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1 Cost-effectiveness analysis of telephone cognitive-behaviour therapy for adolescents with  
2 obsessive-compulsive disorder

3

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6

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10

11 **Abstract**

12 **Background:** Telephone cognitive-behaviour therapy (TCBT) may be a cost-effective  
13 method for improving access to evidence-based treatment for obsessive-compulsive disorder  
14 (OCD) in young people.

15 **Aims:** Economic evaluation of TCBT compared to face-to-face CBT for OCD in young  
16 people.

17 **Method:** Randomised non-inferiority trial comparing TCBT to face-to-face CBT for 72  
18 young people (aged 11 to 18) with a diagnosis of OCD. Cost-effectiveness at 12-month  
19 follow-up was explored in terms of the primary clinical outcome (CY-BOCS) and quality-  
20 adjusted life-years (QALYs).

21 **Results:** Total health and social care costs were higher for face-to-face CBT (mean total cost  
22 £2965, SD £1548) than TCBT (mean total cost £2475, SD £1024) but this difference was  
23 non-significant ( $p=0.118$ ). There were no significant between-group differences in QALYs or  
24 the CY-BOCS and there was strong evidence to support the clinical non-inferiority of TCBT.  
25 Cost-effectiveness analysis suggests a 74% probability that face-to-face CBT is cost-effective  
26 compared to TCBT in terms of QALYs, but the result was less clear in terms of CY-BOCS,  
27 with TCBT being the preferred option at low levels of willingness to pay and the probability  
28 of either intervention being cost-effective at higher levels of willingness to pay being around  
29 50%.

30 **Conclusions:** Although cost-effectiveness of TCBT was sensitive to the outcome measure  
31 used, TCBT should be considered a clinically non-inferior alternative when access to  
32 standard clinic-based CBT is limited, or when patient preference is expressed.

33 **Declaration of interest**

34 Prof. Mataix-Cols reports research grants from the Swedish Research Council  
35 (Vetenskapsrådet), the Swedish Research Council for Health, working life and welfare

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37 Health Research (NIHR), as well as royalties from Wolters Kluwer Health and Elsevier, all  
38 unrelated to the submitted work. All other authors report no conflicts of interest.

39

40

41 **Introduction**

42 Obsessive-compulsive disorder (OCD) is a serious and disabling disorder which often begins  
43 in childhood.<sup>1,2</sup> OCD causes significant disruption to the child's academic, family and social  
44 life, and impairs the child's cognitive and psychosocial development.<sup>2-4</sup> Because OCD is  
45 often a chronic condition, it imposes substantial long-term economic and social burdens at  
46 both the individual and national levels.<sup>5,6</sup> The direct (\$2.1 billion) and indirect costs (\$6.2  
47 billion) of OCD was estimated to be \$8.4 billion a year in 1990 USD prices, accounting for  
48 5.7% of the costs of all mental illnesses.<sup>5</sup> In the UK, the total costs of anxiety disorders  
49 (service costs and lost earnings), including OCD, was projected to be £14.2 billion (at 2007  
50 prices) in 2026.<sup>6</sup> Despite the well-documented effectiveness of cognitive-behaviour therapy  
51 (CBT) in treating this patient group,<sup>7</sup> under-diagnosis and under-treatment are common,  
52 partly due to inequalities in access to treatment.<sup>8-11</sup> Following the call from the National  
53 Service Framework for Mental Health to improve accessibility of effective treatments for  
54 common mental health problems,<sup>12</sup> alternative treatment modalities using current  
55 technologies such as telephone and computer are increasingly being researched and  
56 developed.<sup>10,13</sup> Evidence in adult OCD suggests that telephone CBT (TCBT) shows  
57 promising advantages over face-to-face CBT in terms of reduced service and patient costs,  
58 and improved accessibility and convenience.<sup>14-16</sup> This study reports the results of an  
59 economic evaluation of TCBT in a group of young people with OCD carried out alongside a  
60 randomised controlled trial.<sup>17</sup>

61

62 **Method**

63 *Hypothesis*

64 The economic aim of the trial was to compare the cost-effectiveness of TCBT with face-to-  
65 face CBT in treating young people with OCD. We hypothesised that TCBT would be cost-  
66 effective at a service level compared to face-to-face CBT.

67

68 *Trial design*

69 Participants were recruited by referral from primary care general practitioners, and from  
70 mental health professionals within secondary and tertiary care settings within the National  
71 Health Service (NHS) to a specialist OCD clinic between 2008 and 2011. Information about  
72 the study was conveyed by word of mouth, letter to referring agencies, advertisements  
73 published on webpages of national OCD charities within the UK, and by a research support  
74 organisation within the NHS (the Mental Health Research Network).

75

76 Inclusion criteria were: (a) primary OCD according to DSM-IV criteria,<sup>18</sup> (b) a Children's  
77 Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)<sup>19</sup> score of 16 or greater, indicating  
78 moderate to severe impairment, (c) aged 11 to 18 years; (d) medication free or on a stable  
79 dose of medication for a period of 12 weeks or greater, (e) no suicidal intent, drug or alcohol  
80 abuse, or psychotic symptoms, (f) no learning disability or pervasive developmental  
81 disability, (g) need and want CBT, and agreeable to randomisation, and (h) agreeable to  
82 parental involvement in treatment. Exclusion criteria were: (a) current diagnosis of  
83 psychosis, current alcohol or substance abuse/dependence, (b) English too poor to engage in  
84 treatment, (c) severe disabling neurological disorder, (d) diagnosed global learning disability  
85 or pervasive developmental delay, and (e) characteristics interfering with completion of  
86 treatment within trial (e.g. a life-threatening or unstable medical illness).

87

88 After initial clinical assessments, eligible participants attended a second clinic appointment  
89 approximately 8 weeks later. Participants who remained symptomatic were randomised to  
90 CBT or TCBT in a 1:1 ratio using a computer-generated randomisation sequence prepared  
91 before the study commenced. There were no restrictions or matching. A repeated measures  
92 design was used and assessments were conducted immediately before treatment (i.e.,  
93 baseline), immediately after treatment (i.e., post-treatment), and at follow-up points  
94 scheduled at 3-months, 6-months, and 12-months post-treatment.

95

#### 96 ***Ethics statement***

97 The study protocol was approved by the Joint South London and Maudsley / Institute of  
98 Psychiatry Research Ethics Committee (08/H0807/12).

99

#### 100 ***Consent statement***

101 Written informed consent was obtained from all parents and participants over 16 years, and  
102 informed assent from participants under 16 years after a detailed description of the study had  
103 been given.

104

#### 105 ***Clinical trials registration number***

106 The trial was registered on the International Standard Randomized Controlled Trial Number  
107 Register (ISRCTN27070832).

108

#### 109 ***Interventions***

110 Treatment consisted of 14 sessions of CBT, lasting approximately 60 minutes, delivered by  
111 six experienced clinical psychologists following a detailed treatment manual. Treatment was

112 identical within conditions except that participants randomised to TCBT received all  
113 treatment sessions via telephone. Sessions 1-2 consisted of psycho-education, sessions 3-12  
114 consisted of graduated exposure with response prevention (E/RP) and incorporated various  
115 cognitive strategies as appropriate, sessions 13-14 consisted of relapse prevention and  
116 ongoing symptom management (if required). The treatment protocol incorporated 10 minutes  
117 of parental discussion at the end of each treatment session. Homework E/RP tasks were  
118 assigned between sessions and participants were encouraged to complete daily E/RP. The  
119 treatment protocol has been validated in previous trials.<sup>20,21</sup> All 14 sessions were required to  
120 be completed within 17 weeks, allowing illness, missed appointments, or holidays to be  
121 accommodated. Treating therapists received supervision by senior clinical psychologists who  
122 were specialists in CBT for OCD and all sessions (wherever possible) were audio recorded. A  
123 random sample of n=225 (25%) recorded sessions were audited and independently rated for  
124 integrity to protocol. The rate of adherence to the manual was 93% and there were no  
125 differences in adherence ratings between conditions.<sup>17</sup>

126

### 127 ***Outcomes***

128 Research assessments were completed in face-to-face interviews at baseline, post-treatment,  
129 3-months, 6-months and 12-months post-treatment. The primary outcome measure for the  
130 economic evaluation was the Children's Yale-Brown Obsessive-Compulsive Scale (CY-  
131 BOCS),<sup>19</sup> which was administered by an independent clinician blinded to treatment  
132 condition. CY-BOCS is a detailed semi-structured clinician administered interview,  
133 incorporating a 10-item inventory of paediatric OCD symptoms severity, and is comprised of  
134 an obsession severity score and compulsion severity score. Using a 5-point scale for each  
135 item (score 0 to 4), the total scores range from 0 to 40, where higher scores indicate worse  
136 outcomes. The CY-BOCS has demonstrated robust psychometric properties, with good



137 internal consistency, convergent and divergent validity reported<sup>19</sup> and has been shown to  
138 respond to change.

139

140 Secondary analysis explored cost-effectiveness in terms of quality-adjusted life years  
141 (QALYs), using the self-report EQ-5D-3L (5 dimensions, 3 levels) measure of health-related  
142 quality of life.<sup>22</sup> The EQ-5D is a generic questionnaire that assesses health-related quality of  
143 life on five dimensions including mobility, self-care, usual activities, pain/discomfort, and  
144 anxiety/depression. Each dimension has three levels, leading to a total of 243 possible health  
145 states, each of which is associated with a score used to calculate QALYs. The questionnaire  
146 also contains a visual analogue scale (VAS) which enables participants to rate their current  
147 health state between zero (worst imaginable health state) and 100 (best imaginable health  
148 state).

149

150 Being a generic health state measure, the EQ-5D allows policy makers to make comparisons,  
151 and most importantly, resource allocation decisions, across competing interventions within  
152 the same patient group or more broadly across different disease areas and populations. The  
153 EQ-5D is used extensively in economic evaluations of mental health disorders, despite a lack  
154 of evidence to support the relevance and validity of the measure in all mental health  
155 populations, particularly young populations. Psychometric assessment of the EQ-5D in young  
156 people with persistent major depression provides evidence of weak to moderate validity and  
157 responsiveness.<sup>23</sup> However, further research is needed to test the generalisability of these  
158 results to other child and adolescent mental health populations.<sup>23</sup> For this reason, the EQ-5D  
159 is used to supplement results from the primary cost-effectiveness analysis in this study.

160

161 **Costs**

162 Economic data were collected in interview at baseline, post-treatment and 3-month, 6-month  
163 and 12-month follow-ups. The economic evaluation took a health and social care perspective  
164 but additionally included carer costs which were expected to be influenced by treatment  
165 delivery method (telephone or face-to-face). Service use information was recorded using the  
166 Child and Adolescent Service Use Schedule (CA-SUS), which included hospital and  
167 community health and social services, and concomitant psychotropic medications. Travel  
168 costs and productivity losses of the primary carer were recorded using the Carer Service Use  
169 Schedule (CARER-SUS). Both schedules have been designed based on previous economic  
170 evaluations in child and adolescent mental health populations.<sup>24,25</sup> All unit costs are reported  
171 in Pound Sterling and were for the financial year 2010-2011, which was the most recent year  
172 over which the trial data were collected. No discounting was necessary due to the short  
173 duration of the trial.

174

175 A nationally applicable unit cost for CBT for young people of £115 per hour of face-to-face  
176 contact was applied to all CBT sessions young people attended in the trial.<sup>26</sup> Sessions that  
177 young people did not attend (DNAs) were assumed to have a zero cost on the basis that the  
178 clinician would be able to make use of the time available to do something else. This unit cost  
179 was based on estimates from a randomised controlled trial of interventions for adolescents  
180 with major depression<sup>25</sup> and includes the cost of supervision and relevant overheads  
181 (management, administrative, capital, estates etc.). Expert opinion was sought which  
182 confirmed that this unit cost was reasonable, given similarities in the grade and seniority of  
183 the therapists involved and the length of the sessions. In addition, data collected by therapists  
184 at each session, which included session length, confirmed that the average length of time  
185 spent delivering TCBT sessions was equal to that of face-to-face sessions (mean 62 minutes

186 in both groups) hence the same cost was applied to both treatment conditions. Costs of  
187 psychotropic medication were taken from the British National Formulary,<sup>27</sup> and costs of  
188 hospital contacts, including in-patient and out-patient appointments, and accident and  
189 emergency attendance, were obtained from the National Schedule of Reference Costs.<sup>28</sup>  
190 Contacts with community health and social services were taken from national publications.<sup>26</sup>  
191 Unit costs were multiplied by the corresponding service use data to generate total service  
192 costs per patient.

193

194 Productivity losses of the primary carers were valued using the human capital approach.<sup>29</sup>  
195 This involves multiplying the individual's salary by hours of absence from work due to their  
196 child's illness. Travel costs of public transport, such as train and bus, were self-reported in  
197 the CARER-SUS. To estimate travel cost by private car, mileage between the clinic and  
198 home address was multiplied by the national average standing (basic costs of keeping the car  
199 for use on the road, including annual car tax, insurance, cost of capital used for the car and  
200 depreciation) and running (costs that depend directly on using the car, including fuel costs,  
201 parking and tolls, tyres, servicing and repair costs) cost per mile.<sup>30</sup>

202

### 203 *Statistical method*

204 The trial was designed to test non-inferiority in effects of the two competing interventions, so  
205 one may consider it legitimate to conduct a cost-minimisation analysis (CMA), which is an  
206 analysis method involving comparison of costs alone, given equal outcomes. However, CMA  
207 has been criticised for leading to biased results, causing overestimation or underestimation of  
208 the probability that treatment is cost-effective.<sup>31</sup> For this reason, cost-effectiveness analysis  
209 (CEA) is recommended, regardless of non-inferiority, for exploration of uncertainty  
210 surrounding the cost and effectiveness data and to help interpret the economic results.<sup>31,32</sup>

211

212 Analyses were carried out on an intention-to-treat basis, with the primary objective of  
213 comparing the costs and cost-effectiveness of TCBT and face-to-face CBT at the final 12-  
214 month follow-up point. In order to best utilise all available data, multiple regression was used  
215 to impute missing total cost, QALY and CY-BOCS data in the main cost-effectiveness  
216 analyses using the impute command in STATA. Factors included in the multiple regression  
217 were treatment arm and the following baseline characteristics: gender, age, CY-BOCS scores  
218 and EQ-5D scores. All analyses were adjusted for baseline characteristics including gender,  
219 age, CY-BOCS scores and EQ-5D scores using multiple regression techniques. Results from  
220 the smaller sample with full economic data were reported in sensitivity analyses to explore  
221 the robustness and validity of the imputed data.

222

223 Results from cost-effectiveness analyses were expressed in terms of incremental cost-  
224 effectiveness ratios (ICERs), defined as the difference in mean costs divided by the difference  
225 in mean effects, calculated using the net benefit approach.<sup>33</sup> Non-parametric bootstrapping  
226 (random and repeat re-sampling from the costs and outcome data) was used to generate a  
227 large number of sets of expected incremental costs and effects for both treatment groups  
228 (1000 replications).<sup>29</sup> The proportion of these that were greater than zero gives the probability  
229 that TCBT is the optimal choice, i.e. cost-effective compared to face-to-face CBT, subject to  
230 a range of thresholds which represent decision makers' willingness-to-pay for a unit  
231 improvement in outcome.

232

233 These probabilities were used to generate cost-effectiveness acceptability curves (CEAC),  
234 which are the recommended alternative to confidence intervals around ICERs to overcome  
235 problems associated with ratio estimators in standard statistical methods.<sup>34,35</sup> CEACs account

236 for the uncertainty surrounding the estimates of expected costs and outcomes, and act as a  
237 useful tool to inform decision makers on the probability that an intervention will be cost-  
238 effective at different thresholds.<sup>35</sup> Cost-effectiveness planes were used to illustrate the  
239 distribution of bootstrapped mean differences in costs and outcomes.

240

241 Sensitivity analyses were carried out to investigate the robustness of the economic evaluation,  
242 and to account for uncertainty that exists around some of the input parameters and  
243 assumptions. Firstly, as noted above, a complete case sensitivity analysis was undertaken to  
244 explore the validity of the imputation method used for dealing with missing data. Secondly,  
245 we considered the ongoing debate about the inclusion of various non-healthcare related  
246 costs<sup>36</sup> and repeated the economic analyses by employing the NHS and personal social  
247 services perspective preferred by NICE in guideline development, which involved the  
248 removal of all costs borne by the carers. Finally, we considered the hypothesis that face-to-  
249 face CBT overhead costs may be higher than TCBT overhead costs as a result of the need for  
250 potentially more expensive clinical space, compared to office space, administrative costs  
251 related to the booking of clinical space, and time spent preparing the clinic space. Whilst the  
252 main analysis was conservative, assuming equal overheads for TCBT and face-to-face CBT,  
253 the sensitivity analysis reduced the cost of TCBT by 10%.

254

## 255 **Results**

### 256 *Participants*

257 72 participants were recruited into the trial, 36 randomised to TCBT and 36 to face-to-face  
258 CBT. Baseline demographic and clinical characteristics of the two treatment groups are  
259 shown in [the online supplement](#). The current paper focuses on the economic results; further  
260 detail on participant characteristics and clinical results are reported elsewhere.<sup>17</sup>

261

262 At final 12-month follow-up, full clinical data was available for 27 (75%) participants in the  
263 CBT group and 25 (69%) participants in the TCBT group and full economic data was  
264 available for 21 (58%) in the CBT group and 22 (61%) in the TCBT group. Comparison of  
265 baseline characteristics between those with available and those with missing data revealed a  
266 significant difference in baseline CY-BOCS scores ( $p=0.033$ ), with those missing having  
267 poorer baseline scores, but no differences in any other variables.

268

### 269 *Outcomes*

270 For the primary clinical outcome, CY-BOCS, at all assessment points through to six-month  
271 follow-up, the difference between conditions was non-significant and the 95% confidence  
272 interval lies below the 5-point difference margin, indicating that TCBT was not inferior to  
273 face to face CBT. For the 12-month follow-up point, the difference remained non-significant  
274 but non-inferiority of TCBT could not conclusively be demonstrated as the 95% confidence  
275 interval included the margin of difference.<sup>17</sup> All secondary measures included in the clinical  
276 trial confirmed non-inferiority at all assessment points.<sup>17</sup>

277

278 **Table 1** reports the results for the EQ-5D. Both groups show improvements in health-related  
279 quality of life over time but there were no significant differences between the groups.

280

281 **Table 1 here**

282

### 283 *Resource Use*

284 Mean number of service contacts for participants with full economic data over the treatment  
285 and 12-month follow-up period **are shown in the online supplement**. There were few

286 differences in service utilisation between the two groups, although participants in the face-to-  
287 face CBT group had slightly more outpatient appointments and more contacts with  
288 community health and social services than those in the TCBT group, particularly GP and  
289 clinical psychologist contacts. Despite the different modes of delivery, intervention  
290 attendance was similar in each group (12.3 sessions in the face-to-face CBT group versus  
291 12.8 sessions in the TCBT group out of a possible 14 sessions).

292

### 293 ***Total costs***

294 Total costs per participant over the treatment and 12-month follow-up period are reported in  
295 Table 1. Intervention costs were similar in the two groups, as a result of the similar number of  
296 sessions attended (mean cost in CBT group £1476, SD 289; mean cost in TCBT group £1415,  
297 SD 307). On average, total cost per participant in the face-to-face CBT group was £2965 (SD  
298 1548), which was £490 more costly than the TCBT group (£2475, SD 1024). This difference  
299 was not statistically significant ( $p=0.118$ ). For both groups, the CBT interventions accounted  
300 for the greatest proportion of the total costs (53%), followed by carer costs (20%) and  
301 hospital services (16%).

302

303 Carer costs were relatively low and differed little between groups. Only a small proportion of  
304 parents reported taking any time off work ( $n=13$  at the post-treatment follow-up point) and  
305 travel costs reported in the face-to-face CBT group were small.

306

### 307 ***Cost-effectiveness analysis***

308 Figure 1 shows a scatterplot of the bootstrapped replications for incremental cost and  
309 incremental CY-BOCS score for TCBT on the cost-effectiveness plane. Because lower CY-  
310 BOCS scores are associated with improved outcomes, the standard cost-effectiveness plane is

311 reversed (outcomes deteriorate when moving from left to right on the  $x$ -axis). Compared to  
312 TCBT, face-to-face CBT has higher bootstrapped mean cost per participant (£697) and  
313 slightly better bootstrapped mean effects on the CY-BOCS (-0.07367), giving rise to an ICER  
314 of £9461 per unit reduction (improvement) in CY-BOCS. In other words, a one-point  
315 improvement in CY-BOCS can be realized if decision makers are willing to pay an additional  
316 £9461 for face-to-face CBT.

317

318 It should be noted that, whilst the cost-effectiveness results presented are based on a unit  
319 improvement in CY-BOCS, a clinically meaningful reduction in symptoms has been  
320 suggested to be at least a 35% reduction in CY-BOCS score.<sup>37</sup> Taking the minimum for  
321 inclusion in this study of a CY-BOCS score of 16, a 35% reduction would be 6 points. Thus,  
322 whilst the incremental cost per unit improvement in CY-BOCS is £9,461, willingness to pay  
323 for a clinically meaningful improvement would need to be a minimum of £56,766 for face-to-  
324 face CBT to be considered cost-effective compared to TCBT using the CY-BOCS. This  
325 minimum would increase with increasing severity of impairment at baseline. For example,  
326 taking the average baseline score for trial participants of approximately 25, a 35% reduction  
327 would be equivalent to approximately 9 points on the CY-BOCS and thus willingness to pay  
328 for a clinically meaningful improvement would need to be at least £85,149 per participant for  
329 face-to-face CBT to be considered cost-effective compared to TCBT.

330

331 The results for QALYs are shown in Figure 2, where, in this case, lower scores are associated  
332 with poorer outcomes so the standard cost-effectiveness plane applies (outcomes improve  
333 when moving from left to right on the  $x$ -axis). Face-to-face CBT was again associated with  
334 higher bootstrapped mean cost per participant (£697) and improved bootstrapped mean  
335 effects in QALY (0.0794) compared to TCBT, giving rise to an ICER of £8778 per unit



336 increase in QALY. Thus for both measures of outcome, TCBT is associated with lower costs  
337 but also slightly poorer outcomes.

338

339 *Figures 1 and 2 here*

340

341 The cost-effectiveness acceptability curves (CEAC) shown in Figure 3 illustrate that at the  
342 standard NICE willingness-to-pay threshold of £20,000 per QALY (NICE, 2008), the  
343 probability of TCBT being the dominant option is 26% and thus the probability of face-to-  
344 face CBT being cost-effective compared to TCBT is 74%. There is no clear consensus  
345 threshold for a unit improvement in CY-BOCS. Figure 3 suggests that at low levels of  
346 willingness to pay (£4000 and below), there is a higher probability of TCBT being the cost-  
347 effective option. However, as willingness to pay rises above this amount, the probability of  
348 either intervention being cost-effective is around 50%.

349

350 *Figure 3 here*

351

### 352 *Sensitivity analyses*

353 Sensitivity analyses, reported in **the online supplement**, did not alter the overall findings of  
354 the cost-effectiveness analyses. The complete case and the narrower NHS/social services  
355 perspective reduced the mean cost per participant in each group, but the difference between  
356 groups remained very similar (£490 primary analysis; £542 complete case analysis; £421  
357 narrow perspective) and these differences remained non-significant. Differences in costs  
358 became statistically significant between the two groups when the cost of TCBT was reduced  
359 by 10% to £104 per session (mean difference £631, p=0.044). However, this did not alter the  
360 cost-effectiveness results.

361

362 **Discussion**

363 The results of this economic evaluation, and the associated clinical trial,<sup>17</sup> suggest there is  
364 strong evidence to support the clinical non-inferiority of TCBT compared to face-to-face  
365 CBT for young people with OCD, and no evidence to suggest any statistically significant  
366 differences in total cost per participant between the two groups, albeit with lower observed  
367 costs in the TCBT group.

368

369 In terms of cost-effectiveness, whilst our secondary cost-effectiveness analysis based on  
370 QALYs favoured face-to-face CBT, our primary cost-effectiveness analysis based on the CY-  
371 BOCS was less clear. This analysis suggests that TCBT may be the preferred option at low  
372 levels of willingness to pay for additional improvements in CY-BOCS scores, whilst at  
373 higher levels of willingness to pay, the probability of either intervention being cost-effective  
374 is around 50%.

375

376 Taking into consideration evidence to suggest that TCBT is clinically non-inferior to CBT,  
377 evidence from our primary cost-effectiveness analysis to suggest TCBT has a 50% or higher  
378 probability of being cost-effective compared to face-to-face CBT, and potential cost-savings  
379 for TCBT, which were statistically significant in sensitivity analysis hypothesising a 10%  
380 reduction in the cost of TCBT given the potential for lower overhead costs, TCBT presents as  
381 an effective alternative for young OCD sufferers who are unable or unwilling to access face-  
382 to-face CBT.

383 There are a number of limitations of the work presented. First, there is currently no evidence  
384 of the validity or responsiveness of the EQ-5D in young people with OCD, and some  
385 evidence to suggest that the youth version of the EQ-5D (EQ-5D-Y) is not correlated with

386 clinical outcomes in such populations,<sup>38</sup> so the sensitivity of the EQ-5D to clinically  
387 important changes is in doubt. Lack of sensitivity of broadly focused outcome measures  
388 compared to disease-specific measures has been demonstrated in a previous paediatric OCD  
389 population,<sup>39</sup> so this is a real possibility in the current sample. However, both measures of  
390 effect showed consistent improvements over the post-treatment and follow-up periods and  
391 there were no significant between-group differences. This suggests that the EQ-5D may be a  
392 relatively robust and sensitive measure of effect in this patient group, though more research is  
393 required to substantiate this.

394

395 Sample sizes, estimated for the purpose of the primary clinical question,<sup>17</sup> were small, and  
396 thus the economic evaluation may have been underpowered. We attempted to minimise the  
397 further impact of data loss through imputation of missing data and, although the imputation  
398 method was robust in sensitivity analysis, results of the study still require careful  
399 interpretation due to the small sample sizes and large amount of missing economic data at the  
400 12-month follow-up. Significant differences in the baseline CY-BOCS scores ( $p=0.033$ ) were  
401 found between those with missing data and those with full economic data, with those missing  
402 having marginally higher symptom scores at baseline, although this was less than 2 points on  
403 the CY-BOCS scale which is unlikely to be clinically meaningful. No significant differences  
404 were detected in any other baseline characteristics.

405

406 Data collected at each therapy session confirmed that there were no differences in terms of  
407 length of sessions, grade of therapists and thus costs, between TCBT and face-to-face CBT,  
408 and that CBT sessions in young people with OCD are comparable to those with major  
409 depression, which is what the unit cost applied was based on. However, a more detailed  
410 micro-costing (bottom-up) in future research may still be valuable as it would provide more

411 accurate estimates of treatment costs. In an attempt to compensate for the lack of a micro-  
412 costing approach, and the hypothesis that overhead costs associated with TCBT may be lower  
413 than those for face-to-face CBT, the cost of TCBT was reduced by 10% in sensitivity  
414 analysis, and the cost results, although not the cost-effectiveness results, were found to be  
415 sensitive to this parameter.

416

417 In terms of generalisability, all treatments within the trial were delivered by NHS therapists  
418 to NHS patients aged 11 to 18 with a clinical diagnosis of OCD. However, this was a single  
419 site study based in a specialist clinic in London, so generalisability across the UK or other  
420 countries is not proven.

421

422 Finally, the trial enabled comparisons to be made in terms of improving access to treatment  
423 by attempting to remove geographical, social or financial barriers, between the two delivery  
424 modes for CBT in young people with OCD. It was not, however, designed to quantify the  
425 effect of TCBT on commonly long NHS waiting lists that result from therapist shortage.<sup>10</sup>  
426 Since with greater access comes greater demands, improvement in access via waiting list  
427 reduction could only be achieved in this patient group if TCBT is proven to save therapists'  
428 time, and if the treatment could be delivered by more therapists through increased training  
429 and effective dissemination of clinical and training materials.<sup>9</sup> Thus, the implications for the  
430 NHS in terms of availability of resources to provide such service and the impact of such  
431 provision on the NHS waiting list remain unclear. The full economic impact of TCBT in  
432 reducing waiting time or delayed access is unknown and further research is needed.  
433 Similarly, the analysis does not take into consideration resource implications in terms of  
434 therapist location, with face-to-face CBT requiring therapy rooms which are often in great  
435 demand, compared to TCBT which can take place at a desk.

436

437 **Policy implications**

438 There is no evidence to suggest that TCBT is cost-effective compared to face-to-face, clinic-  
439 based CBT in this study, particularly in terms of QALYs, and therefore TCBT may not be the  
440 preferred strategy of policy makers by default. However, taking into consideration the non-  
441 inferiority of effects, the potential for cost savings and the potential to overcome barriers to  
442 treatment, it should be recognised that TCBT has a place in supporting the government's  
443 initiative to increase accessibility of effective treatments for OCD<sup>12</sup> and should be offered  
444 where access to specialist clinic-based CBT is limited or where patient or family preference  
445 for telephone therapy is high.

446

447 It is also important to consider the generalisability of the results and the context within which  
448 the study was undertaken. The study is not able to come to conclusions about the cost-  
449 effectiveness of TCBT for young people who were excluded from the study including those  
450 with mild impairment, with current alcohol or substance abuse or dependence, with psychosis  
451 or psychotic symptoms, or with chaotic medication use. In addition, the study is not able to  
452 come to any conclusion about the cost-effectiveness of TCBT in more rural settings, where  
453 specialist clinic-based services are likely to be particularly inaccessible.

454

455 Further research priorities in this field include (1) comparison of the cost-effectiveness of  
456 TCBT with other less resource-intensive modes of delivering evidence-based treatments,  
457 such as computerised or internet-based CBT for OCD<sup>13,37</sup> or therapist supported self-help  
458 programmes,<sup>10</sup> (2) investigation of the cost-effectiveness and feasibility of TCBT delivered  
459 by other health professionals within the community setting, such as CBT-trained nurses  
460 (mental health nurse or practice-based nurse), or generic CAMHS therapists, and (3)

461 replication of the study with a larger sample of participants recruited from multiple sites,  
462 including both rural and urban sites.

463

464 **Word count: 4486**

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474

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501 **Author contributions**

502 CT, DM-C, KL, IH and SB designed the study, GK, KL and HT collected the data, HT, SB  
503 and JS carried out the analysis, HT, SB and JS drafted the manuscript. All authors  
504 commented on and approved the manuscript. All authors had full access to the data in the  
505 study and take responsibility for the integrity of the data and the accuracy of the data  
506 analysis.

507

508

509 **Data availability**

510 All authors had full access to the data. Data available from corresponding author upon  
511 request.

512



513 **References**

- 514 1. Heyman I, Fombonne E, Simmons H, Ford T, Meltzer H and Goodman R. Prevalence of  
515 obsessive-compulsive disorder in the British nationwide survey of child mental health.  
516 *Br J Psychiatry* 2001; **179**: 324-9.
- 517 2. Freeman JB, Garcia AM, Coyne L, Ale C, Prezeworski A, Himle, M, et al. Early  
518 childhood OCD: preliminary findings from a family-based cognitive-behavioral  
519 approach. *J Am Acad Child Adolesc Psychiatry* 2008; **47** (5): 593-602.
- 520 3. Piacentini J, Bergman RL, Keller M and McCracken J. Functional impairment in  
521 children and adolescents with obsessive-compulsive disorder. *J Child Adolesc*  
522 *Psychopharmacol* 2003; **13** (2, Supplement 1): 61-9.
- 523 4. O’Kearney RT, Anstey K, von Sanden C, Hunt A. Behavioural and cognitive  
524 behavioural therapy for obsessive compulsive disorder in children and adolescents.  
525 *Cochrane Database of Systematic Reviews* 2006; Issue 4.
- 526 5. Dupont R, Rice D, Shiraki S, Rowland C. Economic costs of obsessive-compulsive  
527 disorder. *Med Interface* 1995; **8** (4): 102-9.
- 528 6. McCrone P, Dhanasiri S, Patel A, Knapp M, Lawton-Smith S. *Paying the price: the cost*  
529 *of mental health care in England to 2026*. King’s Fund, 2008.
- 530 7. Watson HJ, Rees CS. Meta-analysis of randomized, controlled treatment trials for  
531 pediatric obsessive compulsive disorder. *J Child Psychol Psychiatry* 2008; **49** (5): 489-  
532 98.
- 533 8. Clark DM, Layard R, Smithies R, Richards DA, Suckling R, Wright B. Improving access  
534 to psychological therapy: Initial evaluation of two UK demonstration sites. *Behav Res*  
535 *Ther* 2009; **47** (11): 910-20.
- 536 9. Layard R. The case for psychological treatment centres. *Br Med J* 2006; **332**: 1030-2.

- 537 10. Mataix-Cols D, Marks I. Self-help with minimal therapist contact for obsessive-  
538 compulsive disorder: A review. *Eur Psychiatry* 2006; **21**: 75-80.
- 539 11. Lovell K, Richards DA. Multiple access points and levels of entry (MAPLE): ensuring  
540 choice, acceptability and equity for CBT services. *Behav Cogn Psychother* 2000; **28**:  
541 379-91.
- 542 12. Department of Health. *National Service Framework for Mental Health*. Department of  
543 Health, 1999.
- 544 13. Kaltenthaler E, Brazier J, De Nigris E, Tumur I, Ferriter M, Beverley C, et al.  
545 Computerised cognitive behaviour therapy for depression and anxiety update: a  
546 systematic review and economic evaluation. *Health Technol Assess* 2006; **10** (33).
- 547 14. Taylor S, Thordarson DS, Spring T, Yeh AH, Corcoran KM, Eugster K, Tisshaw C.  
548 Telephone-administered cognitive behavior therapy for obsessive-compulsive disorder.  
549 *Cogn Behav Ther* 2003; **32** (1): 13-25.
- 550 15. Hammond GC, Croudace TJ, Radhakrishnan M, Lafortune L, Watson A, McMillan-  
551 Shields F, Jones PB. Comparative effectiveness of cognitive therapies delivered face-to-  
552 face or over the telephone: An observational study using propensity methods. *PLoS ONE*  
553 2012; **7** (9): e42916.
- 554 16. Lovell K, Cox D, Haddock G, Jones C, Raines D, Garvey R, et al. Telephone  
555 administered cognitive behaviour therapy for treatment of obsessive compulsive  
556 disorder: randomised controlled non-inferiority trial. *Br Med J* 2006; **333**: 883-7.
- 557 17. Turner CM, Mataix-Cols D, Lovell K, Krebs G, Lang K, Byford S, Heyman I. Telephone  
558 cognitive-behaviour therapy for adolescents with obsessive-compulsive disorder: A  
559 randomised controlled non-inferiority trial. *J Am Acad Child Adolesc Psychiatry* 2014;  
560 **53** (12): 1298-307.

- 561 18. American Psychiatric Association. *Diagnostic and statistical manual of mental*  
562 *disorders*. 4th ed. American Psychiatric Association, 1994.
- 563 19. Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, et al.  
564 Children's Yale-Brown Obsessive-Compulsive Scale: Reliability and validity. *J Am*  
565 *Acad Child Adolesc Psychiatry* 1997; **36** (6): 844-52.
- 566 20. Turner C, Heyman I, Futh A, Lovell K. A pilot study of telephone cognitive-behavioural  
567 therapy for obsessive-compulsive disorder in young people. *Behav Cogn Psychother*  
568 2009; **37**: 469-74.
- 569 21. Mataix-Cols D, Turner C, Monzani B, Isomura K, Murphy C, Krebs G, Heyman I.  
570 Cognitive-behavioural therapy with post-session d-cycloserine augmentation for  
571 paediatric obsessive-compulsive disorder: pilot randomised controlled trial. *Br J*  
572 *Psychiatry* 2014; **204** (1): 77-8.
- 573 22. Brooks R. EuroQol: the current state of play. *Health Policy* 1996; **37**: 53-72.
- 574 23. Byford S. The validity and responsiveness of the EQ-5D measure of health-related  
575 quality of life in an adolescent population with persistent major depression. *J Ment*  
576 *Health* 2013; **22** (2): 101-10.
- 577 24. Byford S, Barrett B, Roberts C, Clark A, Edwards V, Smethurst N, Gowers SG.  
578 Economic evaluation of a randomised controlled trial for anorexia nervosa in  
579 adolescents. *Br J Psychiatry* 2007; **191**: 436-40.
- 580 25. Byford S, Barrett B, Roberts C, Wilkinson P, Dubicka B, Kelvin RG, et al. Cost-  
581 effectiveness of selective serotonin reuptake inhibitors and routine specialist care with  
582 and without cognitive-behavioural therapy in adolescents with major depression. *Br J*  
583 *Psychiatry* 2007; **191**: 521-27.
- 584 26. Curtis L. *Unit costs of health and social care 2011*. Canterbury: Personal Social Services  
585 Research Unit, 2011.

- 586 27. British Medical Association and Royal Pharmaceutical Society. *British National*  
587 *Formulary 62*. BMJ Books and Pharmaceutical Press, 2011.
- 588 28. Department of Health. *NHS Reference Costs*. Department of Health, 2011.
- 589 29. Drummond MF, Sculpher M, O'Brien B, Stoddart GL, Torrance GW. *Methods for the*  
590 *economic evaluation of health care programmes*. 3rd edition. Oxford Medical  
591 Publications, 2005.
- 592 30. Automobile Association. *Monitoring Costs 2010*. Automobile Association website.  
593 Available: [http://www.theaa.com/motoring\\_advice/running\\_costs/petrol2011.pdf](http://www.theaa.com/motoring_advice/running_costs/petrol2011.pdf).  
594 Accessed 21 February 2013.
- 595 31. Dakin H, Wordsworth S. Cost-minimisation analysis versus cost-effectiveness analysis,  
596 revisited. *Health Econ* 2011; **22** (1): 22-34.
- 597 32. Briggs AH, O'Brien BJ. The death of cost-minimization analysis? *Health Econ* 2001; **10**  
598 (2): 179-84.
- 599 33. Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of  
600 uncertainty in cost-effectiveness analysis. *Med Decis Making* 1998; **18**: S68-80.
- 601 34. Briggs AH, Fenn P. Confidence intervals or surfaces? Uncertainty on the cost-  
602 effectiveness plane. *Health Econ* 1998; **7** (8): 723-40.
- 603 35. Fenwick E, Byford S. A guide to cost-effectiveness acceptability curves. *Br J Psychiatry*  
604 2005; **187**: 106-8.
- 605 36. Stant AD, Ten Vergert EM, den Boer PCAM, Wiersma D. Cost-effectiveness of  
606 cognitive self-therapy in patients with depression and anxiety disorders. *Acta Psychiatr*  
607 *Scand* 2008; **117**: 57-66.
- 608 37. Mataix-Cols D, Fernandez de la Cruz L, Nordsletten AE, Lenhard F, Isomura K, Blair  
609 Simpson H. Towards an international expert consensus for defining treatment response,

- 610 remission, recovery and relapse in obsessive-compulsive disorder. *World Psychiatr*  
611 2016; **15** (1): 80-81.
- 612 38. Lenhard F, Ssegonja R, Andersson E, Feldman I, Ruck C, Mataix-Cols D, Serlachius E.  
613 Cost-effectiveness of therapist-guided internet-delivered cognitive behaviour therapy for  
614 paediatric obsessive-compulsive disorder: results from a randomised controlled trial.  
615 *BMJ Open* 2018; **7**: e015246.
- 616 39. Lee W, Jones L, Goodman R, Heyman I. Broad outcome measures may underestimate  
617 effectiveness: An instrument comparison study. *Child Adolesc Ment Health* 2005; **10**:  
618 143-4.

619 Table 1: Outcomes and costs by treatment groups

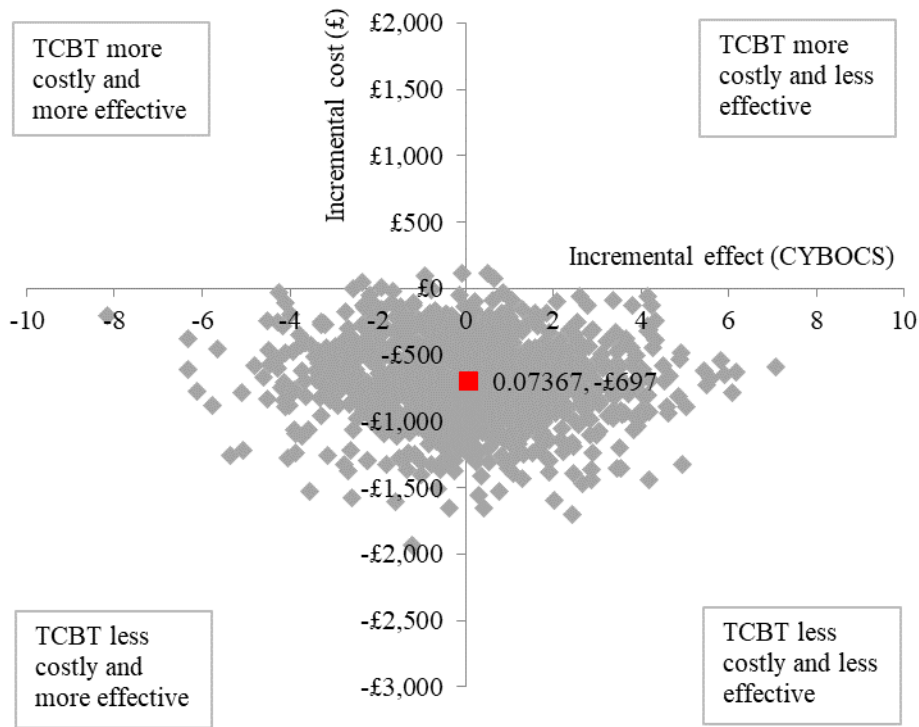
	CBT (n=36)	TCBT (n=36)	Mean difference (95% CI)	p-value
<b>EQ-5D VAS</b>				
Baseline	7.52 (1.45)	7.85 (1.63)	-0.33 (-1.06 to 0.39)	0.366
Post-treatment	8.75 (1.30)	8.48 (1.51)	0.27 (-0.39 to 0.94)	0.412
Final follow-up	8.91 (0.71)	9.10 (0.75)	-0.19 (-0.53 to 0.15)	0.277
<b>EQ-5D Utilities</b>				
Baseline	0.76 (0.15)	0.80 (0.27)	-0.04 (-0.15 to 0.06)	0.396
Post-treatment	0.89 (0.14)	0.89 (0.22)	-0.00 (-0.08 to 0.09)	0.952
Final follow-up	0.93 (0.08)	0.91 (0.08)	0.01 (-0.02 to 0.05)	0.379
<b>QALYs</b>				
Final follow-up	1.19 (0.21)	1.14 (0.29)	0.05 (-0.07 to 0.17)	0.379
<b>Costs between baseline and 12-month post-treatment follow-up (£)</b>				
Intervention	1476 (289)	1415 (307)	61 (-79 to 201)	0.391
Hospital services	550 (1040)	313 (532)	237 (-152 to 625)	0.229
Community services	330 (406)	233 (233)	98 (-61 to 250)	0.230
Medication	40 (110)	14 (5)	19 (-12 to 63)	0.176
Carer cost	569 (658)	500 (692)	69 (-249 to 386)	0.666
Total cost	2965 (1548)	2475 (1024)	490 (-127 to 1107)	0.118

620 VAS=visual analogue scale; QALY=quality adjusted life years

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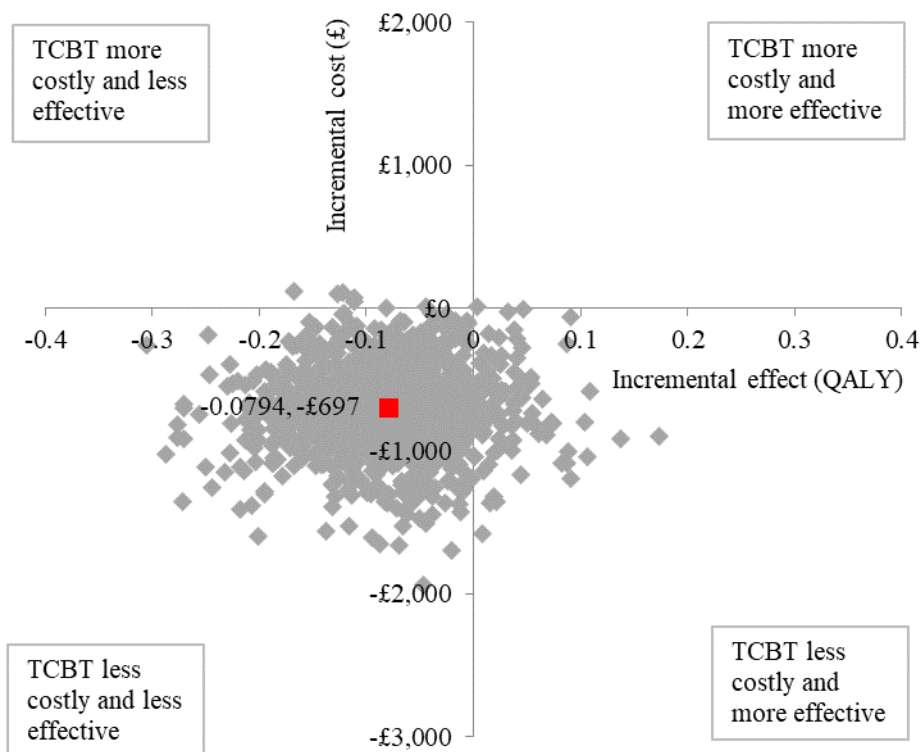
622

623 Figure 1: Bootstrapped mean differences in costs and effects in term of CY-BOCS for TCBT  
624 compared to face-to-face CBT  
625



626  
627 Note: Standard cost-effectiveness plane is reversed as higher CY-BOCS scores reflect poorer outcomes  
628

629 Figure 2: Bootstrapped mean differences in costs and effects in term of QALYs for TCBT  
630 compared to face-to-face CBT  
631

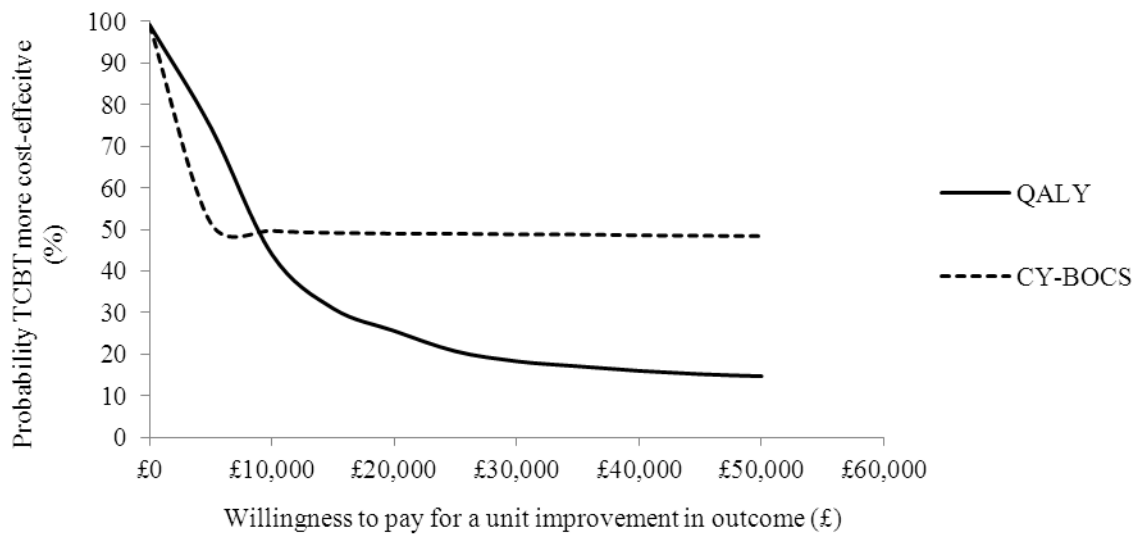


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634 Figure 3: Cost-effectiveness acceptability curves showing the probability that TCBT is cost-  
635 effective compared to face-to-face CBT



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637

Section/item	Item No	Recommendation	Reported on page No/ line No
<b>Title and abstract</b>			
Title	1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	page 1, line 1 to 2
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	page 2, line 12 to 38
<b>Introduction</b>			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	page 4, line 41 to 63
		Present the study question and its relevance for health policy or practice decisions.	page 4, line 61 to 63
<b>Methods</b>			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	page 5, line 79 to 89; online supplement page 1, table 1
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	page 5, line 72 to 74
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	page 9, line 166 to 168; page 9, line 178 to page 10, line 204
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	page 6, line 112 to 128
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	page 7, line 131 to 132
Discount rate	9	Report the choice of discount rate(s) used for	page 9, line 175 to 176

Section/item	Item No	Recommendation	Reported on page No/ line No
		costs and outcomes and say why appropriate.	
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	page 7, line 130 to page 8, line 162
Measurement of effectiveness	11a	<i>Single study-based estimates:</i> Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	page 4, line 61 to 63; page 6, line 91 to 97
	11b	<i>Synthesis-based estimates:</i> Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	<i>Single study-based economic evaluation:</i> Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	page 9, line 164 to 176; page 9, line 178 to page 10, line 204
	13b	<i>Model-based economic evaluation:</i> Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	page 9, line 173 to 175
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly	N/A

Section/item	Item No	Recommendation	Reported on page No/ line No
		recommended.	
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	N/A
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	page 10, line 206 to page 12, line 256
<b>Results</b>			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Online supplement, table 2
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Page 29, table 1; Page 13, line 272 to 282; Page 14, line 296 to 308
Characterising uncertainty	20a	<i>Single study-based economic evaluation:</i> Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	Page 16, line 355 to 363;  Online supplement, table 3;  page 30, figure 1;  page 31, figure 2;  page 32, figure 3
	20b	<i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A
Characterising	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be	N/A

Section/item	Item No	Recommendation	Reported on page No/ line No
heterogeneity		explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
<b>Discussion</b>			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	page 17, line 365 to page 19, line 438; page 20 line 440 to page 21 line 465;
<b>Other</b>			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Page 22, lines 472 to 476
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Page 2, lines 33 to page 3, line 38

639 For consistency, the CHEERS statement checklist format is based on the format of the CONSORT statement  
640 checklist

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