1 Applying an established Exposure Response Prevention protocol for

2 Young People with Tourette syndrome in an intensive, group format: a

- 3 feasibility study
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# 26 **Conflicts of interest**

- 27 The Authors declares that there is no conflict of interest.
- 28
- 29 Ethics statement
- 30 The Great Ormond Street Hospital for Children NHS Foundation Trusts' Clinical Audit Team
- approved this study as part of a service evaluation (audit reference number: 2420). Although it was
- 32 decided that the collection and analysis of data did not require ethical review by an NHS research
- 33 ethics committee, care was taken to ensure ethical standards were met. No personally identifiable
- 34 information was described in this study.

#### 35 Keywords: Exposure Response Prevention<sub>1</sub>, Tourette syndrome<sub>2</sub>, Behaviour therapies<sub>3</sub>, Group 36 Intervention 4 Tiese

- 36 Intervention4, Tics5
- 37
- 38

### 39 Abstract

- 40 Background: The motor and vocal tics that characterise Tourette syndrome (TS) are stigmatizing and
- 41 impact on quality of life (QOL). Behavioural interventions such as Exposure Response Prevention
- 42 (ERP) or Comprehensive Behavioural Interventions for Tics (CBITs) are first line treatment for TS,
- 43 but availability is limited. This study is the first to explore the impact of an established manualised
- 44 ERP treatment protocol, developed for individual therapy, but here uniquely delivered intensively, to
- 45 a group.
- 46 Methods: A naturalistic study comprised of a consecutive series of children (N=20), aged 8-16 years
- 47 (M= 12, SD= 2.17) were offered ERP in one of two groups, delivered in series within a specialist
- 48 clinic. Young people received the equivalent of 12 sessions (matching the manualised individual
- 49 protocol).
- 50 Results: The YGTSS and Giles de la Tourette Syndrome Quality of Life Scale for Children and
- 51 Adolescents (Satisfaction Scale) showed significant improvement following treatment with moderate
- 52 to large effect sizes. Thirty-five percent of children demonstrated a reliable improvement on the
- 53 YGTSS Global Tic Severity score.
- 54 Conclusions: These data suggest an established ERP protocol can be delivered in an intensive, group
- setting with a positive clinical outcome. Replication in a randomized controlled trial is an important
- 56 next step.

### 57 **1. Introduction**

Tourette Syndrome (TS) characterised by motor and vocal tics (APA, 2013), has a prevalence of 0.77– (Knight et al., 2012). It is frequently associated with comorbidities such as Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive Compulsive Disorder (OCD; Abramovitch et al., 2015). Additionally, social and emotional difficulties (Cutler et al., 2009), impaired school functioning (Cubo et al., 2017) behavioural difficulties and a diminished quality of life (Eapen et al., 2016) are also

63 frequently reported.

64 Behavioural therapy is the first-line intervention for TS delivered following psychoeducation (Andren et al., 2022). There are two broad behavioural approaches with an evidence base: first, Comprehensive 65 Behavioural Intervention for Tics (CBITs; Woods et al., 2008) which incorporates Habit Reversal 66 Training techniques (Azrin & Nunn, 1973) and second, Exposure and Response Prevention (ERP) 67 68 originally developed by Meyer (1966) to treat obsessive-compulsive symptoms. Treatment effects of 69 ERP for tics are comparable to those of HRT (Andren et al., 2021; Verdellen et al., 2004). The unique 70 advantage of ERP is that it addresses multiple tics simultaneously in contrast to HRT/CBITs, which treats one tic at a time. Despite effect sizes in these studies being moderate to high (0.57-1.5) with 71 72 significant reduction in tic severity (McGuire et al., 2014), behavioural treatments are not widely available (Hollis et al., 2016; McGuire et al., 2015). 73

To address the treatment bottleneck, various delivery methods have been developed. For example, an abbreviated CBITs program (Chen et al., 2020) and other case studies (Blount et al., 2014; Blount et al., 2018; Flancbaum et al., 2010) suggest intensive delivery offers a promising solution by reducing the number of appointments needed. However, much remains unknown about dose effects and optimum delivery formats (Chen et al., 2020).

79 Another viable option to the treatment shortage is group therapy. Learning in a social context has many unique benefits for young people (Lieberman, 2012), especially during adolescence where peer-to-80 81 peer learning is highly effective, often more so than adult didactic instruction (Yeager et al., 2018), 82 potentially making carefully facilitated group work the optimum modality for psychoeducation, post 83 puberty. For TS affected individuals, tics are suggestible (Tallur & Minns, 2010), so there has been 84 some caution about offering group interventions to young people or adults with TS until relatively recently, however, existing data show a group setting for TS provides general benefits such as 85 86 improved self-efficacy, reduced isolation (Murphy & Heyman, 2007) as well as augmenting TS 87 specific treatment goals (Nussey et al., 2014).

Bata are sparse, and while RCTs show some positive improvements, the pattern of change is variable, with weaker effects using the adapted CBITs intervention on vocal tics (Yates et al., 2016; Zimmerman-Brenner et al., 2021). Nissen et al. (2019) developed an HRT and ERP combined protocol in an RCT and found that group and individual delivery had equivalent efficacy, with large effect sizes reported in both cases. Beneficial effects were maintained at one-year follow-up in both individual and group formats (Nissen et al., 2021). The case for CBIT or a combination of CBIT/ERP behaviour treatment in group therapy is promising.

Though ERP group treatment is well established in other disorders (Whiteside et al., 2018) only one study to date has used a 'pure' ERP group intervention for TS (Heijerman-Holtgrefe et al., 2021) describing good outcomes, including improved tic profiles (d=.4) and quality of life (d=.6). This group (run by experts in tic behavioural treatment) used an innovative, intensive ERP protocol developed in consultation with service users included additional components, rather than strictly adhering to a published menualised ERP protocol. While patient involvement is a valid enpresent to service delivery

100 published manualised ERP protocol. While patient involvement is a valid approach to service delivery

- 101 methods (and one we support), the current paper explores the value of offering an *existing* manualised
- 102 tic management protocol developed for individual therapy, in an intense group format. Establishing the
- 103 effectiveness of an established protocol in a group context means that professionals less experienced
- 104 in tic treatment will be encouraged to offer them to client groups. The importance of treatment fidelity
- in delivery of evidence-based interventions is well described (Breitenstein et al., 2010; Carroll et al.,
- 106 2007; Mihalic, 2004). No investigation to date has examined the feasibility of using an established
- 107 evidence-based ERP protocol, maintaining procedural fidelity, in a group setting.

108 The current study aimed to determine if an established, evidence-based ERP protocol, delivered in an 109 intensive group format, leads to significant improvements in tic severity and quality of life outcomes 110 in children with TS.

- 111 **2. Methods**
- 112
- 113 *2.1 Design*

A consecutive series of twenty children were recruited for two groups (n=10 in each group) of identical format, run 4 months apart (July 2019 and November 2019).

- 116
- 117 2.2 Recruitment

Patients were recruited from a specialist TS clinic which accepts referrals from across the UK. Following a multi-disciplinary team (MDT) assessment, the details of which are described elsewhere (McFarlane et al., 2019), the group was offered to all patients who met the inclusion/exclusion criteria outlined below.

- 122
- 123 *2.3 Participants*

124 Inclusion criteria for the group were: (a) children aged 8 - 16 years old (b) diagnosed with Tourette 125 syndrome (TS) or chronic tic disorder (CTD), according to the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> edition (APA, 2013), (c) with at least moderate tic severity indicated by Yale 126 127 Global Tic Severity Scale (YGTSS; Leckman et al., 1989) Total Score of > 13 (or > 9 for children with 128 motor or vocal tics only) and (d) able to participate in all three days of the intensive group and the 129 "booster day" scheduled 4 weeks after the group ended. None of the children offered the group intervention declined. Children with co-occurring ADHD, OCD, other anxiety or mood disorders were 130 included (Table S1 in supplementary materials), unless the disorder required immediate treatment or 131 132 was severe and would interfere with group participation. No children were excluded based on this 133 criterion.

Exclusion criteria were: (a) insufficient spoken English to participate in the group (b) participation in ERP or CBITS/HRT sessions in the last year (c) substance abuse, (d) suicidality, (e) psychotic disorders, (f) severe autism spectrum disorders (ASD) or ADHD, which could interfere with a child's

- 137 ability to participate in the group. No children were excluded based on these criteria.
- Gender, age, ethnicity and co-occurring conditions were derived from hospital records. Participants all had a diagnosis of Tourette Syndrome and were predominantly white males with a mean age of 12 years (SD = 2.17). High levels of comorbidity were present, consistent with TS populations (Hirschtritt et al., 2015) with 17 children (85%) diagnosed with at least one other psychiatric diagnosis (see Table
- 142 S2 in the supplementary materials). Co-morbid neurodevelopmental conditions were common, 40%

had ADHD and 25% had ASD. Children with ASD (10%) or ADHD traits (40%) were also identified

144 during MDT assessment and required further assessment in order to make a formal diagnosis (see

supplementary materials 1.1 and Table S3 for additional details on baseline characteristics of the sample).

# 147 2.4 Intervention

The Exposure and Response Prevention (ERP) protocol (Verdellen et al., 2011) comprised 12 weekly individual sessions ( $12 \times 60$  mins sessions = total 720 mins). In the present study the same protocol was offered in a group, intensive setting consisting of 9 sessions (720mins). See supplementary materials (Table S4) for a breakdown of sessions and (Section 3.2) for intervention details. A booster day was offered 4 weeks post completion to consolidate learning and review progress (120 mins).

153

# 154 2.5 Procedure

155 Sessions were conducted at the hospital, according to the manualised protocol with minor adaptations 156 for the group context (Verdellen et al., 2011). A schedule of the intervention and assessments of 157 outcome measures is shown in Table S5 (see supplementary materials). Within 2 weeks of starting the 158 group, the YGTSS was carried out by an experienced clinician who was part of the team, but not part 159 of the treatment group, over the telephone. Children and their families completed all other baseline measures at the start of the first group session (time zero; t0) and the 4 week 'booster day' (time two; 160 t2). Goal based outcome measures and feedback forms were additionally completed at the end of the 161 intensive three-day group (time one; t1). ERP exercises as per the protocol, were offered in small 162 163 subgroups of 2 or 3 children with peer-to-peer learning (timing, counting tics and encouragement). Therapists rotated around the small groups and offered support. Sessions were delivered by two 164 165 experienced Clinical Psychologists and an assistant psychologist.

- 166
- 167 *2.6 Outcome Measures*
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2.6.1 Primary outcome measure

171 2.6.1.1 Yale Global Tic Severity Scale (YGTSS)

The YGTSS (Leckman et al., 1989), is the gold standard measure of tic severity and impairment. The Global severity score (range 0–100) is composed of an Impairment score (0–50) and a Total Tic score (0–50), which sums total motor (0–25) and total vocal (0–25) tic scores. We defined a 25% tic reduction as a positive response on the Total Tic Severity scale (Jeon et al., 2013). The YGTSS has good interrater reliability (Leckman et al., 1989) and test re-test reliability is high at 0.94 (Storch et al., 2005).

- 177
- 178 2.6.2 Secondary outcome measures
- 179
- 180 2.6.2.1 Goal Based Outcomes (GBOs)

GBOs (Law & Wolpert, 2014) are routinely used to evaluate progress towards a patient's treatment goals. Each parent and child completed the appropriate version and rated how close they felt they were to achieving their goal on a Likert Scale from 0 (Not at all) to 10 (Goal reached). Participants were invited to establish up to three goals (i.e. GBO 1, GBO 2, GBO 3; parent/ child rating separately), but some chose to create one or two. Goals were typically about finding successful ways to manage tics.

- 186 GBOs have acceptable internal consistency (α coefficient of 0.7; Edbrooke-Childs et al., 2015). We
- 187 considered a reliable change index for GBOs at 2.45 points (Edbrooke-Childs et al., 2015).
- 188 2.6.2.2 The Gilles de la Tourette Syndrome Quality of Life Scale for Children and Adolescents
   189 (C&A-GTS-QOL).

190 Quality of life was measured using the C&A-GTS-QOL (Su et al., 2017), a 27-item patient-reported

- 191 scale with good acceptability, reliability ( $\alpha$ >0.7) and validity. It comprises four subscales describing
- 192 Psychological, Physical, Obsessive compulsive and Cognitive aspects of life. Scores for the subscales
- are generated by summing items and normalising total scores to a 0-100 range Lower scores indicate
- better QOL. A life satisfaction subscale (GTS QOL satisfaction score) presented on a visual analogue scale (0-100 range) is scored in the opposite direction, so higher scores indicate greater satisfaction.
- 196 Additional measures taken at baseline to characterise the sample are described in Section 3.1.
- 197
- 198 2.7 Statistical analyses

199 Measures were collected and where relevant analysed at three time points: t0, t1 and t2. The YGTSS 200 showed one outlier on all subscales apart from the Motor subscale (using inspection of a boxplot). 201 Difference scores were not normally distributed for the Vocal (Shapiro-Wilk's test = 0.002) and 202 Impairment (Shapiro-Wilk's test = 0.016) subscales. Therefore, difference scores were based on the 203 median change in scores; these changes were tested using Wilcoxon signed rank test/Sign test as 204 appropriate and converted into effect sizes (r value; Fritz et al., 2012). The GTS OOL C&A, showed 205 no outliers (assessed by inspection of a boxplot) and difference scores were normally distributed 206 (lowest p value on Shapiro-Wilk's test > .281), so difference scores were based on the mean change in 207 scores; these changes were tested using paired samples t-tests and converted into effect sizes (Cohen's 208 d; Cohen, 2013). GBO scores had outliers and were not normally distributed (Shapiro Wilk's < 0.05). 209 Here difference scores were based on the median change in scores. To maintain a conservative 210 approach, we limited analysis of GBO data to a descriptive comparison of change against benchmark 211 data i.e. the UK Increasing Access to Psychological Therapies program for children and young people 212 - CYP IAPT - data set from 2011 to June 2015, which includes data from 75 separate services (Law & 213 Wolpert, 2014). Results on the YGTSS Global severity score, GTS QOL Total, GTS Satisfaction and 214 GBOs were analysed at the individual level by reliable change analysis, which determines whether the 215 degree of change on each measure was statistically reliable, and not due to measurement-error 216 (Jacobson & Truax, 1991). This allows for classification of participants as either (i) reliably improved, 217 (ii) reliably deteriorated, or (iii) not changed. Differences in patient characteristics/outcome measures 218 between the first and second ERP groups were tested using independent t-tests/Mann-Whitney U tests 219 for continuous variables and chi-square/fisher's exact tests for categorical variables (results are 220 presented in supplementary materials sections 1.2 and 1.3 and Figures S1, S3 and S5).

- 221
- 222 2.8 Qualitative Feedback

Patient feedback is an important part of the acceptability and feasibility assessment. We developed an 8-item questionnaire (see 'Feedback form' in supplementary materials). Questions 1-5 were answered using a set of predefined categorical answers, 6 to 8 were open-ended, in which participants could provide free text responses. For the open-text questions only, responses were grouped into categories based on the principles of content analysis (Cole, 1988).

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- 229

- **3. Results**
- 231232 *3.1 Feasibility*
- 233 There were no patient dropouts or missing data on the primary outcome measure.
- 234

*3.2 Outcomes* 

236 3.2.1 Primary – tic severity (YGTSS)

237 Results for the primary outcome are presented in Table 1, Figure 1 and Figure S1 (see supplementary 238 materials). Improvements in Global, Total and Motor YGTSS scores were statistically significant 239 (p<.05) with moderate to large effect sizes. Reliable improvement on the YGTSS Global score was 240 seen in 7/20 (35%) of the sample. 2/20 (10%) showed reliable deterioration. One of these children is 241 described in supplementary materials 1.4 (case 2). The other experienced a significant life event 242 between the last session and the booster, which may have contributed to his deterioration. At follow-243 up, 9/20 (45%) of participants were classed as 'treatment responders' (defined as 25% reduction in tics 244 on YGTSS Total Tic Severity scale).

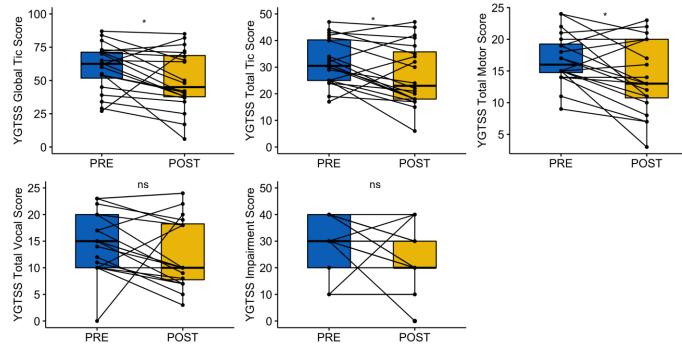
# 245 3.2.2 Secondary – quality of life (GTS QOL) and patient rated goal-based outcomes (GBO)

Results for the secondary outcomes are presented in Tables 2 and 3 and Figures S2-S5(see supplementary materials). Patient-reported life satisfaction, (GTS QOL satisfaction score), demonstrated an improvement from a mean score of 64.7 (25.55) pre-intervention (t0) to 76.8 (15.63) at follow-up (t2), a statistically significant increase of 12.1, 95% CI [2.37; 21.83], t(19) = 4.99, p=.017, d=0.58. Improvements on all other subscales did not reach statistical significance, with effect sizes mostly in the 'small' range. Reliable improvement on the GTS QOL Total score was seen in 3/20 (15%) of the sample. 1/20 (5%) showed reliable deterioration.

253 All child and parent-reported GBO scores showed median increases (implying patients reported being 254 closer to their therapeutic goal following treatment) from t0 - t1 and t0 - t2. All child GBOs and parent 255 GBO 3 showed a small decrease from t1 - t2, the period post the group ending to follow-up. The mean 256 increases in goal ratings from t0 - t2 were 3.72 (self-reported) and 3.51 (parent-reported). This 257 compares to a mean increase in goal ratings of 3.73 (self-reported) and 3.7 (parent-reported) in the 258 CYP-IAPT study (Wolpert et al., 2016; median increases in GBOs were not available for 259 benchmarking, which is why mean difference scores are reported here). Reliable improvement between 260 t0 and t2, was seen in 14/20 (70%) for child-rated GBOs and 15/20 (75%) for parent-rated GBOs (using 261 averaged GBO 1, GBO 2 and GBO 3 scores where available for each rater). None showed reliable 262 deterioration between t0 and t2.

263

#### Intensive group ERP feasibility study



264PREPOSTPREPOST265Figure 1. Change in tic severity pre and post-intervention on the Yale Global Tic Severity266Scale's (YGTSS) Global Severity Score and YGTSS Subscales (Total Tic, Motor, Vocal and267Impairment Scores)

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	tO	t2			
	All (n=20)	All (n=20)		r (CI)	
	median (IQR)	median (IQR)	р		
YGTSS - Motor	16 (14.25 - 19.75)	13 (10.25 - 20)	.010*	0.54 (0.16, 0.80)	
YGTSS - Vocal	15 (10 - 20)	10 (7.25 - 18.75)	.064	0.43 (0.05, 0.83)	
YGTSS - Total	30.5 (25 - 30.75)	23 (18 - 37.25)	.033*	0.48 (0.10, 0.82)	
YGTSS - Impairment	30 (20 - 40)	20 (20 - 30)	.065	0.44 (0.07, 0.76)	
YGTSS - Global	62.5 (47.25 - 71.75)	45 (37.25 - 70.25)	.012*	0.56 (0.23, 0.88)	

270 **Table 1.** Median score (interquartile range) by time point and effect sizes for YGTSS subscales.

271 Note: \* p<.05;

Effect sizes were computed using the r value; 0.1 - <0.3 (small effect), 0.3 - <0.5 (moderate effect) and  $\ge 0.5$  (large effect).

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Table 2. Mean difference scores (time 0 – time 2), paired samples t-tests results and effect sizes (Cohen's d) for GTS QOL subscales.

	t0	t2				
	All (n=20)	All (n=20)				
	Mean (SD)	Mean (SD)	mean difference (CI)	t	р	d (CI)
GTS QOL Satisfaction <sup>1</sup>	64.7 (25.55)	76.8 (15.63)	-12.1 (-21.83 ; -2.37)	-2.60	.017*	0.58 (0.09, 1.07)
GTS QOL Psychological	22.25 (11.39)	19.5 (11.48)	2.75 (-0.81; 6.31)	1.62	.123	0.36 (-0.11, 0.83)
GTS QOL Physical	13.55 (7.49)	12.15 (7.48)	1.4 (-0.31 ; 3.11)	1.72	.102	0.38 (-0.09, 0.85)
GTS QOL OCD	8.15 (5.08)	7.6 (4.63)	0.55 (-1.4 ; 2.5)	0.59	.563	0.13 (-0.32, 0.59)
GTS QOL Cog	8 (4.23)	7.15 (3.94)	0.85 (-0.66 ; 2.36)	1.18	.252	0.26 (-0.20, 0.72)
GTS QOL Total	51.95 (26.13)	46.85 (25.79)	5.1 (-1.94 ; 12.14)	1.52	.146	0.34 (-0.13, 0.81)

277 Note: \* p<.05;

278 Effect sizes were computed using Cohen's d; 0.2 - <0.5 (small effect), 0.5 - <0.8 (moderate effect) and  $\ge 0.8$  (large effect).

<sup>&</sup>lt;sup>1</sup> Scored in the opposite direction to the specific subscales, where a higher score indicates greater satisfaction

	t0		t1 All (n=20)		t2	
	All (n=20	)			All (n=20)	
Measure	n	median (IQR)	n	median (IQR)	n	median (IQR)
Child GBO 1	20	5 (1-6)	20	8 (6-9)	20	7 (6-9)
Child GBO 2	19	4 (2-5)	19	9 (8-10)	19	8 (5-10)
Child GBO 3	13	4 (1-5)	13	10 (9-10)	13	9 (7-10)
Parent GBO 1	20	2 (1-4)	20	7 (4-9)	20	7 (5-7)
Parent GBO 2	19	2 (1-4)	19	6 (4-8)	19	6 (3-7)
Parent GBO 3	14	3 (2-3)	14	7 (3-8)	14	5 (3-6)

**Table 3.** Descriptive statistics by time point for parent and child GBOs.

#### 281 *3.3 Qualitative Feedback*

Overall, responses from the feedback questionnaire suggested high levels of acceptability (see Figures S6 and S7 in the supplementary material). The majority of young people described the group as enjoyable, useful and effective and stated they would recommend it to a friend. 80% of young people had no suggestions for future improvements according to free text questions.

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### **4. Discussion**

The current study is unique in examining whether an established manualised evidence-based ERP 288 protocol, developed for individual therapy, maintains efficacy when delivered in an intensive group 289 290 format. We found positive treatment outcomes with an overall large effect size (r = 0.56) for the YGTSS Global severity score. Thirty-five percent of participants achieved reliable improvement with 291 292 45% showing clinically meaningful change overall. These findings align with previous trials using a 293 clinically developed ERP group treatment, which showed positive effects of a similar magnitude 294 (Heijerman-Holtgrefe et al., 2021). Our data show an adapted group intensive delivery of an evidence-295 based manualised ERP intervention for tics is effective and feasible. ERP has potential advantages over 296 the CBITs protocol as all tics are treated simultaneously rather than one by one as in the CBITs 297 approach. Therefore, an ERP group could offer efficiencies on a number of dimensions. Clinicians less experienced in tic treatment delivery may find these data useful as it suggests an existing ERP 298 299 manualised treatment can be used 'off the shelf' in intensive treatment groups, an important 300 consideration given the current treatment bottleneck.

301 There was a marked improvement in motor tics and though there was a moderate effect size 302 improvement in vocal tics, it did not reach statistical significance, reflecting a pattern in previous 303 CBITS (Yates et al., 2016) and ERP TS groups (Heijerman-Holtgrefe et al., 2021), but this may be a 304 reflection of the group tic profile (Yates et al., 2016). While impairment and most QoL scores did not 305 improve significantly as a result of the group, this may be due to the complexity of the group recruited. 306 The population of children recruited had high levels of co-occurring conditions alongside tics, which 307 are commonly described as more impactful on OoL than tics themselves (Atkinson-Clement et al., 308 2022) and may have impacted impairment ratings. Although the samples were too small to test for statistical difference, on visual inspection of the data, the first group appeared to have better outcomes 309 310 (see Figures S1 and S3 in supplementary materials). Similar differences comparing children 311 participating in a group intervention at different times of the year were found by Yates and colleagues (2016), who hypothesised this was due to one group coinciding with the return to school, which some 312 participants found stressful and may have impacted on QoL. Similarly, in our study the first group was 313 314 carried out in July, during the summer, whereas the second was carried out in November, where young 315 people were in school and may have been experiencing additional stressors. Though tics are suggestible 316 for young people with existing tics, there was no clear evidence participants' tics increased following 317 exposure to other young people's tics in the group, providing reassurance to families who might be 318 concerned about this (Woods et al., 2010). Overall QOL 'satisfaction' improved following treatment 319 and, while physical aspects on the QOL measure improved they did not reach significance. Heijerman-320 Holtgrefe et al. (2021) reported an improvement on the summed QOL subscales of the same QOL 321 measure but neither individual subscale nor 'satisfaction' scores were reported. In broad terms, the message is similar across both studies: improvements in both tic profile and QoL following treatment. 322 323 These outcomes might be considered cornerstones of viable treatment for the TS population.

324 All participants described getting closer to reaching their therapeutic goal following the group, and 325 70% reached threshold for a reliable change on GBOs. The magnitude of change was similar to reports 326 from CAMHS nationwide studies (CYP-IAPT study; Wolpert et al., 2016). The study's low attrition 327 and high attendance rates also suggest acceptability and feasibility of the group intervention. As is true 328 for any TS behavioural treatment (Capriotti et al., 2014) intensive group treatment was not universally 329 effective (55% did not show clinically meaningful change), and for some children, may not be 330 appropriate. Possible reasons for this are discussed in more detail by Heijerman-Holtgrefe and 331 colleagues (2021) and include reduced time to practise in between sessions compared to individual 332 treatment and less flexibility/time to address a child's individual difficulties.

333 The results on the primary outcome measure are promising, nonetheless, it is important to consider the 334 study's limitations. This is a small study with no control group, randomisation or blinding. Participants 335 were all children and adolescents with mild to severe TS symptoms and complex comorbidities typical 336 of the wider TS population (Eapen et al., 2004). Still, our centre is more likely to manage relatively 337 complex cases given its tertiary referral status. Showing a positive response in a relatively complex 338 group, is likely to indicate the treatment protocol will be effective (and possibly more so) in TS 339 populations in community services. The 4 week follow-up period may inadvertently capture natural 340 course fluctuations (Roessner et al., 2011), and longer follow-up studies are needed. While careful 341 attention was paid to the treatment protocol described by (Verdellen et al., 2011), we did not use a 342 fidelity checklist, similar to those used in previous studies (Sukhodolsky et al., 2009).

Replication of the study with a larger sample as an RCT - including a health economic analysis - is warranted. It is possible non-specific group factors such as social support, feeling accepted or reducing stigma had a generalised positive effect on well-being which could theoretically indirectly impact on tic profiles. These non-specific group effects are important to explore as "fitting in with peers" is a key factor influencing QOL in children with TS (Cutler et al., 2009). Such effects are discussed elsewhere in an RCT comparing psychoeducation and HRT treatment groups in a TS population (Yates et al., 2016).

350 This study provides promising indications that a manualised ERP tic treatment developed for individual

therapy can be delivered in an intensive group format as an acceptable, feasible and effective option,

352 offering increased accessibility to treatment, reducing tic severity and improving quality of life for

353 young people with TS.

### 354 **References**

- Andren, P., Jakubovski, E., Murphy, T. L., Woitecki, K., Tarnok, Z., Zimmerman-Brenner, S., van de
  Griendt, J., Debes, N. M., Viefhaus, P., Robinson, S., Roessner, V., Ganos, C., Szejko, N.,
  Muller-Vahl, K. R., Cath, D., Hartmann, A., & Verdellen, C. (2022). European clinical
  guidelines for Tourette syndrome and other tic disorders-version 2.0. Part II: psychological
  interventions. *Eur Child Adolesc Psychiatry*, *31*(3), 403-423. <a href="https://doi.org/10.1007/s00787-021-01845-z">https://doi.org/10.1007/s00787-021-01845-z</a>
- Andren, P., Wachtmeister, V., Franze, J., Speiner, C., Fernandez de la Cruz, L., Andersson, E., de
   Schipper, E., Rautio, D., Silverberg-Morse, M., Serlachius, E., & Mataix-Cols, D. (2021).
   Effectiveness of Behaviour Therapy for Children and Adolescents with Tourette Syndrome
   and Chronic Tic Disorder in a Naturalistic Setting. *Child Psychiatry Hum Dev*, 52(4), 739 <u>https://doi.org/10.1007/s10578-020-01098-y</u>
- APA. (2013). *Diagnostic and statistical manual of mental disorders, 5th ed.* . American Psychiatric
   Association. <u>https://doi.org/10.1176/appi.books.9780890425596</u>
- Atkinson-Clement, C., Duflot, M., Lastennet, E., Patsalides, L., Wasserman, E., Sartoris, T. M.,
  Tarrano, C., Rosso, C., Burbaud, P., Deniau, E., Czernecki, V., Roze, E., Hartmann, A., &
  Worbe, Y. (2022). How does Tourette syndrome impact adolescents' daily living? A text
  mining study. *Eur Child Adolesc Psychiatry*. https://doi.org/10.1007/s00787-022-02116-1
- Azrin, N. H., & Nunn, R. G. (1973). Habit-reversal: a method of eliminating nervous habits and tics.
   *Behav Res Ther*, *11*(4), 619-628. <u>https://doi.org/10.1016/0005-7967(73)90119-8</u>
- Blount, T. H., Lockhart, A. L., Garcia, R. V., Raj, J. J., & Peterson, A. L. (2014). Intensive outpatient
  comprehensive behavioral intervention for tics: A case series. *World J Clin Cases*, 2(10), 569577. https://doi.org/10.12998/wjcc.v2.i10.569
- Blount, T. H., Raj, J. J., & Peterson, A. L. (2018). Intensive Outpatient Comprehensive Behavioral
   Intervention for Tics: A Clinical Replication Series. *Cognitive and Behavioral Practice*,
   25(1), 156-167. <u>https://doi.org/10.1016/j.cbpra.2017.02.001</u>
- Breitenstein, S. M., Gross, D., Garvey, C. A., Hill, C., Fogg, L., & Resnick, B. (2010).
   Implementation fidelity in community-based interventions. *Res Nurs Health*, *33*(2), 164-173.
   <a href="https://doi.org/10.1002/nur.20373">https://doi.org/10.1002/nur.20373</a>
- Capriotti, M. R., Himle, M. B., & Woods, D. W. (2014). Behavioral Treatments for Tourette
   Syndrome. *J Obsessive Compuls Relat Disord*, *3*(4), 415-420.
   <u>https://doi.org/10.1016/j.jocrd.2014.03.007</u>
- Carroll, C., Patterson, M., Wood, S., Booth, A., Rick, J., & Balain, S. (2007). A conceptual
   framework for implementation fidelity. *Implement Sci*, 2, 40. <u>https://doi.org/10.1186/1748-</u>
   <u>5908-2-40</u>
- Chen, C. W., Wang, H. S., Chang, H. J., & Hsueh, C. W. (2020). Effectiveness of a modified
  comprehensive behavioral intervention for tics for children and adolescents with tourette's
  syndrome: A randomized controlled trial. *J Adv Nurs*, 76(3), 903-915.
  https://doi.org/10.1111/jan.14279

- Cohen, J. (2013). Statistical Power Analysis for the Behavioral Sciences. Routledge.
   <u>https://doi.org/https://doi.org/10.4324/9780203771587</u>
- Cole, F. L. (1988). Content analysis: process and application. *Clin Nurse Spec*, 2(1), 53-57.
   <u>https://doi.org/10.1097/00002800-198800210-00025</u>
- 401 Cubo, E., Gonzalez, C., Ausin, V., Delgado, V., Saez, S., Calvo, S., Garcia Soto, X., Cordero, J.,
  402 Kompoliti, K., Louis, E. D., & de la Fuente Anuncibay, R. (2017). The Association of Poor
  403 Academic Performance with Tic Disorders: A Longitudinal, Mainstream School-Based
  404 Population Study. *Neuroepidemiology*, 48(3-4), 155-163. <u>https://doi.org/10.1159/000479517</u>
- Cutler, D., Murphy, T., Gilmour, J., & Heyman, I. (2009). The quality of life of young people with
   Tourette syndrome. *Child Care Health Dev*, 35(4), 496-504. <u>https://doi.org/10.1111/j.1365-</u>
   2214.2009.00983.x
- Eapen, V., Cavanna, A. E., & Robertson, M. M. (2016). Comorbidities, Social Impact, and Quality of
   Life in Tourette Syndrome. *Front Psychiatry*, 7, 97. <u>https://doi.org/10.3389/fpsyt.2016.00097</u>
- 410 Eapen, V., Fox-Hiley, P., Banerjee, S., & Robertson, M. (2004). Clinical features and associated
  411 psychopathology in a Tourette syndrome cohort. *Acta Neurol Scand*, *109*(4), 255-260.
  412 <u>https://doi.org/10.1046/j.1600-0404.2003.00228.x</u>
- Edbrooke-Childs, J., Jacob, J., Law, D., Deighton, J., & Wolpert, M. (2015). Interpreting
  standardized and idiographic outcome measures in CAMHS: what does change mean and
  how does it relate to functioning and experience? *Child Adolesc Ment Health*, 20(3), 142-148.
  <u>https://doi.org/10.1111/camh.12107</u>
- Flancbaum, M., Rockmore, L., & Franklin, M. E. (2010). Intensive Behavior Therapy for Tics:
  Implications for Clinical Practice and Overcoming Barriers to Treatment. *Journal of Developmental and Physical Disabilities*, 23(1), 61-69. <u>https://doi.org/10.1007/s10882-010-</u>
  9222-0
- 421 Fritz, C. O., Morris, P. E., & Richler, J. J. (2012). Effect size estimates: current use, calculations, and
  422 interpretation. *J Exp Psychol Gen*, 141(1), 2-18. <u>https://doi.org/10.1037/a0024338</u>
- Heijerman-Holtgrefe, A. P., Verdellen, C. W. J., van de Griendt, J., Beljaars, L. P. L., Kan, K. J.,
  Cath, D., Hoekstra, P. J., Huyser, C., & Utens, E. (2021). Tackle your Tics: pilot findings of a
  brief, intensive group-based exposure therapy program for children with tic disorders. *Eur Child Adolesc Psychiatry*, *30*(3), 461-473. <u>https://doi.org/10.1007/s00787-020-01532-5</u>
- Hirschtritt, M. E., Lee, P. C., Pauls, D. L., Dion, Y., Grados, M. A., Illmann, C., King, R. A., Sandor,
  P., McMahon, W. M., Lyon, G. J., Cath, D. C., Kurlan, R., Robertson, M. M., Osiecki, L.,
  Scharf, J. M., Mathews, C. A., & Tourette Syndrome Association International Consortium
  for, G. (2015). Lifetime prevalence, age of risk, and genetic relationships of comorbid
  psychiatric disorders in Tourette syndrome. *JAMA Psychiatry*, 72(4), 325-333.
  https://doi.org/10.1001/jamapsychiatry.2014.2650
- Hollis, C., Pennant, M., Cuenca, J., Glazebrook, C., Kendall, T., Whittington, C., Stockton, S.,
  Larsson, L., Bunton, P., Dobson, S., Groom, M., Hedderly, T., Heyman, I., Jackson, G. M.,
  Jackson, S., Murphy, T., Rickards, H., Robertson, M., & Stern, J. (2016). Clinical
  effectiveness and patient perspectives of different treatment strategies for tics in children and
  adolescents with Tourette syndrome: a systematic review and qualitative analysis. *Health Technol Assess*, 20(4), 1-450, vii-viii. https://doi.org/10.3310/hta20040

- Jacobson, N. S., & Truax, P. (1991). Clinical significance: a statistical approach to defining
   meaningful change in psychotherapy research. *J Consult Clin Psychol*, 59(1), 12-19.
   https://doi.org/10.1037//0022-006x.59.1.12
- Jeon, S., Walkup, J. T., Woods, D. W., Peterson, A., Piacentini, J., Wilhelm, S., Katsovich, L.,
  McGuire, J. F., Dziura, J., & Scahill, L. (2013). Detecting a clinically meaningful change in
  tic severity in Tourette syndrome: a comparison of three methods. *Contemp Clin Trials*,
  36(2), 414-420. https://doi.org/10.1016/j.cct.2013.08.012
- Knight, T., Steeves, T., Day, L., Lowerison, M., Jette, N., & Pringsheim, T. (2012). Prevalence of tic
  disorders: a systematic review and meta-analysis. *Pediatr Neurol*, 47(2), 77-90.
  <u>https://doi.org/10.1016/j.pediatrneurol.2012.05.002</u>
- Law, D., & Wolpert, M. (2014). Guide to using outcomes and feedback tools with children, young
   *people and families*. C. Press.
   <u>https://www.corc.uk.net/media/1950/201404guide\_to\_using\_outcomes\_measures\_and\_feedb</u>
   ack\_tools-updated.pdf
- Leckman, J. F., Riddle, M. A., Hardin, M. T., Ort, S. I., Swartz, K. L., Stevenson, J., & Cohen, D. J.
  (1989). The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic
  severity. *J Am Acad Child Adolesc Psychiatry*, 28(4), 566-573.
  https://doi.org/10.1097/00004583-198907000-00015
- Lieberman, M. D. (2012). Education and the social brain. *Trends in Neuroscience and Education*, *1*(1), 3-9. <u>https://doi.org/10.1016/j.tine.2012.07.003</u>
- McFarlane, F. A., Allcott-Watson, H., Hadji-Michael, M., McAllister, E., Stark, D., Reilly, C.,
  Bennett, S. D., McWillliams, A., & Heyman, I. (2019). Cognitive-behavioural treatment of
  functional neurological symptoms (conversion disorder) in children and adolescents: A case
  series. *Eur J Paediatr Neurol*, 23(2), 317-328. <u>https://doi.org/10.1016/j.ejpn.2018.12.002</u>
- McGuire, J. F., Piacentini, J., Brennan, E. A., Lewin, A. B., Murphy, T. K., Small, B. J., & Storch, E.
  A. (2014). A meta-analysis of behavior therapy for Tourette Syndrome. *J Psychiatr Res*, 50, 106-112. <u>https://doi.org/10.1016/j.jpsychires.2013.12.009</u>
- McGuire, J. F., Ricketts, E. J., Piacentini, J., Murphy, T. K., Storch, E. A., & Lewin, A. B. (2015).
  Behavior Therapy for Tic Disorders: An Evidenced-based Review and New Directions for
  Treatment Research. *Curr Dev Disord Rep*, 2(4), 309-317. <u>https://doi.org/10.1007/s40474-</u>
  015-0063-5
- 470 Meyer, V. (1966). Modification of expectations in cases with obsessional rituals. *Behav Res Ther*,
  471 4(4), 273-280. <u>https://doi.org/10.1016/0005-7967(66)90023-4</u>
- 472 Mihalic, S. (2004). The Importance of Implementation Fidelity. *Report on Emotional & Behavioral*473 *Disorders in Youth*, 04, 83-90.
  474 https://civicresearchinstitute.com/online/article\_abstract.php?pid=5&iid=176&aid=1192
- 474 <u>https://civicresearchinstitute.com/online/article\_abstract.php?pid=5&iid=176&aid=1192</u>
  475 Mumbu T & Hayman L (2007) Crown Work in Young Boople with Tourstte Syndrome. *Child*
- Murphy, T., & Heyman, I. (2007). Group Work in Young People with Tourette Syndrome. *Child Adolesc Ment Health*, *12*(1), 46-48. <u>https://doi.org/10.1111/j.1475-3588.2006.00427.x</u>
- Nissen, J. B., Carlsen, A. H., & Thomsen, P. H. (2021). One-year outcome of manualised behavior
  therapy of chronic tic disorders in children and adolescents. *Child Adolesc Psychiatry Ment Health*, 15(1), 9. <u>https://doi.org/10.1186/s13034-021-00362-w</u>
- Nissen, J. B., Kaergaard, M., Laursen, L., Parner, E., & Thomsen, P. H. (2019). Combined habit
   reversal training and exposure response prevention in a group setting compared to individual

- 482 training: a randomized controlled clinical trial. *Eur Child Adolesc Psychiatry*, 28(1), 57-68.
  483 <u>https://doi.org/10.1007/s00787-018-1187-z</u>
- Nussey, C., Pistrang, N., & Murphy, T. (2014). Does it help to talk about tics? An evaluation of a
   classroom presentation about Tourette syndrome. *Child Adolesc Ment Health*, *19*(1), 31-38.
   <u>https://doi.org/10.1111/camh.12000</u>
- 487 Roessner, V., Plessen, K. J., Rothenberger, A., Ludolph, A. G., Rizzo, R., Skov, L., Strand, G., Stern,
  488 J. S., Termine, C., Hoekstra, P. J., & Group, E. G. (2011). European clinical guidelines for
  489 Tourette syndrome and other tic disorders. Part II: pharmacological treatment. *Eur Child*490 *Adolesc Psychiatry*, 20(4), 173-196. <u>https://doi.org/10.1007/s00787-011-0163-7</u>
- 491 Storch, E. A., Murphy, T. K., Geffken, G. R., Sajid, M., Allen, P., Roberti, J. W., & Goodman, W. K.
  492 (2005). Reliability and validity of the Yale Global Tic Severity Scale. *Psychol Assess*, *17*(4),
  493 486-491. <u>https://doi.org/10.1037/1040-3590.17.4.486</u>
- Su, M. T., McFarlane, F., Cavanna, A. E., Termine, C., Murray, I., Heidemeyer, L., Heyman, I., &
  Murphy, T. (2017). The English Version of the Gilles de la Tourette Syndrome-Quality of
  Life Scale for Children and Adolescents (C&A-GTS-QOL). *J Child Neurol*, *32*(1), 76-83.
  <u>https://doi.org/10.1177/0883073816670083</u>
- Sukhodolsky, D. G., Vitulano, L. A., Carroll, D. H., McGuire, J., Leckman, J. F., & Scahill, L.
  (2009). Randomized trial of anger control training for adolescents with Tourette's syndrome and disruptive behavior. *J Am Acad Child Adolesc Psychiatry*, 48(4), 413-421.
  <u>https://doi.org/10.1097/CHI.0b013e3181985050</u>
- Tallur, K., & Minns, R. A. (2010). Tourette's syndrome. *Paediatrics and Child Health*, 20(2), 88-93.
   <u>https://doi.org/10.1016/j.paed.2009.10.010</u>
- Verdellen, C., Van de Griendt, J., Kriens, S., & Van Oostrum, I. (2011). *Tics Therapist manual & workbook for children*. Uitgeverij Boom.
- Verdellen, C. W., Keijsers, G. P., Cath, D. C., & Hoogduin, C. A. (2004). Exposure with response
   prevention versus habit reversal in Tourettes's syndrome: a controlled study. *Behav Res Ther*,
   42(5), 501-511. <u>https://doi.org/10.1016/S0005-7967(03)00154-2</u>
- Whiteside, S. P. H., Dammann, J. E., Tiede, M. S., Biggs, B. K., & Hillson Jensen, A. (2018).
  Increasing Availability of Exposure Therapy Through Intensive Group Treatment for
  Childhood Anxiety and OCD. *Behav Modif*, 42(5), 707-728.
  https://doi.org/10.1177/0145445517730831
- Wolpert, M., Jenna, J., Napoleone, E., Whale, A., Calderon, A., & Edbrooke-Childs, J. (2016). *Child and parent reported outcomes and experience from child and young people's mental health services 2011 2015*. C. Press. <u>https://www.corc.uk.net/child-and-parent-reported-outcomes-</u>
  and-experience-from-child-and-young-peoples-mental-health-services-2011-2015/
- Woods, D. W., Conelea, C. A., & Himle, M. B. (2010). Behavior therapy for Tourette's disorder:
  Utilization in a community sample and an emerging area of practice for psychologists. *Professional Psychology: Research and Practice*, 41(6), 518-525.
  <u>https://doi.org/10.1037/a0021709</u>
- Woods, D. W., Piacentini, J., Chang, S., Deckersbach, T., Ginsburg, G., Peterson, A., Scahill, L. D.,
  Walkup, J. T., & Wilhelm, S. (2008). *Managing Tourette Syndrome*. https://doi.org/10.1093/med:psych/9780195341287.001.0001

- Yates, R., Edwards, K., King, J., Luzon, O., Evangeli, M., Stark, D., McFarlane, F., Heyman, I., Ince,
  B., Kodric, J., & Murphy, T. (2016). Habit reversal training and educational group treatments
  for children with tourette syndrome: A preliminary randomised controlled trial. *Behav Res Ther*, 80, 43-50. <u>https://doi.org/10.1016/j.brat.2016.03.003</u>
- Yeager, D. S., Dahl, R. E., & Dweck, C. S. (2018). Why Interventions to Influence Adolescent
   Behavior Often Fail but Could Succeed. *Perspect Psychol Sci*, 13(1), 101-122.
   https://doi.org/10.1177/1745691617722620
- Zimmerman-Brenner, S., Pilowsky-Peleg, T., Rachamim, L., Ben-Zvi, A., Gur, N., Murphy, T.,
   Fattal-Valevski, A., & Rotstein, M. (2021). Group behavioral interventions for tics and
   comorbid symptoms in children with chronic tic disorders. *Eur Child Adolesc Psychiatry*.
   <u>https://doi.org/10.1007/s00787-020-01702-5</u>

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