = Chronic Motor Tic Disorder; ADHD = Attention Deficit Hyperactivity Disorder; OCD = Obsessive Compulsive Disorder; ASD = Autism Spectrum Disorder; PTSD = Post Traumatic Stress Disorder; ODD = Oppositional Defiant Disorder.

[a] Fisher's exact test conducted comparing British and non-British participants in a 2 x 2 contingency table.

[b] This included all of the diagnoses listed in the table. No other diagnoses were reported at preliminary interview. One child had three comorbidities, six children had two and eleven children had one.

[c] Fisher's exact test not conducted for these diagnoses as the numbers of each were too few.

[d] Ten children were taking non-stimulant medication. One child in the HRT group was taking stimulant medication.

Previous talking therapy. Seven children had received previous formal talking therapy or counselling. Three were in the HRT group and four in the psycho-education group. Two of them had attended a six-session psycho-education group at the clinic more than two years previously. One of the children had also attended fewer than four individual HRT sessions and the other had attended family therapy sessions over a three-year period. Three children had received Cognitive Behavioural Therapy (CBT) in their local Child and Adolescent Mental Health Service (CAMHS), although this related to conditions such as anxiety rather than to their tics. One received social skills support through their local CAMHS and another was reported to have had extensive therapy since the age of six including CBT and play therapy for anxiety.

Concurrent therapy. One child attended local weekly counselling sessions in relation to mood, which they had been attending prior to the study and continued throughout. A second child received CBT locally for anxiety in a local CAMHS service, which began three weeks prior to the pre-assessment. A third child received four sessions of psycho-education in relation to anger, which had been agreed with the GOSH team prior to their involvement in the study. These three children were all in the HRT group. The parents of a fourth child in the psycho-education group attended a group for parents of children with anxiety in their local CAMHS service concurrent with the study. The analyses were run excluding these children to see if this affected results. In addition, children in the study received ongoing school liaison support from the clinical team at GOSH where necessary, as is the case for all children attending the clinic.

Medication changes. Five children had medication changes between Time 1 and Time 2. Three were in the HRT group and two in the psycho-education group. In the HRT group one child began taking Sertraline about a week after the pre-assessment and then stopped again three weeks before follow-up. A second child had a 50% dosage increase in epilepsy medication towards the end of the group sessions and before follow-up. The third child had a 17% reduction in their dose of stimulant medication (Ritalin) during this time. In the psycho-education group two children stopped taking non-stimulant medication between pre-assessment and follow-up. These changes involved both increases and reductions in medication so any influence on results is likely to have been balanced. Nonetheless, the analyses were repeated excluding these children to see if this affected results.

Stressful or adverse life events. One child in the HRT group developed additional unexplained medical symptoms during the study following completion of the group intervention but before Time 2 assessment, resulting in absence from school, frequent additional medical appointments and increased family stress levels. This raised the question of whether this participant was representative of the population under study. A parent of a child in the psycho-education group reported that their child's great grandfather had been very ill during the study. For this reason the analysis was run both including and excluding these participants to see if this affected results. A child in the psycho-education group had a new sibling born during the study but the parents felt their child had not experienced undue stress as a result.

Four children had started secondary school in the first set of groups, which ran from September to October and for whom the pre-assessment was conducted during the summer holiday. It was felt that the return to school for all the children in the

September groups may have impacted on scores at Time 2 compared to Time 1, when they were on holiday. Main analyses were therefore repeated for the September and November groups separately to assess for any differences in results. Where differences occurred these are discussed below.

Attendance rates. In the psycho-education group (September, *n* = 6; November, *n* = 10), the average number of children present in each session was 6.06 compared to an average of 7.06 in each HRT session (September, *n* = 10; November, *n* = 7). This was because the psycho-education group had slightly lower attendance rates overall and one fewer child randomised to this condition.

The 33 participants attended a mean of 6.36 sessions (*SD* = 2.71). This figure was 6.06 (*SD* = 2.93) in the psycho-education group and 6.65 (*SD* = 2.55) in the HRT group. The mode in both groups was eight. In the HRT group, two children never attended any sessions but all those who began to attend (*n* = 15) then came to seven or eight sessions. In the psycho-education group, one child never attended any sessions, six children attended fewer than five sessions and the remaining eleven attended seven or eight sessions.

3.5 Main Analyses

Hypothesis 1. *Participants in the HRT group will show greater reductions in tic severity compared to those in the psycho-education group.*

Repeated Measures ANOVA was chosen for this comparison to allow examination not only of differences between the groups but also of the effect of time point on tic severity. This was based on a 2 x 2 mixed design looking for main effects

of group (HRT or psycho-education) as a between-subjects factor and time point (Time 1 or Time 2) as a within-subjects factor. The alternative of using Analysis of Covariance with Time 1 scores as covariates was rejected because of the possibility that tic severity might have reduced in both groups and, given this was a pilot for a future larger study, it was important this was assessed. In addition, using the Repeated Measures ANOVA reduces error variance (Dancey & Reidy, 2011, p. 357). It was decided to conduct the MANOVA analyses prior to separate ANOVA analyses to protect against inflated Type I error from multiple tests (Tabachnick & Fidell, 2013). This was conducted where appropriate when correlations between dependent variables were moderate.

The tic severity measures used in this analysis were motor and phonic severity scores on the YGTSS and the direct tic count. The two YGTSS measures were included separately to allow for the possibility that the different types of tics may respond differently to the intervention. Examination of Pearson's correlations between these variables (see Table 3.3) showed no relationship between the direct tic count and the YGTSS phonic tics measure. It was therefore decided to analyse the direct tic count variable separately in a Repeated Measures ANOVA and the two YGTSS measures together in a MANOVA.

Table 3.3

Summary of Inter-correlations on Measures of Tic Severity

Measure	1	2	3
1. YGTSS Motor Severity	–	.48*	.31
2. YGTSS Phonic Severity	.46*	–	-.02
3. Direct Tic Count	.15	.14	–

Note. Inter-correlations for Time 1 scores are represented above the diagonal and those for Time 2 scores below. For all scales, higher scores indicate more severe tics. YGTSS = Yale Global Tic Severity Scale.
* $p < 0.05$.

Results of the MANOVA. The multivariate tests showed a significant interaction between group and time point ($F(2,30) = 3.89$, $p = .032$, partial $\eta^2 = .206$). The main multivariate effect of time point was also significant ($F(2,30) = 6.94$, $p = .003$, partial $\eta^2 = .316$). The main multivariate effect of group was non-significant ($F(2,30) = 0.09$, $p = .917$, partial $\eta^2 = .006$).

Univariate repeated measures ANOVAs were then conducted to examine the significant effects for each dependent variable separately. The interaction found between time point and group was significant only in relation to the motor tic severity scale ($F(1,31) = 6.90$, $p = .013$, partial $\eta^2 = .182$), and not the phonic tic severity scale ($F(1,31) = 0.821$, $p = .372$, partial $\eta^2 = .026$). Similarly, the main effect of time point was only significant in relation to the motor tic severity scale ($F(1,31) = 13.87$, $p = .001$, partial $\eta^2 = .309$) and not the phonic tic scale ($F(1,31) = 0.821$, $p = .372$, partial $\eta^2 = .026$).

Inspection of the means showed that participants in both groups reported reductions in motor tics from Time 1 to Time 2. This effect was significantly bigger in the HRT group as compared to the psycho-education group. Means and standard deviations are reported in Table 3.4. Effect sizes and confidence intervals for the main effect of time point and the time point x group interaction of the separate ANOVAs for each variable are displayed in Table 3.6. Percentage change values are given in Table 3.7.

This result partially supports Hypothesis 1 suggesting that both groups led to a reduction in motor tics but that the effect was stronger in the HRT group. The hypothesis was not supported in relation to phonic tics, which did not appear to have been altered by the intervention.

Table 3.4

YGTSS Motor and Phonic Tic Severity Means and Standard Deviations by Group and Time Point, with Confidence Intervals for the Means

		YGTSS Motor tic severity			YGTSS Phonic tic severity		
		M	*SD*	95% CI	*M*	*SD*	95% CI
Psych-Ed (*n* = 16)	Time 1	16.31	3.03	[14.27, 18.36]	12.63	5.93	[9.31, 15.94]
	Time 2	15.88	2.28	[14.11, 17.65]	11.13	5.82	[8.21, 14.04]
HRT (*n* = 17)	Time 1	17.65	4.74	[15.67, 19.63]	12.71	6.99	[9.49, 15.92]
	Time 2	15.12	4.30	[13.40, 16.84]	12.71	5.61	[9.88, 15.53]
All (*n* = 33)	Time 1	16.98	0.70	[15.56, 18.40]	12.67	1.13	[10.36, 14.97]
	Time 2	15.50	0.60	[14.26, 16.73]	11.92	0.99	[9.89, 13.94]

Results of the ANOVA analysis. There was no statistically significant interaction between intervention group and time point on direct tic count ($F(1,28) = 0.02$, $p = .882$, partial $\eta^2 = .022$). The main within-subjects effect of time point showed a statistically significant difference in tic counts between Time 1 and Time 2, with the two groups considered together ($F(1,28) = 9.63$, $p = .004$, partial $\eta^2 = .256$). The main between-subjects effect of group showed no significant difference in tic count scores between the groups across time points ($F(1,28) = 0.77$, $p = .387$, partial $\eta^2 = .027$). Means and standard deviations are reported in Table 3.5. Effect sizes and confidence intervals for the main effect of time point and the time point x group interaction are displayed in Table 3.6. Percentage change scores are given in Table 3.7. The result does not support the hypothesis that tics would be more reduced in the

Table 3.5

Tic Count Means and Standard Deviations by Group and Time Point, with Confidence Intervals for the Means

		Tic Count (Tics per minute)		
		M	*SD*	95% CI
Psych-Ed (*n* = 15)	Time 1	7.68	1.07	[5.49, 9.88]
	Time 2	5.95	0.85	[4.22,7.68]
HRT (*n* = 15)	Time 1	6.50	1.07	[4.30, 8.70]
	Time 2	4.92	0.85	[3.19, 6.66]
All (*n* = 30)	Time 1	7.09	0.76	[5.54, 8.64]
	Time 2	5.44	0.60	[4.21, 6.66]

HRT group compared to the psycho-education group but suggests instead that on this measure tics reduced significantly and in a similar pattern in both groups.

Secondary analyses. The analyses for Hypothesis 1 were repeated with various subsets of the sample removed to see if this had any effect on outcomes. The analyses were run including only those who had attended at least five sessions of the intervention (*n* = 26); who had not had changes to their medication during the study (*n* = 28); who had not had other therapy concurrently (*n* = 29) and who had not experienced stressful life events during the study (*n* = 31). None of these changes altered the significance of the tests conducted. The analyses were also repeated separately for the children who attended in September (*n* = 16) and the children who attended in November (*n* = 17). Again, the overall pattern of the results was the same, although in the September group the interaction between time and group on the motor tic severity measure became non-significant and in the November group the main effect of time on the direct tic count measure became non-significant. This is perhaps unsurprising given the much smaller sample size available.

Table 3.6

Tic Measure Cohen's d and Mean-Difference Effect Sizes for Time 2 Group Differences and Mean Differences Across Time in Whole Sample

	YGTSS Motor Tic Severity	YGTSS Phonic Tic Severity	Tic Count (Tics per minute)
Group Differences at Time 2 (Interaction effect)			
Time 2 mean difference	0.76	-1.58	1.03
Adjusted mean difference[a]	2.1	-1.5	-0.15
d	0.22	-0.28	1.21
Adjusted *d*[a] [95% CI]	0.55 [-0.16, 1.27]	-0.26 [-0.97, 0.44]	0.11 [-0.63, 0.85]
p	.013	.372	.882
Observed power	.72	.14	.05
Time 1 to Time 2 Differences in Whole Sample (Main Effect of Time)			
Mean difference	1.48	0.75	1.65
d [95% CI]	1.58 [1.13, 2.03]	0.49 [0.20, 0.78]	1.67 [1.17,2.18]
p	.001	.372	.001
Observed power	.95	.14	.85

Note. Effect sizes are reported such that for interaction effects positive values indicate greater improvement in the HRT group and improvement in symptoms over time for the main effect of time. CI = Confidence interval.
[a] Effect size measures (both mean difference and Cohen's *d*) adjusted for Time 1 group differences on each measure, as recommended by Durlak (2009). Non- adjusted figures are also reported.

Table 3.7

Percentage Change Scores on Tic Measures from Time 1 to Time 2

	YGTSS Motor tic severity	YGTSS Phonic tic severity	Tic Count (tics per minute)
Psych-Ed (*n* = 16)	2.6%	10.5%	22.5%
HRT (*n* = 17)	14.3%	0%	24.3%
All (*n* = 33)	8.7%	5.9%	23.3%

Hypothesis 2. *Participants in both HRT and psycho-education groups will show significant post-treatment improvements in QoL.*

Repeated Measures ANOVA was chosen for this analysis because it allows assessment of not only group differences but also the effect of time point on QoL. This analysis was based on a 2 x 2 mixed design looking for main effects of group (HRT or psycho-education) as a between-subjects factor and time point (Time 1 or Time 2) as a within-subjects factor.

The measures of QoL used as the dependent variables were the GTS-QoL Total score and the one-item satisfaction rating from the same measure. Examination of Pearson's correlations between these variables (see Table 3.8) showed moderate correlations. It was therefore decided to analyse the variables together in a MANOVA.

Table 3.8

Summary of Inter-correlations on QoL Measures

Measure	1	2
1. GTS-QoL Total Score	–	-.49*
2. GTS-QoL Satisfaction Score	-.64*	–

Note. Pearson's correlations for Time 1 scores are represented above the diagonal and those for Time 2 scores below the diagonal. For the GTS-QoL Total score, higher scores are indicative of increased impairment, whereas for the GTS-QoL Satisfaction scale increased scores indicate greater satisfaction. GTS-QoL = Gilles de la Tourette Syndrome Quality of Life Scale.
* $p < 0.05$.

Results of the MANOVA analysis. The multivariate tests showed no significant main effect of time point ($F(2,30) = 2.01$, $p = .152$, partial $\eta^2 = .118$). The interaction between group and time point was found to be non-significant ($F(2,30) = 0.08$, $p = .925$, partial $\eta^2 = .005$) as was the main effect of group ($F(2,30) = 0.004$, $p =$

.996, partial $\eta^2 < .001$). Means and standard deviations are reported in Table 3.9. Effect sizes and confidence intervals for the main effect of time point and the time point x group interaction of the individual univariate ANOVAs are displayed in Table 3.10. Percentage change scores are given in Table 3.11. Overall this result does not provide support for Hypothesis 2.

Table 3.9

GTS-QoL Scale Total and Satisfaction Score Means and Standard Deviations by Group and Time Point, with Confidence Intervals for the Means

		GTS-QOL Total Score			GTS-QoL Satisfaction Score		
		M	*SD*	95% CI	*M*	*SD*	95% CI
Psych-Ed	Time 1	34.38	4.01	[26.20, 42.55]	73.06	4.10	[64.70, 81.43]
(*n* = 16)	Time 2	30.31	3.60	[22.96, 37.66]	75.50	4.89	[65.53, 85.47]
HRT	Time 1	34.82	3.89	[26.89, 42.75]	74.18	3.98	[66.06, 82.29]
(*n* = 17)	Time 2	30.18	3.50	[23.05, 37.31]	74.94	4.74	[65.27, 84.61]
All	Time 1	34.60	2.79	[28.91, 40.29]	73.62	2.86	[67.79, 79.45]
(*n* = 33)	Time 2	30.24	2.51	[25.12, 35.36]	75.22	3.40	[68.28, 82.16]

Secondary analyses. The analyses for Hypothesis 2 were repeated with the same data subsets as conducted for Hypothesis 1. The main effect of time on GTS-QoL Total Score was found to be significant when only including those who had attended more than five sessions; those who had not had concurrent therapy and when only including those who had not experienced stressful life events during the study. Removing those who had had medication changes did not result in significant effects.

Comparing analyses for participants who attended the September groups (*n* = 16) to those who attended the November groups (*n* = 17) showed that the main effect of time on the GTS-QoL Total Score was much stronger in the November groups than

the September groups across both HRT and psycho-educational groups. The effect was non-significant with a negligible effect size in the September groups (p = .934, η^2 = 0.001), whereas it was significant with a large effect size in the November groups (p = .006, η^2 = 0.405). This value of eta is equivalent to Cohen's d = 1.65, representing a large effect. Similarly, removing only children who had started secondary school from the completed analysis also caused this effect to become significant.

Table 3.10

QoL Measure Cohen's d and Mean-Difference Effect Sizes for Time 2 Group Differences and Mean Differences Across Time in Whole Sample

	GTS-QoL Total	GTS-QoL Satisfaction
Interaction Effect (Time 2 Group Difference)		
Time 2 mean difference	0.13	-0.56
Adjusted mean difference[a]	0.57	-1.68
d	0.04	-0.12
Adjusted *d*[a] [95% CI]	0.15 [-0.56, 0.85]	-0.39 [-1.11, 0.32]
p	.892	.758
Observed power	.05	.06
Main Effect of Time Across Groups		
Mean difference	4.36	1.60
d [95% CI]	1.14 [0.75, 1.53]	0.35 [0.05, 0.66]
p	.050	.555
Observed power	.51	.09

Note. Effect sizes are reported such that for interaction effects positive values indicate greater improvement in the HRT group and improvement in symptoms over time for the main effect of time. CI = Confidence interval.
[a] Effect size measures (both mean difference and Cohen's *d*) adjusted for Time 1 group differences on each measure, as recommended by Durlak (2009). Non- adjusted figures are also reported.

Table 3.11

Percentage Change Scores on QoL Measures from Time 1 to Time 2

	GTS-QoL Total	GTS-QoL Satisfaction
Psych-Ed (*n* = 16)	11.8%	3.3%
HRT (*n* = 17)	13.3%	1.0%
All (*n* = 33)	12.6%	2.2%

In summary, Hypothesis 2 is not supported by the main intention-to-treat analysis, although the tendency of the effect is in the expected direction. Analysis of participant subgroups showed changes in these findings which suggest that those who attended more sessions and those who attended the November as opposed to September groups may have experienced greater changes in GTS-QoL total scores. Effects were also greater when removing participants who had had unusual experiences or changes in circumstances during the study.

Hypothesis 3. *A reduction in the premonitory urge (PU) will be a better predictor of post-treatment improvement in QoL than reduction in tics.*

A hierarchical multiple linear regression analysis was chosen to test this hypothesis. All participants who were followed up at Time 2 were included (*n* = 29). It was felt there would be no extra benefit from including those who were not subsequently followed up as the intention is not to examine effect sizes of the intervention but rather distinguish between factors which predict change in scores. The dependent variable in this analysis represented change in GTS-QoL Total Score from Time 1 to Time 2. Change in the PUTs score was used as the measure of reduction in PU. A single measure of tic severity was chosen given the small sample size for this analysis. Change in the YGTSS Total Tic Severity score was used, as it

encompasses both phonic and motor tics and has higher reliability than the direct tic count measure. GTS-QoL Total scores at Time 1 were used as a covariate and entered first to form Model 1. The two predictor variables were entered into the analysis to form Model 2.

Results of the linear regression analysis. Model 1 showed that Time 1 GTS-QoL total scores explained a significant amount of variance in the dependent variable, which was change in the same scores between Time 1 and Time 2 ($F(1,27) = 13.44$, $p = .001$; $R^2 = .332$, adjusted $R^2 = .308$). The combination of the two main predictor variables added to the model at Step 2 were not shown to contribute to a significant increase in variance explained ($F(2,25) = 1.52$, $p = .238$). Neither change in PUTs score ($t(25) = 1.47$, $p = .154$), nor change in YGTSS Total Tic Severity score ($t(25) = 0.724$, $p = .476$) made significant contributions to explaining change in GTS-QOL Total score. The large difference between *R* square (.41) and adjusted *R* square (.33) in the complete model shows the degree to which the model has been adjusted for the small sample size. This result does not support Hypothesis 3.

Secondary analyses. This analysis was repeated excluding those who had medication changes, concurrent therapy or stressful life events between Times 1 and 2. The last two of these manipulations had no affect on results, however excluding those who had had medication changes was found to affect the results. In this case Model 2 was found to predict a significant amount of additional variance. Variance explained increased from 27% to 51%, adjusted $R^2 = .44$, with the addition of the two main predictor variables. This change was significant ($F(2,20) = 4.96$, $p = .018$). Reductions in PUTs total score were shown to contribute significantly to predicting reductions in GTS-QoL Total score ($t(20) = 2.83$, $p = .010$), whereas change in

YGTSS Total Tic Severity was not ($t(20) = 1.42$, $p = .171$). This means that reduced intensity of the PU was associated with improved QoL in these children.

Hypothesis 4. *Post-treatment improvements in QoL will be predicted by participants' lower inattention, hyperactivity and impulsivity symptoms.*

A hierarchical multiple linear regression analysis was chosen to test this hypothesis. As for Hypothesis 3, all participants followed up at Time 2 were included in this analysis ($n = 29$). The dependent variable represented change in GTS-QoL Total score from Time 1 to Time 2. The SNAP scale was used as a measure of symptoms of inattention as well as hyperactivity and impulsivity. These two individual SNAP scales were too highly correlated to be used as separate predictor variables as they would present a multicollinearity problem ($r(27) = .86$, $p < 001$). A single composite score was used instead, created by adding the two scales together. This is considered an appropriate way to calculate a score representing overall ADHD symptoms (Swanson et al., 2005). This is preferable to use of parentally reported diagnoses because if ADHD has been medicated it would not be expected to interfere with children's ability to access the intervention, regardless of diagnostic status. The SNAP-IV measure provides a measure of current symptoms, regardless of diagnostic or medication status, and therefore is more helpful in the current analysis. It also provides continuous data on symptom severity which a categorical diagnosis does not. GTS-QoL total scores at Time 1 were used as a covariate and entered first to form Model 1. The predictor variable was then entered into the analysis second to form Model 2.

Results of the linear regression analysis. As shown for Hypothesis 3, Time 1 GTS-QoL total scores explained a significant amount of variance in the dependent

variable, which was change in the GTS-QoL total scores between Time 1 and Time 2 ($F(1,27) = 13.44$, $p = .001$; $R^2 = .332$, adjusted $R^2 = .308$). The predictor variable added at Step 2 failed to contribute to a significant increase in variance explained ($F(1,26) = 0.881$, $p = .356$). This does not support Hypothesis 5.

Secondary analyses. This analysis was repeated excluding those who had medication changes, concurrent therapy or stressful life events between Times 1 and 2. Conclusions were the same in all cases.

Chapter 4. Discussion

In this concluding chapter, the findings of the main results are summarised and discussed in the context of previous research. Strengths, limitations and clinical implications of the study are outlined and suggestions made for future research.

4.1 Main Findings

This study aimed to compare Habit Reversal and psycho-education treatment groups for children with Tourette Syndrome (TS) and Chronic Tic Disorders in relation to both tic severity and quality of life (QoL).

Hypothesis 1. *Participants in the HRT group will show greater reductions in tic severity compared to those in the psycho-education group.*

The effect of the interventions on tic severity outcomes was assessed using YGTSS motor and phonic tic severity scales and a direct observation tic count representing tics per minute. The results were different for each measure.

Motor tics, as hypothesised, were found to have improved significantly more in the HRT group compared to the psycho-education group, with a reduction in score of 14.3% as opposed to only 2.6% in the psycho-education group. This was a medium effect size of $d = 0.55$. This result is consistent with results found for individual HRT (Piacentini et al., 2010). Although the effect size is similar to that found in individual HRT ($d = 0.68$), the small sample size in this case means the confidence intervals on the effect size estimation are large. It is, therefore, difficult to draw confident comparisons and research with larger samples is required to provide a more accurate estimate. The percentage reduction in tic severity shown in the HRT group is smaller

than the 31% reduction reported by Piacentini et al. and smaller than the 25% considered clinically meaningful by Jeon et al. (2013). If replicated, the smaller effect size found in the current study may suggest that group therapy produces a weaker effect than individual therapy.

In contrast to this finding, the expected improvement in the HRT group was not found for the YGTSS phonic tic scale, suggesting the HRT intervention had no effect on phonic tics. In fact, the psycho-education group showed a greater reduction in tics from baseline, although the effect was not significant. Such differences have not been reported by previous studies. Many studies have not examined the effect of HRT on phonic and motor tics separately, but those that have done so report a reduction in both types of tics. Piacentini et al. (2010) found slightly greater effect on phonic tics whereas Wilhelm et al. (2012) found a slightly larger effect on motor tics. The difference in this study may relate wholly or partly to the fact that 73% of tics tackled in the HRT group were motor tics. A larger scale study would benefit from addressing this question directly. Woods, Twohig, Flessner and Roloff (2003) followed five children after HRT treatment for phonic tics and found that motor tics were unchanged in four of the five children. This suggests treatment effects may not generalise between tic types.

The final tic severity measure assessed was the direct tic count. This showed contrasting results to the YGTSS scales. In this case, the hypothesis of greater improvement in the HRT group was not supported, as there was no significant difference in the response of the two groups. Instead, a significant main effect of time demonstrated that children in both groups showed a significant reduction in observed tics. The average reduction in tic count across the whole sample in this case was 23.3%, which represents a large effect (d = 1.67). Here, although the confidence

intervals are again wide, the entire confidence interval falls in the range of a large effect size, so we can be more confident about this effect.

It is worth mentioning here that the direct observation measure had limited inter-rater reliability. This would tend to reduce the likelihood that an effect would be significant. The fact that, in this case, the main effect of time was found to be significant despite low reliability supports the confidence we can have that this is a true effect.

This effect is also likely to be clinically meaningful, representing an average reduction in tics equivalent to nearly 100 tics an hour. However, as there is no waiting list control group in this study, it is difficult to draw firm conclusions about this effect. Comparison to previous studies is also difficult as most recent large scale studies of individual HRT therapy have not used a direct observation measure. Azrin and Peterson (1990) reported reductions of 93% in direct tic count but the study is not directly comparable as participants received a mean of 20 sessions over 8 to 11 months with a sample of only 10 participants.

It is interesting to consider why this result differed from those found for the YGTSS scales. It is likely that this observational measure focussed more on motor tics than phonic tics. Although sound was recorded and clear vocal tics were detected, the sound quality was not great, so quieter or more subtle vocal tics not involving mouth movements, such as throat clearing or squeaking noises, might have been missed. It is, therefore, possible this measure more closely reflected improvements seen on the YGTSS motor tic severity measure than the YGTSS phonic measure, where improvements were not seen.

The lack of correlation found between the direct tic count and the YGTSS scales is consistent with previous research (M. Himle et al., 2006). This suggests that

the measures may be capturing different tic characteristics. While the direct tic count is a pure measure of tic frequency, the YGTSS addresses frequency in addition to the range of different tics, complexity of tics, intensity of tics and the degree to which the tics interfere with the child's activities. This may explain the different findings. It is possible HRT differentially affects these other aspects but not the pure tic frequency measure. During the intervention, children in the HRT group specifically tackled their three most annoying tics, which are likely to have included the more complex, intense and interfering tics. This raises the possibility that tic frequency was less affected than these other tic characteristics measured by the YGTSS. Pure tic frequency may not have changed preferentially in the HRT group, as only three tics had been tackled. This may not have had a significant impact on overall tic count in children presenting with many different tics. Future larger studies should address this in the analysis in order to identify the aspects of tics which HRT addresses best and how these specific changes relate to QoL outcomes.

The question remains why the psycho-education group appears to have led to a significant reduction in tic frequency on the observation measure. It is possible that the psycho-education group impacted on secondary factors which in turn impacted on the tics. Normalising processes and social support may, for example, have led to reduced anxiety and stress. While the present study does not conclusively demonstrate this, it does suggest avenues for further research, discussed below. The lack of a control group in this study means that it is impossible to discount possible alternative explanations for this finding. For example, at the second assessment the children may have been more relaxed as they were meeting the researcher for the second time, leading to reduced tic expression.

In summary, tic severity outcomes in the current study varied according to the measure used. Phonic tics showed no improvement, possibly reflecting the tic choices of the children involved in the intervention, whereas motor tics were found to show preferential but limited improvement in the HRT as compared to the psycho-educational group. Effects were smaller than those found for individual therapy. In contrast, tic frequency on a direct observation measure did not differ between the groups but was significantly reduced in both groups. These contrasting findings suggest that different tic characteristics respond differently to the two interventions.

Hypothesis 2. *Participants in both HRT and psycho-education groups will show significant post-treatment improvements in QoL.*

The GTS-QoL scale total score was the main measure of QoL used and results were somewhat equivocal. In the main intention-to-treat (ITT) analysis, no significant effects were found. The tendency in the mean change scores was in the expected direction, showing improvements in QoL scores of about 12.6% across the two groups but no indication of an interaction between groups. The main effect of time was on the cusp of significance ($p = .05$) with a large effect size (Cohen's $d = 1.14$). This suggests that limited power may have caused Type II error in this case. An effect may in fact exist that was not detectable in this size sample. How to evaluate clinically meaningful changes on QoL measures is a matter of debate. However, effect sizes are considered an adequate estimation where measures do not provide more formal benchmarks (Samsa et al., 1999).

The suggestion that there may be an underlying effect which is not quite detectable in the main analysis is supported by the results of secondary analyses conducted. Using only those participants who adhered to the full protocol by

attending a minimum of six sessions, this effect was significant, which may suggest that the dose of the intervention is important and that those who did not attend sufficient sessions did not benefit significantly. Similarly, the effect was significant when participants who had either experienced stressful life events during the study or had received concurrent therapy were excluded. Children who had experienced significant stressful life events during the study might not be expected to show improved QoL across time points, regardless of the usefulness of the intervention. Their inclusion may, therefore, have obscured a true underlying effect. It is more difficult to understand why children who received concurrent therapy would show less improvement across time points. One possible explanation is that families who sought additional support during the intervention may have been experiencing greater or additional difficulties compared those that did not and arguably this may have limited their ability to benefit from the intervention. Alternatively, participation in two parallel interventions may have been too much for them, making it difficult for them to adequately engage with homework and strategies from both.

Multiple additional analyses were conducted, secondary to the main analysis, so multiple testing should be considered here, as this increases risk of Type I error. While this is possible, it seems unlikely given the consistency of results across the various secondary analyses. Application of a Bonferroni correction to the eight variations of the main effect of time examined would result in most of these variations no longer reaching significance.

One effect which does remain significant even after application of the conservative Bonferroni correction was the effect in the November-January group. Comparison of children who attended the groups in September-October with those who attended in November-January revealed a large difference in response on the

GTS-QoL scale total score. At both time points, one HRT group and one psycho-education group was run. Children in the November-January groups showed a much greater response with a large effect size (Cohen's $d = 1.65$; $p = .006$) while those in the September-October groups showed a negligible effect. Considering the smaller sample sizes as compared to the total sample (September, $n = 16$; November, $n = 17$), the significance of the effect in the November groups is particularly striking. Several possible explanations for this difference are suggested. Several parents commented during the summer assessments that their child had shown fewer tics and been more relaxed during the summer. The most likely explanation appears to be that return to school for the children in the September groups was significantly stressful and has obscured the effect of the group demonstrated in the November-January sample. It is possible that return to school did not impact on the children's QoL directly but rather on their ability to benefit from the intervention. Return to school may demand a great deal from children in terms of adaptation to new expectations, new teachers, new children and, where there has been a change of school, a new environment. The move to secondary school, in particular, places demands on children's executive function as they adjust to taking more responsibility for personal organisation and managing new timetables as well as responding to additional academic and social demands. This may have limited the additional cognitive capacity for learning new skills required for successful application of the intervention or it may simply have reduced their motivation at a time when other things felt a priority for children and families.

An alternative explanation for the difference between results for children attending in September-October and those attending in November-January might be that the second round of groups had a three week gap over the Christmas holidays which did not happen in the first treatment trial. It is possible that this allowed the

children additional time to practice and consolidate strategies taught in the groups, resulting in additional benefit. This would be consistent with previous findings that improvements in QoL increase over time (Woods et al., 2011). It will be interesting to compare these results to those obtained when the same children are followed up one year later. By that stage, it is unlikely that such a small initial difference will still be important. A possible counterargument is that, if this were the case, a similar difference might have been expected on the tic measures but this was not found.

A third possible explanation for this difference is that delivery of both interventions was more effective the second time. It is conceivable that the clinicians' increased familiarity with the protocol or experience in delivering the groups, meant the interventions were delivered more effectively the second time. This explanation seems relatively unlikely, given that Dr Murphy, who has many years' experience, led both groups and that variations of the psycho-education group and individual HRT have been run at Great Ormond Street Hospital (GOSH) for some years.

Unlike the GTS-QoL total score, findings for the visual-analogue life satisfaction scale showed no suggestion of change in either group. Although the findings of the main analyses were non-significant in both cases, they were much more clearly non-significant on the satisfaction scale, with negligible changes across groups. While one measure looks at a range of areas likely to impact QoL in children with TS, the satisfaction questionnaire simply asks them to report their overall satisfaction with life. Perhaps, as might be expected, the interventions impact on aspects of QoL directly linked to TS and, as their TS is only one aspect of their lives, this may not impact on the children's perception of their overall life satisfaction. It has been suggested that, while single point measures show broad reliability (de Boer et

al., 2004)**,** they may not be a suitable means of reflecting changes in more complex constructs (Loo, 2002).

In summary, these analyses do not provide conclusive results regarding the effects of the interventions on QoL. Preliminary results of secondary analyses suggest that both interventions may have led to improvements in QoL but this was not supported by the main ITT analysis. This requires exploration using larger samples. If such a finding were supported, this would be consistent with the hypothesis and with previous research (Woods et al., 2011) showing no difference between HRT and psychosocial support immediately following treatment. That study did show greater improvement in the HRT group over time, suggesting that consolidation of strategies learnt might have led to secondary improvements in other areas and consequent improvements in QoL. It will be interesting to track the progress of the children in the current study to see if similar effects are found.

Hypothesis 3. *A reduction in the premonitory urge (PU) will be a better predictor of post-treatment improvement in QoL than reduction in tics.*

The results here were inconclusive. The main analysis showed that neither variable contributed significantly to explaining changes in QoL scores. However secondary analyses removing data from participants who had experienced changes to their medication during the study led to significant effects. In this analysis, the addition of the two predictor variables led to a 24% increase in variance explained with PUTs total score contributing significantly to this increase, while tic severity did not. These results would appear to support the hypothesis. It is possible that medication changes affected QoL scores much more powerfully than other factors, masking an underlying effect in the main analysis. The limited sample size makes it

difficult to draw firm conclusions about this and further research with participants whose medication remains unchanged is needed to answer this question. Given that three secondary analyses were completed here, the possibility of Type I error should be considered. Application of a Bonferonni correction in this case would render this effect non-significant.

As the data used in this analysis is correlational, conclusions regarding cause and effect would not have been possible even had the findings been less equivocal. However, their longitudinal nature means that they would provide insights into the mechanism by which HRT might achieve change in QoL. If confirmed, this finding would lend support to the notion that the PU plays a key role in the impact of TS on QoL and that reducing its impact through habituation as part of behavioural therapy is key to improving QoL.

Hypothesis 4. *Post-treatment improvements in QoL will be predicted by participants' lower inattention, hyperactivity and impulsivity symptoms.*

No evidence was found to support this hypothesis in the current sample. Given the small sample size, it remains possible that there was simply insufficient power to detect such an effect and so no firm conclusions can be drawn. The non-significant result should be interpreted with caution and additional research with larger samples is required to fully answer the question of whether ADHD symptoms affect treatment outcomes. Research on individual therapy demonstrates an effect of ADHD symptoms on treatment response (McGuire et al., 2014) so a similar finding might be expected here.

4.2 Strengths

The current study has several important strengths. Firstly, the randomisation process means that we can draw stronger conclusions in comparison to observational studies regarding cause and effect. Secondly, the fact that the researchers were blind to treatment allocation strengthens the quality of the evidence by reducing potential sources of bias, particularly when there is a degree of subjectivity to the assessment measures, as was the case with tic counting and coding of the YGTSS scale. Thirdly, only four children were lost to follow-up, which is a small proportion of the total (12%). Finally, the evidence is strengthened by use of an ITT analysis as a primary analysis. These are all important factors contributing to the quality of empirical data (Guyatt et al., 2008).

An additional strength in the current study was the range of outcome measures used. A recent study by Espil, Capriotti, Conelea and Woods (2014) examined the contribution of various aspects of tics and comorbid symptoms to psychosocial impairment in family relationships, at school and socially. They found, in combination with symptoms of comorbid anxiety, that tic intensity, as opposed to tic frequency, was the best predictor of functional impairment. Many studies have used tic frequency as the main measure of treatment outcome but this finding suggests tic intensity may be more relevant a target for interventions. In this study both clinical interview and direct observation measures of tic severity were included, capturing different tic characteristics.

QoL measures were also used, which are not routinely included in assessment of treatment efficacy in TS but which are key to knowing whether interventions have actually made a difference to children's lives from their own perspective. In addition,

the study used a disease specific measure of Health Related QoL, which allows focus on areas of specific relevance to children with TS.

Many children in the study had received previous therapy and medication which reflects the reality of referrals to clinical services. This improves the ecologically validity of the study, reflecting the experiences of the range of children referred to the clinic.

It was felt important to have consistency between the groups in terms of having the same person leading both interventions, as clinician characteristics might otherwise have provided an alternative explanation for findings. Dr Murphy ran both children's groups and is also the principal investigator in the current study. Had only one group been hypothesised to show improvement this potential conflict of interest might have introduced greater risk of bias, but this was not the case.

4.3 Limitations

In addition to its strengths, this study has several important limitations.

Design factors. Firstly, the sample was relatively small and the study was, therefore, underpowered for detecting smaller effects in the main analyses. In particular, power was low for the linear regression analyses meaning risk of Type II error is high and that it is difficult to draw firm conclusions in these cases. Even in cases where significant effects have been identified, the small sample means that confidence intervals around these effects are large. The small sample also limited additional exploratory analyses.

Another consequence of the small sample size was that it may have limited the similarity of the two groups at Time 1. The randomisation process attempts to control for unforeseen confounding variables by evening out group differences. However, the small numbers may limit its effectiveness in achieving this aim. Group differences were explored by comparing the groups on key variables at Time 1. No significant differences were identified but the small sample size and resulting wide confidence intervals around means, result in a lower probability of detecting small group differences.

A second key limitation of the study was the lack of additional control groups. It would have been helpful to include comparison to individual HRT treatment to enable conclusions to be drawn about potential benefits of group based delivery. Secondly, comparison to a waiting list control group would allow conclusions to be drawn with regard to the main effects of time. The lack of such a control means we cannot rule out alternative explanations of results, such as children's tics improving because of reduced anxiety at Time 2 assessment or due to the natural history. Tics are known to show short-term fluctuations and a worsening and then improving pattern over the years with a peak at age 11. We cannot rule out the possibility that tics simply showed improvement over time. Given that some children's tics might wax whilst others' might wane during the study, this is likely to be controlled for across the sample. It is arguable that improvements may simply reflect natural improvements shown in tics over the years. The short timescale of the study compared to the children's development means such a change is unlikely. In addition, as the mean age of the study sample falls at the known average peak of symptom severity, we would expect half the children's symptoms to be broadly getting worse and half to

be broadly improving, providing a natural control for this effect. A future study with a waiting list control group would be able to rule out this possibility.

A key strength of the study was the blinding of the researchers. However, some unblinding occurred in the HRT group, opening the possibility of experimenter bias. In addition, children, families and clinicians were not blinded to condition allocation.

The generalisibility of the current findings is limited to those children included in the sample. The findings cannot be generalised to those excluded from participation, such as children with lower IQs. Recruitment from a single clinic may also limit generalisability. A large number of families declined participation on the basis that it was too difficult or costly to travel to GOSH each week to attend the intervention, so the sample may have overly represented those with greater economic resources or practical support to facilitate attendance.

There was a small amount of overlap in group content between conditions. Both interventions involved relaxation training and a reward system to encourage utilisation of strategies both in sessions and at home. In addition, the groups were similarly structured and offered the chance to meet with other individuals experiencing similar difficulties. Where improvements have been found in both groups there are, therefore, a range of possible aspects which may have been responsible for this and the current study does not provide data on which elements were most useful.

Measures and assessment protocols. Due to time constraints, it was impossible to run a pilot assessment in order to assess the feasibility of the complete assessment protocol for the study. Had there been time, this would have been

desirable prior to commencement of the study itself. Given that this project is a pilot for larger future studies, there are a number of limitations in the measures used that may be corrected for.

The direct tic count measure was not found to have high inter-rater reliability, probably because of difficulties in clearly defining what constitutes a single tic, particularly when children display complex tics or repetitive actions in quick succession. The clinicians who counted the tics were relatively inexperienced in working with children with TS. It is possible that rating by more experienced clinicians might have improved reliability.

A second limitation of this measure was that only the children's head and upper body were visible on recordings so tics involving the legs, feet or stomach were not coded. In addition, although the videos did have sound, quiet vocal tics were not easily detectable. These factors clearly limit the ability of the measure to detect all aspects of change in tic frequency. However, only one child in the HRT group chose to tackle a lower body tic, suggesting that tics may be less common or troubling in those areas.

A third limitation of this method was that the videos shown at Time 1 and Time 2 were different. Although efforts were made to ensure that they contained similar content, a future study would benefit from counterbalancing the videos between time points.

The tic observation measure also has the inherent limitation that tics wax and wane and are frequently suppressed dependent on environmental factors. As a result of the inevitably short time over which they are recorded the score may not be an accurate reflection of their tics as a whole. Generalisability to other contexts may therefore be limited.

The percentage of videos double scored for inter-rater reliability coding of the YGTSS scores and tic counting was consistent with previous studies (Piacentini et al., 2010). However, given the small sample size, the actual number of videos double coded was relatively small and confidence intervals on the reliability estimates consequently large, resulting in low precision.

The GTS-QoL scale questionnaire has yet to be validated in English speaking populations and the PUTs scale has been shown to be less reliable for use with children under 11 (Woods et al., 2005) so findings should be considered in that context. Nonetheless, both measures showed acceptable internal consistency within the current sample providing preliminary evidence of reliability.

At Time 2 families were asked about stressful life events that had taken place since the initial evaluation. Arguably this method was not sufficiently systematic. It may have been preferable to ask about a range of specific pre-defined events which may have happened, in addition to a more open question, in order to increase consistency in events reported. It would also have been desirable to collect systematic data on possible harms that were caused by the intervention following CONSORT guidance (Ioannidis et al., 2004).

The assessment protocols at Time 1 and Time 2 were slightly different because of the difference in measures completed on each occasion. In addition, the children knew the researchers on the second occasion but not on the first. These factors may have affected results systematically between time points.

Four children were assessed in the clinic at Time 1 but none were followed up in the clinic as all subsequent assessments were conducted at weekends. The nature of assessments conducted in the clinic may have been different but this is unlikely to

have affected the group differences as two children from each intervention group were assessed in the clinic at Time 1.

4.4 Clinical Implications

The study had low attrition and good attendance rates, suggesting acceptability of the group interventions to the families involved. The observation that both the HRT and psycho-education groups tended to run over time suggests that either the session time should be extended or the protocols should be slightly modified to ensure they run to time.

Importantly, tics were not found to worsen on any measure following the intervention. This can provide reassurance to families who might be concerned about tic worsening following exposure to other children with tics (Woods et al., 2010). This not only has implications for involvement in group based interventions but also for involvement in support groups and other potentially beneficial contexts in which children with TS might have the opportunity to meet others with similar difficulties.

Although high attendance and retention suggests the interventions themselves were acceptable to families who did attend, the large numbers who chose not to participate suggests that aspects of the service delivery were unacceptable to many families. Many families declined participation on the basis that it was too difficult or costly to attend weekly sessions at GOSH. While this would likely apply to individual sessions as well, it may be more relevant for group treatment, which cannot be arranged flexibly to suit individual families' circumstances. This is relevant for service delivery, suggesting that locally based groups are likely to be more acceptable

and that provision of support to enable attendance may be important in facilitating access, whether in terms of funding travel costs or providing child care for siblings.

It is worth considering the possibility that group based interventions have a slightly slower or weaker effect compared to individually administered interventions. It would be interesting to discover whether, by increasing the number of group sessions, effects could match those found for individual therapy. If so, use of such groups may still be more cost-effective than individual treatments.

The finding that QoL did not increase for children who returned to school between Time 1 and Time 2 assessments has important clinical implications. It probably reflects the significant challenges children face at school and the degree of stress school may cause them, particularly at transitions. This is not a new revelation (Akos & Galassi, 2004; Pellegrini & Long, 2002) but the particular challenges faced by children with TS at these important stages may be a key area for future research. The school experience in general, transitions to new schools, or both may impact heavily on the QoL of children with TS, or on their ability to benefit from psychological interventions.

It would be important that clinicians delivering groups were aware of these additional stressors when delivering groups. It may be that the timing of such interventions in relation to the school year is important for children to benefit maximally. Timing in relation to the child's developmental stage may also be an important factor. Perhaps aiming to deliver the intervention at a time when children are facing minimal additional developmental challenges would allow them to devote more energy to the intervention itself.

Timing interventions according to the school year may not always be practical. If school or school transitions are found to impact on the QoL of children with TS to a

greater extent than it may affect other children, then additional thought should be given to how best to support children in school or when making transitions. This could help of itself and by enabling children to better access concurrent interventions. Perhaps a component could be added to the group or parent sessions covering psycho-education and coping strategies in relation to transitions. Liaison with school would clearly be important in order to support schools in meeting children's needs at this time. It would be interesting to investigate further the elements of school which are most difficult for children and then to target interventions at these specific areas, such as through school-based psycho-educational interventions (Nussey et al., 2014).

In the November groups, improvements were seen both in children receiving HRT and those receiving psycho-education on both direct tic frequency and QoL measures. In the absence of a waiting list control group, these findings are somewhat tentative but they suggest both interventions led to benefits. Given the contrasting content of the interventions, it is interesting to consider what the mechanisms of change were. Although our data do not allow us to draw conclusions about this, we can speculate. Change may have been caused by an element common to both interventions, such as the social support gained from group therapy. It may also have been that differing elements of each intervention produced the same result via different mechanisms, such as via habituation to the PU in the HRT group and via reductions in stigma and improved coping skills in the psycho-education group. A fuller understanding of these mechanisms would potentially allow for the development of an intervention which combines the most beneficial aspects of both groups.

If confirmed by future research, the possible finding that improvements in QoL following intervention were predicted by reductions in the PU would have

clinical implications. The finding would be consistent with the negative reinforcement hypothesis of TS showing a relationship between reductions in the PU to QoL following treatment. This would suggest that the PU is a key variable for clinicians to assess and that interventions should be designed to reduce PU. However, even if confirmed as significant, the relationship is not strong, explaining a maximum of 50% of the variance in improvements in QoL. This suggests that there are other important factors that contribute to improvements in QoL following treatment which would also need to be considered.

Further research is needed to fully determine whether therapy groups are beneficial for children with TS and avenues for such research are discussed below. In the longer term, demonstrating the effectiveness of group therapy for TS would have the potential to increase the number of treatment options available to families, increase the cost-effectiveness of interventions delivered and reduce waiting times for therapy. This could, in turn, mean that interventions could be delivered sooner and more flexibly, to be offered to children at the time when they can benefit maximally.

4.5 Ideas for Future Research

The current study is the first to have systematically evaluated group therapies for TS. Despite its limitations, the study provides sufficient evidence to suggest this area would be worthy of further research. One element of this will be the planned follow-up of the current sample one year on, to assess whether changes increase or decrease over time. Further analyses could also be conducted using the current data to examine the impact of the interventions on individual subscales of the GTS-QoL measure and

on various tic characteristics separately, such as tic intensity, frequency and complexity.

As this project has been designed as a pilot for a future larger scale study, suggestions have been made for improvements to the methodology. Future studies may benefit from including additional group sessions to see if this strengthens effects. A major increase in sample size will also be important. Inclusion of additional control groups, specifically waiting list and individual treatment groups, would allow conclusions to be drawn about the impact of a group based format. It is possible that group based delivery contributes to additional benefits such as normalising the condition for children who may never have met another child with TS. It may also provide a context for families to develop a network of support. Although we have not been able to assess such effects directly in the current study. it would be worthy of further investigation in a study with an individual therapy control group using measure addressing factors such as degree of perceived support, self-stigma and self-esteem.

Although attendance at the groups was high, there were some families who did not attend or dropped out of the intervention. Further research would benefit from assessing the characteristics of those who adhere to the protocol and attend against those who do not, in order to consider possible reasons for non-attendance and potential means of supporting attendance. Similarly, this study has not addressed the issue of degree of response to therapy in different children. Given the huge variability in presentation of TS, its comorbidities and the challenges it presents for treatment, further investigation of predictors of response would be warranted in order to better target interventions. In a larger study it would be important to consider characteristics which may influence children's response to treatment by comparing those who show

benefit to those who do not. This would aid future research addressing how best to support those children who do not appear to benefit from this type of intervention. Detailed assessment of a wider range of possible comorbidities would allow this to be conducted systematically. The current study did not include measures of anxiety or autistic spectrum traits, for example, which are both relatively common comorbidities in TS.

An important variable which has not been addressed in this study is the role of age on treatment response. Given reported differences in the nature of the PU in younger children (Banaschewski et al., 2003; Leckman et al., 1993; Woods et al., 2005), it is possible that they may respond differently or benefit from a slightly different approach in therapy. Future studies with larger samples would be able to address this issue more systematically.

In relation to identifying the children most likely to benefit, future larger studies may be able to expand the inclusion criteria for the study. This would enable investigation of whether findings are generalisable to children not included in the current sample, such as those with lower IQ.

A future qualitative study would also be a valuable contribution to the literature. This could look at parents' and children's experiences of the groups in more detail. This would provide a fuller understanding of what they felt to be useful or otherwise. This could also pave the way for more detailed research into which components of the intervention are the most helpful. Past research has not unequivocally determined which elements of HRT result in most benefit. This is also true of the current psycho-educational intervention. Some components might be more or less useful and could therefore be increased or left out in order to maximise treatment response. For example, as relaxation training his limited support as an individual component

(Bergin et al., 1998), it is possible that this does not contribute helpfully to the overall intervention. Further investigation of which components produce most change would be important in maximising benefits to children. An extension of this would be to examine whether, as suggested by O'Connor et al. (1997), additional benefits could be achieved with the addition of cognitive components to the intervention. Such research would allow examination of the outcomes which are most impacted by different components of the intervention, such as whether the use of competing responses differentially impacts the number of distinct tics and their intensity, rather than the overall frequency of all tics and whether these factors change over time.

Another area worth considering is the impact different interventions may have on children's understanding of their disorder and its causes. The two interventions potentially gave children a different message about the nature of the problem and the appropriate means of tackling it. HRT has been shown to be effective in reducing tics and improving broad measures of QoL in children with TS when delivered individually. This study has provided tentative support for its use in a group based format. There may be a difference between the groups in relation to the degree to which they position the "problem" within the child or external to the child. While both interventions are designed to externalise the difficulty as much as possible, the HRT intervention, by definition, places responsibility for controlling tics largely with the child themselves, whereas the psycho-education intervention arguably considers both aspects over which the child is responsible, such as anger outbursts, but also comprehension of things for which they are not responsible, such as bullying. It may be interesting and important to assess children's perspective on the nature of TS as a difficulty and the degree to which they assign themselves the responsibility for this. Depending on results, it may be that any danger that the HRT intervention may not

sufficiently externalise the difficulty can be mitigated, for example by combining elements of an HRT intervention with elements of a psycho-education intervention which more explicitly externalise difficulties experienced.

Finally, it would be interesting to compare QoL scores for children before and after the return to school when not attending an intervention group. A similar study including a waiting list control group would allow for such comparisons. It would also be interesting to investigate whether the impact of return to school on QoL is similar in children with TS compared to their peers without the condition, as it might be expected that such transitions are especially stressful for children with TS. For example, it would be valuable to explore in more detail the challenges faced by children with TS at school and the nature of the particular challenges faced at transition to secondary school. This may then inform development of appropriate interventions.

4.6 Summary

The present study was a randomised controlled pilot study and is the first to have investigated the feasibility and preliminary efficacy of HRT and psycho-educational groups for children aged 9 to13 years with TS. The groups were evaluated in terms of their ability to reduce tic severity and improve QoL.

Good attendance rates in both groups suggests feasibility and acceptability of the interventions to the families involved. Given the small sample size of the current study, findings with regards to efficacy are highly tentative. Tendencies in the results suggest limited improvements in tic severity and QoL in both groups studied, although perhaps to a lesser extent when compared to previous studies of individual

therapy. There was a suggestion that motor tic severity showed greater reduction in the HRT group on the main outcome measure but this finding was not supported by a measure of direct tic count.

Given the potential for such groups to provide additional treatment options for families, further research in this area is warranted. Suggestions for improvements to the current design for a larger study are outlined as well as indications for wider reaching future research.

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24 May 2013

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Dear Dr Murphy

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**
IRAS project ID:	**126154**

Thank you for your letter of 12 May 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mr Thomas McQuillan, thomas.mcquillan@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. We will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Please ensure you do not put in your mobile number as a contact number, but hospital land lines.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		12 May 2013
GP/Consultant Information Sheets	1	12 February 2013
Investigator CV		
Letter of invitation to participant	2	12 February 2013
Other: CV: Katie Edwards		
Other: CV: Rachel Yates		
Other: CV: Dr John King		
Other: CV: Dr Michael Evangeli		
Other: Letter from Amy Brown re Statistical Review		15 January 2013
Other: Approval Letter		20 December 2013
Other: Comments from Dr John King		16 January 2013
Other: Letter re Funding from Tourettes Action		21 February 2013
Other: Review Letter from UCL		26 February 2013
Other: GOSH Lone Worker Policy		12 June 2012
Participant Consent Form: Parents/Guardians	3	04 May 2013
Participant Consent Form: Child Assent	2	04 May 2013
Participant Information Sheet: Parents and Carers	3	04 May 2013
Participant Information Sheet: Child and Young People	3	10 May 2013
Protocol	2	05 March 2013
Questionnaire: YGTSS		01 January 1999
Questionnaire: P-ChOCI: Part 1 (Parent)		
Questionnaire: ChOCI: Part 1 (Young Person)		
Questionnaire: SNAP - IV 26 Teacher & Parent Rating Scale		
Questionnaire: Premonitory Urge for Tics Scale (Child)		
Questionnaire: Strenght & Difficulties Questionnaire		
Questionnaire: PedsQL - Teen Report (13 - 18)		
Questionnaire: PedsQL Child Report (ages 8 -12)		
Questionnaire: Gilles de la Tourette Syndrome _ QoL for patients aged 6 -12 years		
Questionnaire: Gilles de la Tourette Syndrome _ QoL for patients aged 13 - 18 years		
Questionnaire: Tourettes SAyndrome Questionnaire	1	12 March 2013
Questionnaire: Rage Attacks Questionnaire	1	14 March 2013
Questionnaire: Parents Questionnaire for Tourette Group	2	13 March 2013
Questionnaire: Young Person's Questionnaire for Tourette Group	2	13 March 2013
REC application	126154/4263 04/1/996	13 March 2013
Referees or other scientific critique report		20 December 2012
Response to Request for Further Information		12 May 2013

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.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/LO/0511	**Please quote this number on all correspondence**

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/

With the Committee's best wishes for the success of this project.

Yours sincerely

pp
Dr Yogi Amin
Chair
Email:NRESCommittee.London-QueenSquare@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Ms Emma Pendleton, Division of Research and Innovation*

NRES Committee London - Queen Square
HRA Head Office
Skipton House
80 London Road
London, SE1 6LH

Telephone: 020 7972 2556

28 May 2013

Dr Tara Murphy
Consultant Clinical Psychologist and Paediatric Neuropsychologist
Great Ormond Street Hospital for Children
Department of Paediatric Neuropsychology
Great Ormond Street, London
WC1N 3JH

Dear Dr Murphy

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**
IRAS project ID:	**126154**

Thank you for your e-mail of 28th May. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 24 May 2013

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Other: E-mail Clarification for Requested Changes		28 May 2013

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering Letter		12 May 2013
GP/Consultant Information Sheets	1	12 February 2013
Investigator CV		
Letter of invitation to participant	2	12 February 2013

Other: CV: Katie Edwards		
Other: CV: Rachel Yates		
Other: CV: Dr John King		
Other: CV: Dr Michael Evangeli		
Other: Letter from Amy Brown re Statistical Review		15 January 2013
Other: Approval Letter		20 December 2013
Other: Comments from Dr John King		16 January 2013
Other: Letter re Funding from Tourettes Action		21 February 2013
Other: Review Letter from UCL		26 February 2013
Other: GOSH Lone Worker Policy		12 June 2012
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Participant Consent Form: Child Assent	2	04 May 2013
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Protocol	2	05 March 2013
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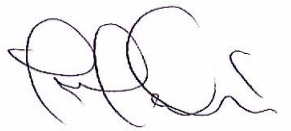
Questionnaire: SNAP - IV 26 Teacher & Parent Rating Scale		
Questionnaire: Premonitory Urge for Tics Scale (Child)		
Questionnaire: Strength & Difficulties Questionnaire		
Questionnaire: PedsQL - Teen Report (13 - 18)		
Questionnaire: PedsQL Child Report (ages 8 -12)		
Questionnaire: Gilles de la Tourette Syndrome _ QoL for patients aged 6 -12 years		
Questionnaire: Gilles de la Tourette Syndrome _ QoL for patients aged 13 - 18 years		
Questionnaire: Tourette's Syndrome Questionnaire	1	12 March 2013
Questionnaire: Rage Attacks Questionnaire	1	14 March 2013
Questionnaire: Parents Questionnaire for Tourette Group	2	13 March 2013
Questionnaire: Young Person's Questionnaire for Tourette Group	2	13 March 2013
REC application	126154/4263 04/1/996	13 March 2013
Referees or other scientific critique report		20 December 2012
Response to Request for Further Information		12 May 2013

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

13/LO/0511 Please quote this number on all correspondence

Yours sincerely



Mr Thomas McQuillan
Assistant Committee Co-ordinator
E-mail: NRESComittee.London-QueenSquare@nhs.net

Copy to: Ms Emma Pendleton, Division of Research and Innovation

Appendix B – Invitation Letter

Great Ormond Street Hospital for Children
NHS Foundation Trust

[Name]
[Address]

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

[Date]

Dear [Name],

I am writing to invite you and your child to participate in a study which my colleagues and I are carrying out at Great Ormond Street Hospital. We are contacting you because your child has been seen at our clinic in relation to their Tourette Syndrome or chronic tic disorder.

Please find enclosed an information sheet explaining the study. It outlines our reasons for conducting the study and what would be asked of you and your child should you choose to participate. There is also a children's version of the information sheet included which you can discuss with your child should you wish.

If you and your child are interested in taking part, or would like to know more, please contact one of my colleagues (Katie Edwards, University College London, tel: 07783644123, or Rachel Yates, Royal Holloway University of London, tel: 07513791931). Further details are provided on the information sheets attached.

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

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

Yours sincerely,

Dr Tara Murphy
Consultant Clinical Psychologist
Great Ormond Street Hospital for Children

Appendix C – Parent Information Sheet

Great Ormond Street Hospital for Children
NHS Foundation Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Information about the project

Project title: Randomised pilot study evaluating two group therapies for Tourette Syndrome

We work at the Tourette syndrome Clinic at Great Ormond Street Hospital (GOSH). We would like to invite you and your child to take part in a research study. Before you decide if you would like to take part, it is important for you to understand why the 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. This would involve attending group therapy as well as completing assessments before and after so that we can evaluate whether the group has been effective.

What is the purpose of the study?

This study is interested in 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.

Currently, treatments are usually delivered individually to each child. This study aims to investigate whether delivering therapies to groups of children could be equally, or more, effective. It is possible the children will benefit from the chance to meet other children experiencing similar difficulties to their own. In the long run, if such treatments are shown to be effective, it could increase the number of treatment options available to families and potentially also reduce waiting times for therapy.

Why have my child and I been asked to help?

We are asking children, aged 9-13 years, who have been seen previously at GOSH or who have recently been referred to the clinic, if they are interested in participating.

Do I have to take part?

No. Taking part in this study is entirely voluntary. If you decide not to take part in this study, 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, even if your child has started attending the group.

Group sessions

To participate in the group based psychological therapy it will be necessary for your child to attend the clinic at GOSH for 8 weekly sessions. These will run either from September to October or November to December 2013. The groups will run from 4:30pm on a week night. The first two sessions will be 90 minutes long and subsequent sessions will last for an hour.

The groups will be a chance for your child to make friends, meet other children with a tic disorder and learn about how others cope with their symptoms. In the groups the children will participate in various games and puzzles and in the final session there will be a party.

The exact content of the group will depend on the group your child is assigned to (see below). One set of groups will be based on Habit Reversal Therapy, in which your child would be taught particular techniques aimed at helping control their tics. The second set of groups will focus on learning about topics such as school and bullying, self-esteem and dealing with difficulties in relation to anger, attention and impulsivity.

Following each session, your child will be set a small 'homework' task. This will be something to practice or do with your child during the week.

During sessions number three to six, parents and carers will also be invited to attend a 4-session parent group which will run at the same time as your child's group. This will include learning about Tourette syndrome and developing strategies to help your child cope with their tics. These sessions are intended to complement the work that your child will be doing in their group.

In which group would my child participate?

As the study will compare two group based therapies using different theoretical approaches, children will participate in either one program or the other. No scientific research has previously investigated the effectiveness of either group and therefore we do not know which may be more beneficial. In order to make it a fair test we need to allocate children to the groups randomly. Therefore, once you decide to take part in the study we would enter your child's participant number into a computer programme, which would randomly assign them to one of the two groups. We would then let you know which group had been assigned and provide you with more information about the days when the group will take place.

Apart from attending the groups, what else will my child and I be asked to do if we take part?

We would initially send you some questionnaires for you, the parents or guardians, to complete at home. We would then telephone you to arrange an initial assessment. We could visit you at home or meet at GOSH depending on which is most convenient for you.

During the first visit, we would complete some puzzles, tasks and questionnaires with your child and expect that these would take about 2 hours and 50 minutes, including rest breaks. During this time, they 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.

Following this initial assessment, your child would be invited to participate in a group therapy program at GOSH. On completion of the group, we would arrange two further assessments to assess any change that may have occurred. These visits would be expected to last about 1 ½ hours, again including rest breaks. The first would take place within a month of finishing the group and the second 1 year later. We would also ask you as parents and carers to complete some additional questionnaires prior to each of these assessments.

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

There are no specific risks from taking part in the study as your child's treatment will not be changed by participating the study in any way. 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.

Will my child's tics increase?

It is possible you may be concerned about your child being exposed to other children with different tics in case your child's tics become worse or they adopt new tics. While this is possible in the short-term, clinical experience has tended to show that this is not a lasting

effect. Nonetheless, should you have any concerns at all during the study you should discuss these with us and you would be entirely free to withdraw from the study at any time should you wish.

Will taking part help my child?
These particular groups have never been tested for children with tic disorders and therefore we do not know whether your child will experience any benefit from their participation. The groups have been designed, based on what is currently known, to help children with chronic tic disorders. We therefore hope that your child might experience some benefit in some areas such as their quality of life or the intensity of their tics.

How will the information help people?
When the study has finished we will write to you to let you know what we found out about the groups. We hope this study will help us find out if 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 Great Ormond Street Hospital, they would continue to be seen as a patient here throughout the study. Any school liaison work, or medication, would continue as normal and be unaffected by participation. If you choose to take part, the only difference would be that your child would not be able to participate in any individual therapy during the study. If your child has been offered this, and you would prefer this to a group based intervention, it would be best not to participate in this study. Should it be felt during the course of the study that your child may benefit from individual therapy, you would be able to withdraw from the study and receive this treatment as appropriate.

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 study.

What will happen to the results of the study?
The results will not be known until the last groups are run and the data is collected for everyone taking part in the study. We hope to complete the short-term outcome of taking part in the groups by early 2014. Following this, we would hope to meet again one year later in order to see whether any effects of the groups are maintained. 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. This research has also been reviewed and approved by ethics committees at Royal Holloway, University of London and University College London. The research is being sponsored by Great Ormond Street Hospital.

Who is funding the research?
Funding for the study has been provided from three sources. These are Royal Holloway, 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 Great Ormond Street Hospital (You can ring them on 020 7829 7862 or email them on pals@gosh.nhs.uk).

What do I do now?
Thank you for reading this information. If you and your child are interested in taking part in this study, please contact Rachel Yates (Tel: 07513791931) or Katie Edwards (Tel: 07783644123) to hear more. If we do not hear from you, we will contact you by phone in about two weeks 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: Katie Edwards, Trainee Clinical Psychologist
Rachel Yates, Trainee Clinical Psychologist

Address: TS Group Study
Dept of Child and Adolescent Mental Health
Level 4, Frontage Building
Great Ormond Street Hospital
Great Ormond Street
London
WC1N 3JH

Email: katie.edwards@ucl.ac.uk
rachel.yates.2011@live.rhul.ac.uk

Tel: Katie Edwards: 07783644123
Rachel Yates: 07513791931

Supervised by: Dr Tara Murphy, Consultant Clinical Psychologist, Great Ormond Street Hospital for Children (Tel: 0207 8298679)

Contact details for London Queen Square Research Ethics Committee:
HRA Head Office, Skipton House, 80 London Road, London, SE1 6LH
Telephone: 020 7972 2584

Great Ormond Street Hospital for Children
NHS Foundation Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Information about the project

Project title: Randomised pilot study evaluating two group therapies for Tourette Syndrome

We work at Great Ormond Street Hospital. We are asking you and your parents to take part in a project. This leaflet will tell you about the project. 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 help with difficulties experienced by children with tic disorders. The treatments involve weekly sessions at the hospital with psychologists (talking doctors) along with a group of other children who also have tic disorders similar to you. During 8 sessions, the psychologists will help teach you all some things you can do to manage your challenges. We would like to find out if coming to these groups helps you in your life or makes your difficulties easier to cope with.

Why have I been asked to take part?

We are asking all children who have visited Great Ormond Street Hospital for help with a tic disorder to take part in the study.

Do I have to take part?

No, you do not have to take part. If you decide not to take part in this 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 or if you have already started attending the groups.

Will taking part help me?

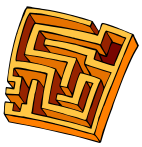
We don't know for sure if the groups will help you. We hope that it will help you to cope with some aspects of your tic disorder. We will evaluate whether it has helped you to reduce your tics or whether it has helped you in other areas such as your satisfaction with your life in general or your ability on certain thinking tasks. Afterwards, we would let you know if the groups helped you in terms of any of the areas we have evaluated.

As an additional reward for taking part, we will enter all children or young people who have attended 6 or more of the group sessions into a prize draw to win £50 of gift vouchers.

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?

Meeting 1



First we would arrange a meeting with you and your parents or carers at home or at Great Ormond Street Hospital. At this meeting:

- One of us would spend about 2 hours 50 minutes with you 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.

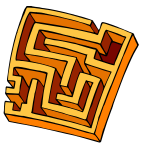
Coming to the groups

If you choose to take part you would come to 8 group therapy sessions at Great Ormond Street Hospital along with a small group of other children or young people with tic disorders. We will invite 12 children to each group. The groups will run in the afternoon, at 4:30pm on one evening a week. The first two sessions will last 1 ½ hours and the rest 1 hour. During each session there will be a variety of things to do and we hope you will find them interesting.

In each session we will also give you a small 'homework' task of something to do or practice at home with the help of your parent or carer.

During some of the sessions we will also invite your parent or carer to come to their own group to learn something about what you have done in the groups and how best to help you keep using the things you learn at home.

Meetings 2 & 3




When you have finished the 8 group sessions we would meet again twice more, either at your home or at the hospital. We would meet a few weeks after the groups and then again 1 year later.

At these visits we would do more games and puzzles and ask you and your parent or carer some more questions. This time the visit would be a bit shorter, probably lasting about 1 ½ hours.

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.
We will make the groups as fun as possible. 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 Great Ormond Street Hospital will not be changed by taking part.

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 will not be known until about September 2014. 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 Katie Edwards or Rachel Yates if you have any other questions.

Contact: Katie Edwards, Trainee Clinical Psychologist
Rachel Yates, Trainee Clinical Psychologist

Address: TS Group Study
Dept of Child and Adolescent Mental Health
Level 4, Frontage Building
Great Ormond Street Hospital
Great Ormond Street
London
WC1N 3JH

Email: katie.edwards@ucl.ac.uk
rachel.yates.2011@live.rhul.ac.uk

Tel: Katie Edwards: 07783644123
Rachel Yates: 07513791931

Supervised by: Dr Tara Murphy, Consultant Clinical Psychologist, Great Ormond Street Hospital for Children

Appendix E – GP Letter

Great Ormond Street Hospital for Children NHS
NHS Foundation Trust

[GP Address]

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

[Date]

Dear Dr [Name],

Patient details:

The above named patient has consented to participate in a research study at Great Ormond Street Hospital, which aims to investigate group work for children with Tourette Syndrome or chronic tic disorders. It is a randomised pilot study to evaluate the efficacy of two treatments: A tic-specific behavioural intervention versus a psycho-educational group.

If you would like any further information on the study, please do not hesitate to contact us (correspondence address: TS Group Study, Dept of Child and Adolescent Mental Health, Level 4, Frontage Building, Great Ormond Street Hospital, Great Ormond Street, London, WC1N 3JH).

Yours sincerely,

Katie Edwards
Trainee Clinical Psychologist

Rachel Yates
Trainee Clinical Psychologist

Supervised by: Dr Tara Murphy, Consultant Clinical Psychologist and Paediatric Neuropsychologist

Appendix F – Randomisation Instructions

Thank you for agreeing to help us with the randomisation process for the Tourette Syndrome Group Study!!

Here are what I hope are some simple instructions on how to carry out the randomisation process.

1. Go to http://qminim.saghaei.net/index.php
2. Login: ########; Password: ########)
3. Go to the subjects tab
4. Click the green plus sign on the left hand side of the screen
5. For each new participant, add their gender and age and then click done. The program will then assign them to either the HRT or the Psych-Ed group.
6. If you add them in order of participant number in the study then the ID number assigned by the program should match our participant number. This may not always be possible, so if they are not matching, then please just keep a track of the numbers assigned by the programme so we know which participant is which.
7. Please do not ever click on the tab at the top that says new, as this will delete the study and we'll need to start from scratch.
8. I have created an Excell spreadsheet called "Randomisation spreadsheet" to help keep track of the group to which each participant has been assigned.

I hope this makes sense. If not, please let me know on [Email address] or [Mobile number] and I will do my best to help.

Best wishes,

Rachel Yates

Trainee Clinical Psychologist

Appendix G – Demographic Information Sheet

Great Ormond Street Hospital for Children NHS Foundation Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

Identification Number_____

Date _____

DEMOGRAPHIC INFORMATION
Parents: Initial telephone conversation

Hi this is name from Great Ormond Street Hospital calling about the Tourette Syndrome Group Study [if appropriate: returning you call]. Is now a good time to talk?

[If returning call] Thank you for contacting me and for your interest in the study. I'm calling today to see if you have any questions about the groups and the study. If you're still interested I'd also like to gather some general demographic information and ask some questions to make sure that your child meets the inclusion criteria to take part, that you would both be available on the necessary days and so on. Is it ok for us to go ahead with that now?

[If first contact from us] I'm calling today to check whether you received the letter and information sheets we sent in the post about our new study, in which we will be running groups for young people with Tourette Syndrome? If no – we can resend. If yes – Were you and your child interested in this? Would you like to ask any questions or like more information? If you are still interested, I'd just like to gather some general demographic information and ask some questions to make sure that your child meets the inclusion criteria to take part, that you would both be available on the necessary days and so on. Is it ok for us to go ahead with that now?

- Received information in the post? Yes No
- Read information sheets?
- Name of person you are speaking to and their relationship to child:
- Parent(s) and child able to attend groups at GOSH from 4.30pm for an hour or 90mins (depending on session) on either Wednesdays or Thursdays?

  Y / N

Child

- Name:
- Age:
- D.O.B:
- Gender:

- Ethnicity:
- What year in school is your child?
- Is English child's first language? Y / N
  - ➔ If not, what is their English ability and what other languages do they speak?
  - ➔ PREVIOUS INPUT: Has your child ever had any counselling, therapy or any other kind of treatment for their tics? *(What? When? Where? How many sessions?)*
  - ➔ CURRENT INPUT: Is your child currently having any counselling, therapy or any other kind of treatment for their tics? *(What? When? Where? How many sessions?)*
- How do you think they would cope with being in a group?

<u>Has your child been diagnosed with:</u>

Tourette's Syndrome □
Chronic Vocal Tic Disorder □
Chronic Motor Tic Disorder □
ASD □
OCD □
ADHD □
Learning Disability □
Other □

<u>List of medications (current):</u> [Name, dose, how long been taking]

Parents/Guardians

- Name (title, first and last names) of other parent/guardian (not spoken to):

- Ethnicity of parents:

- HOLLINGSHEAD SES:

1) Gender of parent(s) in household – [No need to ask if obvious from previous questions]:

Total SES score: ____

Score: ____

2) Marital status *(living together?)*:

Score: ____

3) Parent's/guardian's level of education (both):

Mother:

Father:

Score: ____

4) Parent's/guardian's occupation (both): *Currently working? What?*

Mother:

Father:

Score: ____

- Live in a house/flat? Council-rented? Privately rented/owned?

- Number of other people living in the house:

- Number of brothers/sisters:

Other details

- Contact number(s):
- Best time of day to contact:
- Contact address:
  - ➔ Estimate of travelling time if outside of London:
- Do you have high-speed Wi-Fi at home?

Eligible to take part? Y / N

Child interested in taking part? Y / N

[Check it has been discussed with child – Child info sheet read?]

Parent still interested in taking part? Y / N

[*If no to any, please write down reasons why if known:]*

When would be best to conduct the pre-assessment? (availability)

Re home visit appointment & what will happen next

Is there a quiet space and table available at home that we could use?

Please could they have their internet passwords available on the day?

We'll send them out the questionnaire packs in the post – They can complete them, or hang onto them and do them on the day we come, whichever is more convenient.

We'll pass their details on to the clinical team who will carry out the randomisation. They'll then be in touch about the groups.

Reminder of what will happen re randomisation and that we will not be involved. Therefore we ask them please to not mention when we meet the group to which they have been assigned.

Pre-assessment date arranged?

Thank you very much for speaking with me today. [Confirm meeting date arranged or say "I'll be in contact as soon as possible to arrange a meeting date with you to meet child and conduct the pre-group assessment].

General comments: *(Any concerns? Things for clinicians to keep in mind?)*

Post-Assessment follow-up **Date:**

- Since pre-assessment have there been any changes in medication?
- Since pre-assessment 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 study?
- Ok to possibly be contacted in 1 year for long-term follow-up?

General comments:

Participant ID #: **Appendix G – Demographic Information Sheet**

SNAP-IV 26 – Teacher and Parent Rating Scale

James M. Swanson, Ph.D.

For each item, check the column which best describes this child:	**Not At All**	**Just A Little**	**Quite A Bit**	**Very Much**
1. Often fails to give close attention to details or makes careless mistakes in schoolwork or tasks				
2. Often has difficulty sustaining attention in tasks or play activities				
3. Often does not seem to listen when spoken to directly				
4. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties				
5. Often has difficulty organizing tasks and activities				
6. Often avoids, dislikes, or reluctantly engages in tasks requiring sustained mental effort				
7. Often loses things necessary for activities (e.g., toys, school assignments, pencils, or books)				
8. Often is distracted by extraneous stimuli				
9. Often is forgetful in daily activities				
10. Often has difficulty maintaining alertness, orienting to requests, or executing directions				
11. Often fidgets with hands or feet or squirms in seat				
12. Often leaves seat in classroom or in other situations in which remaining seated is expected				
13. Often runs about or climbs excessively in situations in which it is inappropriate				
14. Often has difficulty playing or engaging in leisure activities quietly				
15. Often is “on the go” or often acts as if “driven by a motor”				
16. Often talks excessively				
17. Often blurts out answers before questions have been completed				
18. Often has difficulty awaiting turn				
19. Often loses temper				
20. Often argues with adults				
21. Often actively defies or refuses adult requests or rules				
22. Often deliberately does things that annoy other people				
23. Often blames others for his or her mistakes or misbehavior				
24. Often touchy or easily annoyed by others				
25. Often is angry and resentful				
26. Often is spiteful or vindictive				

Appendix I – Yale Global Tic Severity Scale Semi-Structured Interview

ID #:

Y G T S S

Yale Global Tic Severity Scale

Yale Child Study Center

October 1992 version

NAME:	TODAY'S DATE : / /
RATER:	

MOTOR TIC SYMPTOM CHECKLIST

Description of Motor Tic Symptoms. Motor tics usually begin in childhood and are characterized by sudden jerks or movements, such as forceful eye blinking or a rapid head jerk to one side or the other. The same tics seem to recur in bouts during the day and are worse during periods of fatigue and/or stress. Many tics occur without warning and may not even be noticed by the person doing them. Others are preceded by a subtle urge that is difficult to describe (some liken it to the urge to scratch an itch). In many cases it is possible to voluntarily hold back the tics for brief periods of time. Although any part of the body may be affected, the face, head, neck, and shoulders are the most common areas involved. Over periods of weeks to months, motor tics wax and wane and old tics may be replaced by totally new ones.

Simple motor tics can be described as a sudden, brief, "meaningless" movement that recurs in bouts (such as excessive eye blinking or squinting). Complex motor tics are sudden, stereotyped (i.e., always done in the same manner) semi-purposeful (i.e., the movement may resemble a meaningful act, but is usually involuntary and not related to what is occurring at the time) movements that involve more than one muscle group. There may often be a constellation of movements such as facial grimacing together with body movements. Some complex tics may be misunderstood by other people (i.e., as if you were shrugging to say "I don't know"). Complex tics can be difficult to distinguish from compulsions; however, it is unusual to see complex tics in the absence of simple ones. Often there is a tendency to explain away the tics with elaborate explanations (e.g., "I have hay fever that has persisted" even though it is not the right time of year). Tics are usually at their worst in childhood and may virtually disappear by early adulthood, so if you are completing this form for yourself, it may be helpful to talk to your parents, an older sibling, or a relative, as you answer the following questions.

- Age of **first** motor tics? _____ years old

- Describe **first** motor tic**:** _____

- Was tic onset sudden or gradual? _____

- Age of **worst** motor tics? _____ years old

Motor Tic Symptom Checklist

*In the boxes on the left below, please check with a mark (**x**) the tics the patient*

*1) has **EVER** experienced*
*2) is **CURRENTLY** experiencing (during the past week)*

*State **AGE OF ONSET** (in years) if patient has had that behavior.*

*Also, in the tic descriptions below, please **circle** or **underline** the specific tics that the patient has experienced (circle or underline the words that apply).*

[*In Years*]

Ever	Cur-rent	Age of onset	**The patient has experienced, or others have noticed, involuntary and apparently purposeless bouts of:**	Ver
			-eye movements.	
			eye blinking, squinting, a quick turning of the eyes, rolling of the eyes to one side, or opening eyes wide very briefly.	
			eye gestures such as looking surprised or quizzical, or looking to one side for a brief period of time, as if s/he heard a noise.	
			-nose, mouth, tongue movements, or facial grimacing.	
			nose twitching, biting the tongue, chewing on the lip or licking the lip, lip pouting, teeth baring, or teeth grinding.	
			broadening the nostrils as if smelling something, smiling, or other gestures involving the mouth, holding funny expressions, or sticking out the tongue.	
			-head jerks/movements.	
			touching the shoulder with the chin or lifting the chin up.	
			throwing the head back, as if to get hair out of the eyes.	
			-shoulder jerks/movements.	
			jerking a shoulder.	
			shrugging the shoulder as if to say "I don't know."	
			-arm or hand movements.	
			quickly flexing the arms or extending them, nail biting, poking with fingers, or popping knuckles.	
			passing hand through the hair in a combing like fashion, or touching objects or others, pinching, or counting with fingers for no purpose, or writing tics, such as writing over and over the same letter or word, or pulling back on the pencil while writing.	
			-leg, foot or toe movements.	
			kicking, skipping, knee-bending, flexing or extension of the ankles; shaking, stomping or tapping the foot.	
			taking a step forward and two steps backward, squatting, or deep knee-bending.	

Ever	Cur-rent	Age of onset	**The patient has experienced, or others have noticed, involuntary and apparently purposeless bouts of:**	*Ver*
			-abdominal/trunk/pelvis movements.	
			tensing the abdomen, tensing the buttocks.	
			-other simple motor tics.	
			Please write example(s): _____ _____	
			-other complex motor tics.	
			touching	
			tapping	
			picking	
			evening-up	
			reckless behaviors	
			stimulus-dependent tics (a tic which follows, for example, hearing a particular word or phrase, seeing a specific object, smelling a particular odor). Please write example(s): _____	
			rude/obscene gestures; obscene finger/hand gestures.	
			unusual postures.	
			bending or gyrating, such as bending over.	
			rotating or spinning on one foot.	
			copying the action of another (echopraxia)	
			sudden tic-like impulsive behaviors. Please describe: _____	
			tic-like behaviors that could injure/mutilate others. Please describe: _____	
			self-injurious tic-like behavior(s). Please describe: _____	
			-other involuntary and apparently purposeless motor tics (that do not fit in any previous categories).	
			Please describe any other patterns or sequences of motor tic behaviors: _____ _____ _____ _____ _____	

Phonic (Vocal) Tics

Description of Phonic (or Vocal) Tic Symptoms Phonic tics usually begin in childhood, typically after motor tics have already started, but they can be the first tic symptoms. They are characterized by a sudden utterance of sounds such as throat clearing or sniffing. The same tics seem to recur in bouts during the day and are worse during periods of fatigue and/or stress. Many tics occur without warning and may not even be noticed by the person doing them. Others are preceded by a subtle urge that is difficult to describe (some liken it to the urge to scratch an itch). In many cases it is possible to voluntarily hold back the tics for brief periods of time. Over periods of weeks to months, phonic tics wax and wane and old tics may be replaced by totally new ones. Simple phonic tics are utterances of fast, meaningless sounds whereas complex phonic tics are involuntary, repetitive, purposeless utterances of words, phrases or statements that are out of context, such as uttering obscenities (i.e., coprolalia), or repeating over and over again what other people have said (i.e., echolalia). Complex tics can be difficult to distinguish from compulsions; however, it is unusual to see complex tics in the absence of simple ones. Often there is a tendency to explain away the tics with elaborate explanations (e.g., "I have hay fever that has persisted" even though it is not the right time of year). Tics are usually at their worst in childhood and may virtually disappear by early adulthood, so if you are completing this form for yourself, it may be helpful to talk to your parents, an older brother or sister, or older relative, as you answer the following questions.

- Age of **first** vocal tics? _____ years old.
- Describe **first** vocal tic**:** _____
- Was tic onset sudden or gradual? _____
- Age of **worst** vocal tics? _____ years old.

Phonic Tic Symptom Checklist

*In the boxes on the left below, please check with a mark (**x**) the tics the patient*

*1) has **EVER** experienced*
*2) is **CURRENTLY** experiencing (during the past week)*

*State **AGE OF ONSET** (in years) if patient has had that behavior.*

*Also, in the tic descriptions below, please **circle** or **underline** the specific tics that the patient has experienced (circle or underline the words that apply).*

[*In Years*]

Ever	**Cur-rent**	**Age of onset**	**The patient has experienced, or others have noticed, bouts of involuntary and apparently purposeless utterance of:**	***Ver***
			-**coughing.**	
			-**throat clearing.**	
			-**sniffing.**	
			-**whistling.**	
			-**animal or bird noises.**	
			-Other simple phonic tics. Please list:	
			-**syllables**. Please list:	
			-**words**. Please list:	
			-**rude or obscene words or phrases**. Please list:	
			-**repeating what someone else said**, either sounds, single words or sentences. Perhaps repeating what's said on TV (echolalia).	
			-**repeating something the patient said** over and over again (palilalia).	
			-**other tic-like speech problems**, such as sudden changes in volume or pitch. Please describe:	
			Describe any other patterns or sequences of phonic tic behaviors:	

SEVERITY RATINGS

NUMBER (clinician rated)

	Motor	Phonic	
None	o	o	**0**
Single tic	o	o	**1**
Multiple discrete tics (2-5)	o	o	**2**
Multiple discrete tics (>5)	o	o	**3**
Multiple discrete tics plus as least one orchestrated pattern of multiple simultaneous or sequential tics where it is difficult to distinguish discrete tics	o	o	**4**
Multiple discrete tics plus several (>2) orchestrated paroxysms of multiple simultaneous or sequential tics that where it is difficult to distinguish discrete tics	o	o	**5**

FREQUENCY (patient rated)

	Motor	Phonic	
NONE No evidence of specific tic behaviors	o	o	**0**
RARELY Specific tic behaviors have been present during previous week. These behaviors occur infrequently, often not on a daily basis. If bouts of tics occur, they are brief and uncommon.	o	o	**1**
OCCASIONALLY Specific tic behaviors are usually present on a daily basis, but there are long tic-free intervals during the day. Bouts of tics may occur on occasion and are not sustained for more than a few minutes at a time.	o	o	**2**
FREQUENTLY Specific tic behaviors are present on a daily basis. tic free intervals as long as 3 hours are not uncommon. Bouts of tics occur regularly but may be limited to a single setting.	o	o	**3**
ALMOST ALWAYS Specific tic behaviors are present virtually every waking hour of every day, and periods of sustained tic behaviors occur regularly. Bouts of tics are common and are not limited to a single setting.	o	o	**4**
ALWAYS Specific tic behaviors are present virtually all the time. Tic free intervals are difficult to identify and do not last more than 5 to 10 minutes at most.	o	o	**5**

INTENSITY (clinician rated)

	Motor	Phonic	
ABSENT	o	o	**0**
MINIMAL INTENSITY Tics not visible or audible (based solely on patient's private experience) or tics are less forceful than comparable voluntary actions and are typically not noticed because of their intensity.	o	o	**1**
MILD INTENSITY Tics are not more forceful than comparable voluntary actions or utterances and are typically not noticed because of their intensity.	o	o	**2**
MODERATE INTENSITY Tics are more forceful than comparable voluntary actions but are not outside the range of normal expression for comparable voluntary actions or utterances. They may call attention to the individual because of their forceful character.	o	o	**3**
MARKED INTENSITY Tics are more forceful than comparable voluntary actions or utterances and typically have an "exaggerated" character. Such tics frequently call attention to the individual because of their forceful and exaggerated character.	o	o	**4**
SEVERE INTENSITY Tics are extremely forceful and exaggerated in expression. These tics call attention to the individual and may result in risk of physical injury (accidental, provoked, or self-inflicted) because of their forceful expression.	o	o	**5**

COMPLEXITY (clinician rated)

	Motor	Phonic	
NONE If present, all tics are clearly "simple" (sudden, brief, purposeless) in character.	o	o	**0**
BORDERLINE Some tics are not clearly "simple" in character.	o	o	**1**
MILD Some tics are clearly "complex" (purposive in appearance) and mimic brief "automatic" behaviors, such as grooming, syllables, or brief meaningful utterances such as "ah huh," "hi" that could be readily camouflaged.	o	o	**2**
MODERATE Some tics are more "complex" (more purposive and sustained in appearance) and may occur in orchestrated bouts that would be difficult to camouflage but could be rationalized or "explained" as normal behavior or speech (picking, tapping, saying "you bet" or "honey", brief echolalia).	o	o	**3**
MARKED Some tics are very "complex" in character and tend to occur in sustained orchestrated bouts that would be difficult to camouflage and could not be easily rationalized as normal behavior or speech because of their duration and/or their unusual, inappropriate, bizarre or obscene character (a lengthy facial contortion, touching genitals, echolalia, speech atypicalities, longer bouts of saying "what do you mean" repeatedly, or saying "fu" or "sh").	o	o	**4**
SEVERE Some tics involve lengthy bouts of orchestrated behavior or speech that would be impossible to camouflage or successfully rationalize as normal because of their duration and/or extremely unusual, inappropriate, bizarre or obscene character (lengthy displays or utterances often involving copropraxia, self-abusive behavior, or coprolalia).	o	o	**5**

INTERFERENCE (therapist rated)

	Motor	Phonic	
NONE	o	o	**0**
MINIMAL When tics are present, they do not interrupt the flow of behavior or speech.	o	o	**1**
MILD When tics are present, they occasionally interrupt the flow of behavior or speech.	o	o	**2**
MODERATE When tics are present, they frequently interrupt the flow of behavior or speech.	o	o	**3**
MARKED When tics are present, they frequently interrupt the flow of behavior or speech, and they occasionally disrupt intended action or communication.	o	o	**4**
SEVERE When tics are present, they frequently disrupt intended action or communication.	o	o	**5**

IMPAIRMENT (rated by patient)

NONE	o	**0**
MINIMAL Tics associated with subtle difficulties in self-esteem, family life, social acceptance, or school or job functioning (infrequent upset or concern about tics vis a vis the future, periodic, slight increase in family tensions because of tics, friends or acquaintances may occasionally notice or comment about tics in an upsetting way).	o	**10**
MILD Tics associated with minor difficulties in self-esteem, family life, social acceptance, or school or job functioning.	o	**20**
MODERATE Tics associated with some clear problems in self-esteem family life, social acceptance, or school or job functioning (episodes of dysphoria, periodic distress and upheaval in the family, frequent teasing by peers or episodic social avoidance, periodic interference in school or job performance because of tics).	o	**30**
MARKED Tics associated with major difficulties in self-esteem, family life, social acceptance, or school or job functioning.	o	**40**
SEVERE Tics associated with extreme difficulties in self-esteem, family life, social acceptance, or school or job functioning (severe depression with suicidal ideation, disruption of the family (separation/divorce, residential placement), disruption of social tics - severely restricted life because of social stigma and social avoidance, removal from school or loss of job).	o	**50**

SCORING

	Number (0-5)	***Frequency (0-5)***	***Intensity (0-5)***	***Complexity (0-5)***	***Interference (0-5)***	***Total (0-25)***
Motor Tic Severity						
Vocal Tic Severity						

Total Tic Severity Score = Motor Tic Severity + Vocal Tic Severity (0-50)	
Total Yale Global Tic Severity Scale Score (Total Tic Severity Score + Impairment) (0-100)	

Appendix J – Simpson Episode Scores

"Mr Lisa Goes to Washington" – Season 3, Episode 2

1. **How stressful/ anxiety provoking was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

2. **How boring was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

3. **How relaxing was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

4. **How stimulating was this episode? (i.e. funny/exciting?)**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

5. **How upsetting or sad was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

6. **How frightening was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

“Lemon of Troy” – Season 6. Episode 24

1. **How stressful/ anxiety provoking was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

2. **How boring was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

3. **How relaxing was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

4. **How stimulating was this episode? (i.e. funny/exciting?)**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

5. **How upsetting or sad was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

6. **How frightening was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

“Homer Simpson, This is your Wife” – Season 17, Episode 15.

1. **How stressful/ anxiety provoking was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

2. **How boring was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

3. **How relaxing was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

4. **How stimulating was this episode? (i.e. funny/exciting?)**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

5. **How upsetting or sad was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

6. **How frightening was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

“Bart Vs Australia” – Season 6, Episode 16

1. **How stressful/ anxiety provoking was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

2. **How boring was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

3. **How relaxing was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

4. **How stimulating was this episode? (i.e. funny/exciting?)**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

5. **How upsetting or sad was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

6. **How frightening was this episode?**

Not at all 0 – 1 – 2 – 3 – 4 – 5 – 6 – 7 – 8 – 9 – 10 Extremely?

Appendix K – Tic Count Protocol

TS Group Study: Tic Counting Protocol

Some background information:

- In this study children are seen once before (**pre**) and once after (**post**) attending group therapy for tics.

- In the pre- and post-visits, children are filmed using the laptop Webcam whilst watching a Simpson's episode for **15 minutes** in order for us to count how many tics they display within that time (**non-suppression task - NS**). They are then asked to hold in their tics for **5 minutes** (**tic-suppression task - TS**) whilst watching the rest of the Simpsons episode. You will hear us say "Simpsons 1" at the beginning of a video to indicate that the task is non-suppression, and "Simpsons 2" to indicate that the task is tic-suppression.

- You will be asked to **count tics** (vocal and motor) that you observe within those time periods, following the directions outlined below and using a tic counter.

- You will **find the videos** for each participant on the **hard-drive** in the drawer below the printer in room #### with the **yellow label "tic counting"**.

- The videos are separated into **"M" and "K" videos** – This relates to whether the videos were taken in **pre- or post**-group visits (these letters have been chosen at random to refer to a particular set of videos). This is to allow you to remain unaware of the time point to ensure fair scoring.

- Each person should have a total of 4 videos, 2 in "M" and 2 in "K" (at each pre- and post-visit each child will have done 1 x 15min NS and 1 x 5min TS).

- We would like you to score all of one participant's videos (M and K) before moving onto the next participant. We would like you to change the order for each new participant you score. For example, if for one participant you scored the M videos and then the Ks, for the next participant you should score the K videos and then the M. We have reminded you to do this by changing the order each time on the Excel data entry file (which will be explained below).

- Each participant has a semi-structured interview with parents and children in pre- and post-group visits. This is called the Yale Global Tic Severity Scale (**YGTSS**) and involves us noting down on a list all of the motor and vocal tics the child has had in the last week. We have written out a complete list of tics for each person ("tic list"). **You will just be rating these only, and no other tics that you see in the videos that are not on the list. You can find a list of tics for each person [description of location].**

DIRECTIONS

- Ensure you have a tic counter (there is one in Katie's top drawer), scrap paper, pen, stopwatch (can use ones on phones) and headphones (if possible/necessary).

- Get one of the hard-drives from the drawer and plug both of the hard-drive USB connectors into the computer. Go to My Computer and double click on McAfee then Start. Click login - Password is [password]. Then go back to My Computer and open the Private (E:) file that has now appeared. Go to the **"TS Group Study Videos"** and then the **"Tic counting" file**.

- Open the Excel spreadsheet for tic counting, where you will enter the data. Start at the top and work your way down. 1 participant = 2 rows, 1 for M and 1 for K time points.

- Look at the first column and get the ID number of the participant you will score on the Excel sheet. Find their tic list (on the shelf above my desk, see-through folder, yellow label "tic counting") and look through the list of tics that came up for that person on both visits, so that you are aware of which tics you will be counting in the videos.

- Now go to the file "tic counting videos: first (or second, depending on participant number you're looking for) set of groups", and find their videos in the "M" file or "K" videos file for that participant, starting with whatever is first (working top to bottom) on the two rows in the Excel file for that person.

- Within the "M"/"K" file, look at the 15min NS video first. Have your tic counter ready. We would like you to **click on the counter every time you see any tic (motor or vocal) that is on the list for that person (DO NOT COUNT TICS THAT ARE NOT ON THE LIST).** Make sure you **do this for exactly 15mins and no more or less** ("time start/stop" in the table below i.e. 0m 40s / 15m 40s is to remind you this should be exact). Videos often go on for longer but shouldn't be scored for more than the allocated time. You can pause the video if you need to check the list at any point.

- If during this time there are moments when it is difficult to observe the participant fully (e.g. they turn away, put their head down, leave the room) you should time these with your stopwatch. It is probably easiest to pause the stopwatch and continue it the next time, so at the end of that task you have a total number of seconds in which the tics were not fully observable. If the video is paused that is fine, just continue when we say start again. [NB: This method of measuring tics is not perfect and we understand it's limitations i.e. difficulty in observing tics from the waist down due to filming on the table, children often fidgeting etc – Please only rate tics as unobservable/nonvisible if it is quite significant e.g. they turn around, they get up and walk away briefly, they bend down to the ground to get something, and so on]

- **Fill all information in on the table below the tic list for that participant (hard copy)** – start/stop time, total tics, total time tics were unobservable/nonvisible, comments and any other tics you saw that were not on the list and so were not counted (write these down as you go along – you may need to pause the video).

So BASICALLY as you are watching the video make sure you:

- Write down the **start/stop time**
- **Count the number of tics** you see (only ones that roughly correspond to those on the tic list)
- Use your stopwatch to record **total time** tics/participant was **unobservable** (pausing your stopwatch each time)
- **Tick off the tics on the tic list** that you see during the videos
- **Write down any other tics you see in the videos that are not on the tic list** (don't count them, just write down what they were i.e. head jerk, repetitive "uh" vocal tic, etc)
- Write down any **comments**

NB: *Make sure you write down the results for M/K in the correct columns on the tic list*

- **Excel data entry:** Go to the database and the row for that participant and the time point (remember **M and K** time points mean that each person has two rows). Write the number of tics counted (e.g. 20) and the total time the tics were unobservable/nonvisible (as measured using your stopwatch - SECONDS). The pale green columns are calculated automatically.

- Now go back to the videos and do the same for the 5min TS video (i.e. count the tics using the tic counter, use the stopwatch to monitor time tics were not fully observable).

- Record this data on the tic list sheet and in the Excel data entry file - in the columns to the right on the same row of the Excel sheet for that participant.

- You have now entered all of the data for the "M" or "K" time point for that participant, and need to do the same for the other time point ("M" or "K" video files) that have not yet been rated for that participant.

- Enter these results on the row below for that participant.

- DONE! Onto the next participant/row… ☺

COMMON DIFFICULTIES AND A FEW THINGS TO REMEMBER!..

Please be very careful to enter the correct data in the 2 rows for each person, relating to the "M" and "K" time points.

Make sure that you are only counting tics for EXACTLY 15 or 5 minutes, as videos often go on slightly longer.

On very few occasions we may have forgotten to press stop on the video and the 15min NS and 5min TS tasks may all be on one video – Just listen out for "Simpsons 1/2" to indicate the start of timing, and "stop" (or something like saying we're finished now) to indicate the end of timing.

Sometimes us saying "Simpsons 1" or "Simpsons 2" at the beginning of each video may not be audible. In this case simply start at an appropriate point, such as when the examiner walks away, and then count for the allotted time.

Do not count general fidgetiness as tics (e.g. playing with face, hair, objects etc).

If something really goes wrong you can re-do the video again, but this will take much more time so we'll avoid that if we can. PLEASE COME AND FIND US IF THERE ARE ANY PROBLEMS OR YOU HAVE ANY QUESTIONS – This data is very important so we would rather you asked us more than less questions! There is also a comments section on the right in the Excel file in which you can record any difficulties or issues, but these should always be discussed with us first ideally.

NB: An error/danger message often comes up when using the hard-drive. Rather than continually pressing close just drag it to the bottom of the screen and continue with your work.

What if…?

- ➔ **I am unsure whether or not a vocalisation/movement is a tic or not?** You will have seen the YGTSS so will know some tics to look out for, but if you are not sure just make sure you are consistent. If you have counted something as a tic before then the best thing to do is keep counting it as a tic throughout, and vice versa if you have not.

- ➔ **The child has very complex tics and it is hard to tell what is one tic e.g. long juddering tic with eye twitching and vocal tics at the same time.** Generally count complex tics ONCE (e.g. a sequence of orchestrated tics – there may be breaks of only a second between bouts of complex tics but try to spot these and count separately. <u>We will go through some examples beforehand.</u>

If someone has tics in which they say lots of words all at once without a break count these as one tic.

If someone says sentences then count each sentence as one tic.

- ➔ **I can't hear quiet vocalisations well on the video?** Sometimes quieter sound tics are not quite audible on the videos and this is a limitation of this method. Unless you can see mouth movements that clearly indicate a sound tic, it is not possible to improve the sound quality to capture less audible vocal tics.

**** THANK YOU FOR YOUR HELP! ****

Please let us know if you have any questions – One of us should usually be around or you are welcome to phone us.

Premonitory Urge for Tics Scale (To be completed by the child)

	Not at all true	A little true	Pretty much true	Very much true
Before I do a tic, I feel like my insides are itchy				
Right before I do a tic, I feel pressure inside my brain and body				
Right before I do a tic, I feel 'wound up' or tense inside				
Right before I do a tic, I feel like something is not 'just right'				
Right before I do a tic, I feel like something isn't complete				
Right before I do a tic, I feel like there is energy inside my body that needs to get out				
I have these feelings almost all the time before I do a tic				
These feelings happen for every tic I have				
After I do a tic, the itchiness, energy, pressure, tense feelings or feelings that something isn't 'just right' or complete, go away, at least for a little while				

(PUTS - Woods et al, 2005)

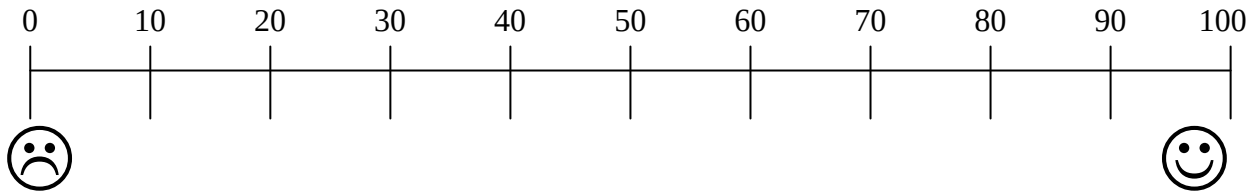
Gilles de la Tourette Syndrome – Quality of Life scale for patients aged 6-12 years (GTS-QOL-C&A 6-12)

Having a health problem can affect a person's quality of life in many different ways. This questionnaire addresses the issue of how your illness affects your well-being. Please put one cross in the box corresponding to the answer that fits your feelings best.
Note that this list includes many problems that you may never experience.

In the last 4 weeks have you…	NEVER	RARELY	SOMETIMES	OFTEN	ALWAYS
1. Been unable to control all your movements?	☐	☐	☐	☐	☐
2. Had difficulty with your favourite school or sport activities?	☐	☐	☐	☐	☐
3. Suffered pain or injuries as a result of your tics?	☐	☐	☐	☐	☐
4. Been upset by noises you could not stop making?	☐	☐	☐	☐	☐
5. Been worried about using bad words you did not mean to say?	☐	☐	☐	☐	☐
6. Been worried about making rude gestures you did not mean to make?	☐	☐	☐	☐	☐
7. Had to repeat words over and over?	☐	☐	☐	☐	☐
8. Had to repeat things that other people did or said that you did not mean to do or say?	☐	☐	☐	☐	☐
9. Had to do things over and over again, in a certain way (e.g. checking, touching...)?	☐	☐	☐	☐	☐
10. Experienced unpleasant thoughts or pictures going through your mind?	☐	☐	☐	☐	☐
11. Had difficulty concentrating?	☐	☐	☐	☐	☐
12. Had problems with your memory?	☐	☐	☐	☐	☐
13. You lost or misplaced important things (e.g. books, keys, mobile)?	☐	☐	☐	☐	☐
14. Had difficulty finishing your tasks once you have started them?	☐	☐	☐	☐	☐
15. Felt generally in poor health?	☐	☐	☐	☐	☐

16. Felt sad of depressed?	☐	☐	☐	☐	☐
17. Felt suddenly sad or suddenly happy without an apparent reason?	☐	☐	☐	☐	☐
18. Given up doing something because you thought you could not do it?	☐	☐	☐	☐	☐
19. Felt unhappy?	☐	☐	☐	☐	☐
20. Felt fidgety?	☐	☐	☐	☐	☐
21. Had difficulty to control your anger?	☐	☐	☐	☐	☐
22. Felt you were not in control of what you are doing?	☐	☐	☐	☐	☐
23. Felt angry, when you did not manage to do something?	☐	☐	☐	☐	☐
24. Felt you needed more help or support from other people?	☐	☐	☐	☐	☐
25. Had difficulty spending time with your friend?	☐	☐	☐	☐	☐
26. Had difficulty going out with other people (e.g. cinema, parties)?	☐	☐	☐	☐	☐
27. Felt lonely or isolated?	☐	☐	☐	☐	☐

Please indicate how satisfied you feel overall with your life at the moment by putting a cross on the line between 0 and 100.



Extremely unhappy with my life

Extremely happy with my life

Thank you very much for completing this questionnaire!

Appendix N – Parent Consent Form

Identification Number_____

Great Ormond Street Hospital for Children NHS
NHS Foundation Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

CONSENT FORM FOR PARENTS/ GUARDIANS

Title of Project: Randomised pilot study evaluating two group therapies for Tourette Syndrome

Names of Researchers: Rachel Yates, Trainee Clinical Psychologist
Katie Edwards, Trainee Clinical Psychologist
Dr Tara Murphy, Consultant Clinical Psychologist
Dr Isobel Heyman, Consultant Child Psychiatrist

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

Please initial the box after each statement.

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 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. ☐
5. 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. ☐
6. 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. ☐
7. I agree to my child's GP being informed of their participation in the study. ☐
8. I agree to taking part in the above study. ☐

Name of Child_____

_____ _____ _____
Name of Parent or Guardian Date Signature

_____ _____ _____
Researcher Date Signature

Appendix O – Child Assent Form

Identification Number_____

Great Ormond Street Hospital for Children NHS

NHS Foundation Trust

Great Ormond Street
London WC1N 3JH

Tel: 020 7405 9200

PARTICIPANT ASSENT FORM

Title of Project: Randomised pilot study evaluating two group therapies for Tourette Syndrome

Names of Researchers: Rachel Yates, Trainee Clinical Psychologist
Katie Edwards, Trainee Clinical Psychologist
Dr Tara Murphy, Consultant Clinical Psychologist
Dr Isobel Heyman, 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 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

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 → Stretchy man REWARD! 
- Talking together with your parents/carers about your tics this week 
- 1 form 

THE END

THANK YOU! ☺

Appendix Q – Time 1 Assessment Protocol

Beforehand

- Tell other Katie/Rachel where you will be and time of visit.
- Take contact details for Tara and Katie/Rachel
- Agree a time after which you will speak.
- Input demographic information into empty Excel file and save on F drive under ppt number
- Double check age and date of birth for eligibility
- Set up login for that child on the assessment centre and add password and login to the spreadsheet
- Make sure we know if they've had a WISC already and input data if so
- Book travel. Bring address and contact details and give this information to Katie/Rachel

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

Safety Procedure if do not hear from each other following visit:

1. **Call person doing home visit**
2. **Call household of assessment**
3. **Call contact for researcher (significant other)**
4. **Call Tara**

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**
- Three-way plug adaptor
- Monitor, connector cable + power cable
- Keyboard, mouse, speakers
- **Encrypted memory stick**
- Pegboard, pegs and spares
- Something to stop pegboard slipping
- WISC-IV Blocks, stimulus book, scoring manual
- Stopwatch
- Pencil without rubber x 2
- **Little rubber man reward**
- **Bluetak**
- Internet dongle
- DVD for watching during obs
- Full assessment protocol
- **Questionnaire pack for right age range (i.e. 13/ under 13)**:
    - *Participant assent form*
    - *YGTSS form*
    - *Young person CHOCCI*
    - *WISC record form response booklet*
    - *Tourette Syndrome Questionnaire*
    - *PUTs*
    - *PEDs-QL (version different if aged 13)*
    - *GTS-QOL (version different if aged 13)*
- **Spare parent questionnaire pack in case they've lost theirs**:
    - *Parent consent form*
    - *Parent CHOCCI*
    - *Rage attacks questionnaire*
    - *SNAP-IV 26*
    - *SDQ*

Equipment for Scoring: Ruler, WISC-IV scoring templates, Clicker counter

Introduction
Introductions
Outline of assessment
Reminder not to disclose group allocation if possible
Remind about GP letter if not already mentioned
Collect parent questionnaires and consent forms
Request internet password (2 mins)

Consent
Discuss study with child and collect their assent (5 mins)

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 while we set up the computer equipment etc.
Monitor to the left of the laptop

Unlock Encrypted file F by clicking on key icon.
Highlight file F and click mount. Enter usual password.

Right click desktop -> Screen resolution
Set up:
Display – 2. Acer (laptop)
Resolution – 1440 x 900
Orientation – Landscape
Multiple displays – Extend these displays

Open Excell spreadsheet for that participant number.

Setup three dongle or internet connection depending which is being used.
If dongle:
Plug in dongle and double click 3 icon.

If nesc turn on wifi on laptop – press fn then f3 (on laptop keyboard)

Go to Internet Explorer and Favourites – Choose TSGroupStudy
Get login and password from spreadsheet and type in.

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)
Ask about handedness:

"Are you… or Is your child right- or left- handed?"

If unsure, ask the following three questions:
1) ***"Which hand do you (does your child) use to pick up and throw a ball?"***
2) ***"Which hand do you (does your child) use to write or draw?"***
3) ***"Which foot do you (does your child) use to kick a ball?"***

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. WISC – 7 subtests (40 mins)

	Block design		
	Look at these blocks. They are all alike. On some sides they're all red; on some sides, all white and on some sides, half red and half white.		Blocks. Stimulus book. Stopwatch. Record form.
		Trial 2	
Item 1 (30 secs)	Watch me put the blocks together to make something. Now you make one just like mine. Go ahead.	Watch me again. Now you try it again and make it just like mine. Go ahead.	Reverse until 2 perfect scores. Discontinue after 3 zeros.
Item 2 (45 secs)	Watch me put four blocks together to make something else. Now you make one just like mine. Work as quickly as you can and tell me when you're finished. Go ahead.	Watch me again. Now you try it again and make it just like mine. Go ahead. **(use child's blocks)**	**See, it goes this way.**
	Start here		
Item 3 (45 secs)	Watch me put the blocks together to look like this picture.You see, the tops of these blocks look the same as this picture. Now you make one just like the picture. Work as quickly as you can and tell me when you have finished. Go ahead.	Watch me again. You see, the tops of these blocks look the same as this picture. Now you try it again and make sure it looks just like the picture. Go ahead.	
Items 4 -10	Now you make one just like this. Work as quickly as you can and tell me when you are finished. Go ahead.		
Items 11-14	Now make one like this using all nine blocks. Work as quickly as you can an tell me when you have finished. Go ahead.		

Similarities			
	Now, I am going to say two words and ask you how they are alike. In what way are RED and BLUE alike? How are they the same?	Red and blue are both colours.	Administation manual. Record form.
	Lets try another one.		
Item 1	In what way are MILK and WATER alike?	Milk and water are both liquids or fluids and you drink them.	Reverse until 2 perfect scores. Discontinue after 5 zeros.
	Lets try another one.		
Item 2	In what way are a PEN and a PENCIL alike?	A pen and a pencil are both things you write or draw with.	
	Lets try another one.		
Ages 9-11	**Sample then item 3**		
Ages 12-16	**Sample then item 5**		**What do you mean? Tell me more about it**
			Can repeat items as often as necessary.

Digit Span			
I am going to say some numbers. Listen carefully, and when I am finished, say them straight after me. Just say what I say.			Administation manual. Record form.
Backwards digit span			
Now I am going to say some more numbers, but this time when I stop, I want you to say them backwards. If I say 8-2, what would you say?	That's not quite right. I said 8-2, so to say it backwards, you should say 2-8. Let's try again: 8-2.	That's not quite right. I said 8-2, so to say it backwards, you should say 2-8. Let's try again: 8-2.	**Just make your best guess. (no repeats)**
That's right.	That's right.		
Lets try these numbers. Remember you're to say them backwards: 5-6.	That's not quite right. I said 5-6, so to say it backwards, you should say 6-5. Let's try again: 5-6.	That's not quite right. I said 5-6, so to say it backwards, you should say 6-5. Let's try again: 5-6.	
That's right.	That's right.		
Then proceed to item 1			

Coding			
Age 8-16			
Look at these boxes. Each box has a number in the top part and a special mark in the bottom part. Each number has its own mark. Down here the boxes have numbers in the top parts but are empty in the bottom parts. You are to draw the marks that belong in the empty boxes like this. Here is a 2, the 2 has this mark. So I draw that mark in the empty box, like this. Here is a 1. The 1 has this mark. So I draw the mark in the empty box. This is a 4. The 4 has this mark. So I draw the mark in the box. Now you do these. Stop when you get to this line.		(Correct any errors until clearly understood.)	Administration manual. Stopwatch. Record form. Response booklet.2 pencils without erasor.
Right, now you know how to do them			Discontinue after 2 minutes.
When I say go, do these in the same way. Start here, go in order, and don't skip any. Work as fast as you can without making mistakes until I tell you to stop. Are you ready?			**(if mistake) That's okay. Just keep working as fast as you can.**
			Do them in order. Don't skip any. Do this one next.

	Vocabulary		
	I am going to say some words. Listen carefully and tell me what each word means.		Stimulus book. Record form. Administration manual.
Item 5	What is a hat?	A hat is something you wear on your head.	Reverse until 2 perfect scores. Discontinue after 5 zeros.
Item 6	What is an umbrella?	An umbrella is something that keeps you from getting wet in the rain.	**Yes, but what else is it called? Yes, but what kind of…is it?**
Ages 9-11	**Start item 7**		
Ages 12-16	Start item 9		**Yes, but what is it called? What do you mean? Tell me more about it. Listen carefully, wht does……..mean? Tell me in words what a……..is.**
			Can repeat items as often as necessary

Matrix Reasoning		
Look at these pictures. Which one here goes here?		Stimulus book. Record form. Administration manual.
Right. Lets try another one.	Let's look again. All of these butterflies are blue. This one is also blue, so it goes here. Lets try another one.	Reverse until 2 perfect scores. Discontinue after 4 zeros or 4 zeros on 5 items.
Which one here, goes here?		**Show me.**
Right. Lets try another one.	Let's look again. These two lightbulbs are yellow. Here is a green light bulb. We need another green lightbulb like this one, so this one goes here. Lets try another one	**There is only one correct answer to each problem. Just choose the best one.**
Which one here, goes here?	Lets look again. All of these boxes are blue and have a line through them going this way. This one is also blue and has the same line through it, so it goes here. Lets try another one.	
Right. Lets try another one.		
Ages 9-11	Item7	
Ages 12-16	Item 11	
Which one here, goes here?		

Symbol Search		
Age 8-16		
Look at these shapes. One of these shapes is the same as one of the shapes here. This shape here is the same as this shape here, so I will mark the YES box like this. Now look at these shapes. Neither of these shapes here is the same as any of the shapes here, so I will mark the NO box like this. You are to mark the YES box if one of the shapes here is the same as any of these shapes here and mark the NO box if none of the shapes are the same. Do you understand?		Record form. Administration manual. Response booklet. 2 pencils without eraser. Stopwatch
Now you do these here. Go ahead.		After 2 minutes
Yes, Right. Now you know how to do them.	That's not quite right. Look here. Here is the shape. Now look over here. Here is the same shape. The shapes are the same, so you should mark the YES box.	**Keep working as fast as you can**
	That's not quite right. Look here. Here is the shape. Now look over here. None of these shapes is the same, so you should mark the NO box.	**That's OK. Just keep working as fast as you can.**
When I say go, do these in the same way. Start here, go in order and don't skip any. Work as quickly as you can without making mistakes. When you finish the first page, go to the second page and the following page. Are you ready?		**Do them in order. Don't skip any. Do this one next.**
Go		
Stop		

9. Direct Obs while watching video (20 mins)

Set up video and camera
"Now we're 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 stretchy man as a reward."
Then say **"Simpsons 2".** Start stopwatch.
Say **"stop"** after 5 minutes and stop video.
Label second video (see above)
Give jelly man.

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

10. YGTSS (30 mins)

Video this (parent and child).
"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

<u>Coding notes</u>
Complex – if includes a series of muscle groups or appears purposeful (e.g. motor hand through hair/obscene gestures or touching things; or vocal, saying a word).
Ver = verify (i.e. see in room).
Try to add e.gs. for the scores given where possible.
<u>Ask</u> initial questions about age of onset etc (but then for individual tics just ask about **<u>current</u>**)

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 ticing 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.

Additional points
Noticeability is due to INTENSITY or STRENGTH, not frequency or complexity!

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

Additional points:
Usually rated based on observations and symptom checklist
If a complex tics includes both phonic and motor decide which is more dominant – do not rate twice.

Follow up questions:

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

- 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?"

Additional points:
The key is the extent to which tics disrupt planned actions or speech
First establish if tics do interfere, then rate the extent
Use observations

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

Additional points
Impairment rated as a single item (not specified for motor/vocal, but rating the whole tic package concurrently)
0-50 scale

11. Child CHOCCI (15 mins)
Enter data directly onto computer as they complete the paper form

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

13. Check parent questionnaires (check over any missing items)

Save spreadsheet
Dismount the F drive

After visit

Enter data for:

- GTS-QoL
- WISC
- Tourette Syndrome Questionnaire
- Parent questionnaires (SNAP-IV; Rage attacks questionnaire; SDQ)
- Get NIH data and add to Excel
- Double check eligibility (YGTSS score and WISC score)
- 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 (#### has password)
Put questionnaires in Tara’s office

Extra info

To Log in to Assessment centre if necessary:
www.assessmentcenter.net in internet explorer
Login: ##########; Usual study password.

To access data:

- We need to click the "request" buttons for participant data on the administration tab each time we run a new participant.
- Click F5 to refresh the page and make sure the links on the right have the current date on them to ensure they have been updated.
- "Assessment scores" show age-adjusted scores and percentiles.
- "Pivoted assessment data" at the bottom is also very useful, presenting all summary data for one participant on one row rather than multiple rows (it pivots it round to fit one row.. you can do this manually with the assessment data if necessary apparently but we shouldn't need to!)

Appendix R – Time 2 Assessment Protocol

Beforehand

- Tell other Katie/Rachel where you will be and time of visit.
- Take contact details for Tara and Katie/Rachel
- Agree a time after which you will speak.
- Copy demographic information into new empty Excel file from time 1 spreadsheet and change assessment date. Save on F drive under ppt number and make clear T2.
- **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 Katie/Rachel

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

Safety Procedure if do not hear from each other following visit:

1. **Call person doing home visit**
2. **Call household of assessment**
3. **Call contact for researcher (significant other)**
4. **Call Tara**

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 slinky reward**
- **Bluetak**
- Internet dongle
- DVD for watching during obs – **new disk**
- 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
Outline of assessment – show visual timetable
Reminder not to disclose group allocation if possible
Give parent questionnaires
Request internet password (2 mins)

Go over T2 questions from demographic sheet:

- Since pre-assessment have there been any changes in medication?
- Since pre-assessment 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 study?
- Ok to possibly be contacted in 1 year for long-term follow-up?

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 while we set up the computer equipment etc.
Monitor to the left of the laptop

Unlock Encrypted file F by clicking on key icon.
Highlight file F and click mount. Usual password.

Right click desktop -> Screen resolution
Set up:
Display – 2. Acer (laptop)
Resolution – 1440 x 900
Orientation – Landscape
Multiple displays – Extend these displays

Open Excell spreadsheet for that participant number.

Setup three dongle or internet connection depending which is being used.
If dongle:
Plug in dongle and double click 3 icon.

If nesc turn on wifi on laptop – press fn then f3 (on laptop keyboard)

Go to Internet Explorer and Favourites – Choose TSGroupStudy
Get login and password from spreadsheet and type in.

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 – **Mr Lisa Goes to Washington – Season 3 episode 2.**
"Now we're 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 slinky as a reward."
Then say **"Simpsons 2".** Start stopwatch.
Say **"stop"** after 5 minutes and stop video.
Label second video (see above)
Give slinky.

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).

"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

Coding notes

Complex – if includes a series of muscle groups or appears purposeful (e.g. motor hand through hair/obscene gestures or touching things; or vocal, saying a word).

Ver = verify (i.e. see in room).

Try to add e.gs. for the scores given where possible.

Ask initial questions about age of onset etc (but then for individual tics just ask about **current**)

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

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

Follow up questions

  - Do you have at least one motor tic every day?
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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)**

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Parents Questionnaire for Tourette Group

We would like to evaluate the usefulness of this first group for young people with Tourette Syndrome. It is therefore very helpful for us to get some feedback from you and we would appreciate it if you could fill in the questionnaire. Please also feel free to add any additional comments.

Having brought your child to the group and possibly discussed the sessions with your child did you get a sense of:

1. **For you and your child, was the amount of information about the group:**

Much too little	Too little	Sufficient	Too much	Far too much
☐	☐	☐	☐	☐

2. **Would you have liked the frequency of the group to be:**

Every week	every 2 weeks	every 3 weeks	every 4 weeks	less frequent
☐	☐	☐	☐	☐

3. **Would you have liked the group to take place at:**

10am	12pm	2pm	4pm	6pm
☐	☐	☐	☐	☐

4. **Would you have liked the number of sessions to be:**

2	4	6	8	more
☐	☐	☐	☐	☐

5. **Would you have liked the duration of the group to be:**

1 hour	1 ½ hours	2 hours	3 hours	more
☐	☐	☐	☐	☐

6. **Was the group:**

Not at all helpful				Extremely helpful
1	2	3	4	5
☐	☐	☐	☐	☐

7. Any other comments on how the group could be improved?

Young Person's Questionnaire for Tourette Group

We would like to evaluate the usefulness of this first group for young people with Tourette Syndrome. It is therefore very helpful for us to get some feedback from you and we would appreciate it if you could fill in the questionnaire. Please also feel free to add any additional comments.

1. **Was the amount of information about the group:**

much too little	too little	sufficient	too much	far too much
☐	☐	☐	☐	☐

2. **Would you have liked the frequency of the group to be:**

Every week	every 2 weeks	every 3 weeks	every 4 weeks	less frequent
☐	☐	☐	☐	☐

3. **Would you have liked the group to take place at:**

10am	12pm	2pm	4pm	6pm
☐	☐	☐	☐	☐

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2	4	6	8	more
☐	☐	☐	☐	☐

5. **Would you have liked the duration of the group to be:**

1 hour	1 ½ hours	2 hours	3 hours	more
☐	☐	☐	☐	☐

6. **Was the group:**

Not at all enjoyable				Enjoyable extremely
1	2	3	4	5

7. Was the group:

Not at all helpful				Extremely helpful
1	2	3	4	5

8. Were the group leaders:

Not at all helpful				Extremely helpful
1	2	3	4	5

9. What did you enjoy most about the group:

a.

b.

c.

10. What did you learn in the group:

a.

b.

c.

11. What other areas would you have liked covered in the group:

a.

b.

c.

12. Any other comments on how the group could be improved?

Appendix U – Effect Size (Cohen's *d*) and Confidence Interval Formulae

Equations as taken from Nakagawa and Cuthill (2007)

$$\text{Cohen's } d = \frac{m_2 - m_1}{\text{Pooled } SD}$$

$$\text{Pooled } SD = \sqrt{\frac{(n_2 - 1)s_2^2 + (n_1 - 1)s_1^2}{(n_1 + n_2 - 2)}}$$

Approximate 95% Confidence Interval for Cohen's *d*,

$$95\%\text{CI} = ES - 1.96se \text{ to } ES + 1.96se$$

For independent unpaired *d*,

$$se_d = \sqrt{\left(\frac{n_1 + n_2 - 1}{n_1 + n_2 - 3}\right)\left[\left(\frac{4}{n_1 + n_2}\right)\left(1 + \frac{d^2}{8}\right)\right]}$$

For dependent, paired or repeated measures *d*,

$$se_d = \sqrt{\frac{2(1 - r_{12})}{n} + \frac{d^2}{2(n - 1)}}$$

Where s^2 the variance; *se* is standard error; *r* is the correlation coefficient between the two groups; *ES* is effect size (*d*).