Cost-effectiveness of psychological interventions for children and young people with post-traumatic stress disorder

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Abstract

Background: PTSD in youth may lead to long-lasting psychological implications, educational difficulties and increased healthcare costs. Psychological interventions have been shown to be effective in its management. The objective of this study was to assess the cost-effectiveness of a range of psychological interventions for children and young people with PTSD.

Methods: A decision-analytic model was constructed to compare costs and quality-adjusted life years (QALYs) of 10 psychological interventions and no treatment for children and young people with PTSD, from the perspective of the National Health Service and personal social services in England. Effectiveness data were derived from a systematic review and network meta-analysis. Other model input parameters were based on published sources, supplemented by expert opinion.

Results: Cognitive therapy for PTSD, a form of individual trauma-focused cognitive behavioural therapy (TF-CBT), appeared to be the most cost-effective intervention for children and young people with PTSD (with a probability of 0.78 amongst the 11 evaluated options at a cost-effectiveness threshold of £20,000/QALY), followed by narrative exposure (another form of individual TF-CBT), play therapy, and other forms of individual TF-CBT. After excluding cognitive therapy from the analysis, narrative exposure appeared to be the most cost-effective option with a 0.40 probability of being cost-effective amongst the remaining 10 options. EMDR, parent training and group TF-CBT occupied middle cost-effectiveness rankings. Family therapy and supportive counselling were less cost-effective than other active interventions. There was limited evidence for some interventions, in particular cognitive therapy for PTSD and parent training.

Conclusions: Individual forms of TF-CBT and, to a lesser degree, play therapy appear to be cost-effective in the treatment of children and young people with PTSD. Family therapy and supportive counselling are unlikely to be cost-effective relative to other interventions. There is a need for well-conducted studies that examine the long-term clinical and cost-

effectiveness of a range of psychological treatments for children and young people with PTSD.

Keywords: post-traumatic stress disorder; economic evaluation; decision-analytic modelling; intervention

INTRODUCTION

A considerable proportion of children and young people who are exposed to traumatic events, around 16%, will develop post-traumatic stress disorder (PTSD) (Alisic et al., 2014). Those who still have PTSD symptoms six months after the traumatic event are unlikely to recover without intervention (Hiller et al., 2016). If untreated, PTSD may lead to long-lasting psychological implications, educational difficulties and increased healthcare costs (Makley & Falcone, 2010). A number of psychological interventions have been shown to be effective in the treatment of PTSD in youth, predominantly trauma-focused cognitive behavioural therapy (TF-CBT) and, to a lesser extent, eye movement desensitisation and reprocessing (EMDR) (Mavranezouli et al., 2019). Published economic evaluations in this field have concluded that cognitive therapy for PTSD, an individual form of TF-CBT (Shearer et al., 2018), individual TF-CBT (Mihalopoulos et al., 2015) and group TF-CBT (Aas, Iversen, Holt, Ormhaug, & Jensen, 2018) were more cost-effective than waitlist or treatment as usual; TF-CBT was also found to be more cost-effective than counselling (Gospodarevskaya & Segal, 2012) whereas group psychotherapy was likely more cost-effective than individual psychotherapy (McCrone et al., 2005). These economic studies evaluated a limited range of interventions available for the treatment of PTSD in youth and made very few comparisons between active interventions. Given the variety of available interventions and the need for efficient use of healthcare resources, the objective of this study was to examine the cost-effectiveness of a range of psychological interventions for the treatment of PTSD in children and young people from the perspective of the National Health Service (NHS) and Personal Social Services (PSS) in England, using decision-analytic economic modelling.

METHODS

The analysis presented here informed the updating of national guidance for the management of PTSD in England, published by the National Institute for Health and Care Excellence (NICE) (National Institute for Health and Care Excellence, 2018). The guideline was developed by a guideline committee, an independent multi-disciplinary group of clinical

academics, health professionals and service user and carer representatives with expertise and experience in the field of PTSD. The committee contributed to the development of the economic model by providing advice on issues relating to the natural history and treatment patterns of PTSD in children and young people in the UK, as well as on model inputs in areas where evidence was lacking.

Population

The study population comprised children and young people (aged under 18 years) with clinically important post-traumatic stress symptoms, defined by a diagnosis of PTSD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM), the World Health Organization (WHO) International Classification of Diseases (ICD) or similar criteria, or by clinically significant PTSD symptoms, indicated by a PTSD symptom score above threshold on a validated scale, that are present for more than 3 months after a traumatic event.

Interventions

The psychological interventions considered in the economic analysis were selected amongst interventions that were considered in a systematic review and NMA of randomised controlled trials (RCTs) of psychological, psychosocial and other non-pharmacological treatments for children and young people with PTSD (Mavranezouli et al., 2019; see Appendix S2 of that paper for the study protocol and the inclusion criteria for the NMA). For the economic analysis we considered only interventions that had been tested on at least 40 individuals across RCTs included in the NMA of changes in PTSD symptoms at treatment endpoint, as this was deemed the minimum size of evidence base that could support a practice recommendation. Treatment as usual was not considered in the economic analysis as it comprised a heterogeneous group of non-specific interventions that were not clearly defined across studies. The NMA assessed different interventions within the TF-CBT class. TF-CBT is a broad class of psychological interventions that predominantly use trauma-focused

cognitive, behavioural or cognitive-behavioural techniques and exposure approaches to treatment. Although some interventions place their main emphasis on exposure (e.g. imaginal reliving, producing a written narrative or in vivo exposure) and others on cognitive techniques (e.g. restructuring of trauma-related appraisals), most use a combination. Interventions belonging to the TF-CBT class were considered separately in the economic analysis to explore potential substantial differences in their relative cost-effectiveness. We decided to consider cognitive therapy for PTSD, one of the interventions within the TF-CBT class, in an exploratory economic analysis, although it had only been tested on 25 trial participants, because it was shown to be the most effective intervention in the NMA, and this finding, in combination with the robust evidence of effectiveness for all other interventions within the TF-CBT class, increased our confidence that cognitive therapy for PTSD was effective, despite of its limited evidence base. Nevertheless, we have also presented and interpreted results of the economic analysis after excluding cognitive therapy for PTSD from consideration.

The economic analysis evaluated the following interventions:

- Cognitive therapy for PTSD [TF-CBT] (included in exploratory analysis)
- Cohen TF-CBT/cognitive processing therapy (CPT) [TF-CBT]
- Narrative exposure therapy [TF-CBT]
- Exposure/prolonged exposure therapy [TF-CBT]
- Group CBT [TF-CBT]
- EMDR
- Family therapy
- Play therapy
- Parent training
- Supportive counselling
- No treatment, reflected in waitlist or no treatment RCT arms included in the NMA.

Economic model structure

A hybrid decision-analytic model consisting of a decision-tree followed by a two-state Markov model was constructed using Microsoft Office Excel 2013 to estimate total costs and quality-adjusted life years (QALYs) associated with each treatment. The model structure was determined by the natural history of PTSD in youth, its treatment patterns in the UK, and the availability of relevant clinical and epidemiological data (Figure 1).

The model followed hypothetical cohorts of children and young people with PTSD, initiated on each of the treatment options assessed. The duration of treatment equalled 3 months (12 weeks), according to the average treatment duration for children and young people with PTSD in trials and routine clinical practice (range 6-14 weeks). Following a course of treatment, children and young people in each cohort either remitted (entering a state of 'no-PTSD') or failed to remit, remaining in a 'PTSD' state. In the next 3 months of follow-up, those who had remitted could remain in remission or relapse to PTSD. Conversely, those who had not remitted, could remain in the 'PTSD' state or remit (and move to 'no-PTSD'). The length of the follow-up period immediately post-treatment was set at 3 months as this is the period for which most follow-up data are reported in RCTs of psychological interventions for PTSD.

After that point, children and young people in each cohort entered the Markov model, run in 3-month cycles, for consistency with the duration of the two periods of the decision-tree. In each cycle, children and young people could remain in the same health state or move between the states of 'PTSD' and 'no-PTSD'. A half-cycle correction was applied.

The time horizon of the analysis was 3 years (36 months), comprising 6 months in the decision tree and 2.5 years (10 x 3-month cycles) in the Markov component of the model. This time frame was deemed adequate to capture longer-term costs and effects of

treatment, without making significant extrapolations and assumptions over the course of PTSD.

Death was not considered as there is no published evidence that mortality in children and young people with PTSD is higher than that of those in the general population.

Effectiveness data

We obtained effectiveness data from a systematic review and NMA of psychological and psychosocial interventions for children and young people with PTSD (Mavranezouli et al., 2019). We utilised the results of 2 NMAs of changes in PTSD symptoms: between baseline and treatment endpoint; and between baseline and 1-4 month follow-up. Details on the selection of the effectiveness data and the transformations required for use in the economic model are provided in Appendix S1.

The outputs of the NMA of changes in PTSD symptoms between baseline and treatment endpoint informed the intervention effects in the model period of 0-3 months. For the 3-6 month follow-up period, the base-case economic analysis conservatively assumed that the active intervention effects were not retained and equalled the effect of no treatment; this was decided because the results of the NMA of changes in PTSD symptoms between baseline and 1-4-month follow-up showed considerable uncertainty. Data from this NMA were used in secondary analyses, to inform effects for each active intervention during 3-6 months after treatment initiation.

Baseline probability of remission

The probability of remission for no treatment (baseline) and for all model arms beyond treatment endpoint (i.e. for all treatment options during 3-6 months after treatment initiation in the base-case analysis and for all treatment options during 6-36 months after treatment initiation in both the base-case and secondary analyses) was estimated using naturalistic

data on children and young people with PTSD in the community, who participated in a global mental health survey (Rosellini et al., 2018). We considered the community survey participants to be representative of our study population, which was children and young people presenting in primary care with symptoms of PTSD. We preferred using community data on absolute effects for baseline (no treatment) to RCT data, as the latter reflect trial conditions and not necessarily care received in community (for a discussion on the selection of data for the baseline natural history model see Dias, Welton, Sutton, & Ades, 2013). Details on the methods used for the estimation of the baseline probability of remission are provided in Appendix S2.

Risk of relapse

An annual risk of relapse of 0.10 was assumed across all treatment arms, based on the committee's expert opinion and due to lack of relevant published evidence; this was translated into a 3-month probability of relapse of 0.026 assuming exponential function, which was applied in the 3-month follow-up period of the decision-tree and over the whole duration of the Markov model. This assumption was tested in sensitivity analysis.

Utility data

Utility scores express preferences for the health-related quality of life (HRQoL) in distinct health states and are necessary for the estimation of QALYs. Following a systematic literature search of utility data for PTSD, the base-case economic analysis used utility scores generated from HRQoL ratings of Australian adolescents and young adults aged 16-21 years, some of whom had developed PTSD, who participated in a mental health survey (Gospodarevskaya, 2013). HRQoL was assessed with the Assessment of Quality of Life measure (http://www.aqol.com.au). The study sample was large (N=993) but its age was higher than the age of our study population. Moreover, the utility value of 'no-PTSD', derived from adolescents and young adults who had never experienced PTSD, is likely to be higher

than the utility of ‘no-PTSD’ following remission, therefore use of utility data from this study has likely overestimated the utility value of the ‘no-PTSD’ state.

A secondary economic analysis was conducted that used utility data from children and young people aged 8-17 years with PTSD who participated in a RCT of cognitive therapy for PTSD 2-6 months after single trauma (Shearer et al., 2018). HRQoL was rated using the parent-completed Strengths and Difficulties Questionnaire, and subsequently mapped onto the Child Health Utility index 9D using a published algorithm (Furber, Segal, Leach, & Cocks, 2014). Utility values were adjusted for baseline utility differences and potential clinical predictors (age, gender, group). Baseline HRQoL data from all trial participants determined the utility of the PTSD state. Data obtained from PTSD-free children at trial follow up, irrespective of group allocation, determined the utility of no-PTSD. The study sample, although very small (N=29), was directly relevant to the population of our analysis. The reported utility values suggested very narrow utility gains after remission from PTSD, resulting in the face validity of these data being questioned by the guideline committee; for this reason these data were only utilised in secondary analyses.

Resource use and cost data

The analysis included intervention costs (healthcare professional time), and costs relating to the ‘PTSD’ and ‘no-PTSD’ health states, including costs of primary, community and secondary healthcare and costs of personal social services.

Intervention costs (Table 1) were calculated by combining resource use reported in RCTs included in the NMA that informed the economic analysis (i.e. number and duration of therapeutic sessions, number of therapists and participants for group interventions), modified to represent routine UK practice, with respective national unit costs. Descriptions of interventions in the RCTs that informed the NMAs and, subsequently, the economic analysis suggested that interventions were delivered by a range of therapists, including

psychologists, social care professionals, counsellors, teachers, psychology graduate students or postdoctoral fellows, nurses, social workers, and lay counsellors. For the economic analysis, all interventions were assumed to be delivered by Band 7 therapists (clinical psychologists) according to the NHS Agenda for Change for qualified Allied Health Professionals, to reflect routine practice in the UK.

The therapists' unit cost was estimated using a combination of data derived from national sources (British Association for Behavioural & Cognitive Psychotherapies, 2016; Curtis & Burns, 2017; National College for Teaching and Leadership, 2016) and included wages/salary, salary oncosts, capital and other overheads, qualification and supervision costs. The ratio of direct (face-to-face) to indirect (preparation and administrative tasks) therapists' time was taken into account. Combining this information, the unit cost of a band 7 clinical psychologist was estimated at £101 per hour of direct client contact. Details on the methods and sources used to estimate this figure are reported in Appendix S3.

Costs associated with the PTSD and no-PTSD health states were taken from the study by Shearer and colleagues (2018). NHS/PSS costs including staff time (general practitioner, nurse, paediatrician, clinical psychologist, etc.), hospital services, advice services, social services and medication were collected for all participants at baseline and over the trial period. Costs were adjusted for baseline cost differences and potential clinical predictors (age, gender, group). The reported 3-month baseline costs for all trial participants were attached to the PTSD state; reported 3-month costs for children who were PTSD-free at trial follow up, irrespective of allocation arm, were attached to the 'no-PTSD' state.

Costs were expressed in 2017 prices, uplifted, where necessary, using the Hospital and Community Health Services Pay and Prices Index (Curtis & Burns, 2017).

Discounting

Costs and QALYs were discounted at 3.5% annually as recommended by NICE (National Institute for Health and Care Excellence, 2014).

Analysis

To account for the uncertainty around input parameter point estimates, a probabilistic analysis was undertaken, in which input parameters were assigned probabilistic distributions (Briggs, Sculpher, & Claxton, 2006). Subsequently, 10,000 iterations were performed, each drawing random values out of the distributions fitted onto the model input parameters. Mean costs and QALYs for each treatment were calculated by averaging across the 10,000 iterations. The Net Monetary Benefit (NMB) for each intervention was estimated for each iteration and averaged across the 10,000 iterations, determined by the formula

$$NMB = E \bullet \lambda - C$$

where E and C are the effects (QALYs) and costs of each intervention, respectively, and λ represents the willingness-to-pay per unit of effectiveness, set at the NICE lower cost-effectiveness threshold of £20,000/QALY (National Institute for Health and Care Excellence, 2014). The intervention with the highest NMB is the most cost-effective option (Fenwick, Claxton, & Sculpher, 2001).

The mean ranking by cost-effectiveness is reported for each intervention (out of 10,000 iterations), where a rank of 1 suggests that an intervention is the most cost-effective amongst all evaluated treatment options. The probability of the intervention with the highest NMB being the most cost-effective option is also provided, calculated as the proportion of iterations in which the intervention has had the highest NMB amongst all interventions considered in the analysis. The probability of cost-effectiveness has been estimated in a step-wise approach, according to which the most cost-effective intervention is omitted at each step, and the probability of cost-effectiveness of the next most cost-effective intervention amongst the remaining treatment options is re-calculated. The probabilities estimated following this approach reflect the uncertainty around the cost-effectiveness not

only of the most cost-effective intervention, but also the second, third, fourth, etc. most cost-effective intervention in ranking, after more cost-effective interventions have been omitted from analysis. Finally, the cost-effectiveness acceptability frontier has been plotted, showing the treatment with the highest mean NMB over different cost-effectiveness thresholds (λ), and the probability that this treatment is the most cost-effective among those assessed (Fenwick et al., 2001). We present two cost-effectiveness acceptability frontiers, one for the analysis that has considered all 11 treatment options, and another for the analysis that has included 10 treatment options, after excluding cognitive therapy for PTSD.

Table 2 reports the values of all model input parameters. Deterministic values were used in deterministic one-way sensitivity analyses. The probability distributions show the types and range of distributions assigned to each parameter; estimation of distribution ranges was based on data reported in the published sources of evidence.

Four probabilistic analyses were undertaken by combining the 2 alternative assumptions on the effectiveness of interventions at the 3-month follow-up with the 2 sets of utility data:

- Scenario A (base-case analysis): use of utility data from Gospodarevskaya (2013); treatment effect between 3-6 months equalled that of no treatment
- Scenario B: use of utility data from Gospodarevskaya (2013); treatment effect between 3-6 months estimated from the NMA of changes in PTSD symptoms between baseline and 1-4 month follow-up
- Scenario C: use of utility data from Shearer and colleagues (2018); treatment effect between 3-6 months equalled that of no treatment
- Scenario D: use of utility data from Shearer and colleagues (2018); treatment effect between 3-6 months was estimated from the NMA of changes in PTSD symptoms between baseline and 1-4 month follow-up

One-way deterministic sensitivity analyses explored the impact of a change in the annual risk of relapse, which was varied between zero and 0.20.

Validation of the economic model

The economic model was developed in collaboration with members of the guideline committee. All inputs and model formulae were systematically checked. The model was tested for logical consistency by setting input parameters to null and extreme values and examining whether results changed in the expected direction. All results were discussed with the committee to confirm their plausibility.

RESULTS

Table 3 shows the results of the base-case economic analysis [utility data from Gospodarevskaya (2013); no beneficial effect beyond treatment endpoint]. Interventions have been ordered from the most to the least cost-effective. The table provides, for each treatment, the mean number of QALYs, intervention costs and total costs per person, the mean NMB and ranking of each intervention, and its probability of being cost-effective in a step-wise approach, as explained earlier, at a threshold of £20,000/QALY.

Cognitive therapy for PTSD was shown to be the most cost-effective intervention for children and young people with PTSD, with the highest NMB at the cost-effectiveness threshold of £20,000/QALY. This was followed by narrative exposure and play therapy. Exposure/prolonged exposure and Cohen TF-CBT/CPT completed the top 5 likely most cost-effective treatments. These were followed by EMDR, parent training, group TF-CBT, family therapy, supportive counselling and no treatment. Therefore, the 4 individual forms of TF-CBT included in the economic analysis occupied 4 out of the 5 top places in cost-effectiveness ranking. It can be seen that, with the exception of cognitive therapy for PTSD, the next most cost-effective interventions up to (and including) parent training have probabilities of being cost-effective among remaining options that do not exceed 0.40,

although increasingly fewer interventions are included in the analysis, indicating the uncertainty characterising the results for high-to-middle rankings. Notably, supportive counselling had a higher mean NMB but worse mean ranking than no treatment and, also, a 0.49 probability of being cost-effective when compared with no treatment alone, suggesting considerable uncertainty around its cost-effectiveness; these findings are attributable to the skewed distributions of NMBs, combined with the fact that, according to the NMA that informed the economic analysis (Mavranezouli et al., 2019), the 95% credible intervals around the mean effect of supportive counselling versus no treatment crossed the line of no effect, indicating uncertainty in its clinical effectiveness. The cost-effectiveness plane (Figure 2) depicts the mean incremental costs and QALYs of all psychological interventions versus no treatment (placed at the origin). According to the cost-effectiveness acceptability frontier, cognitive therapy appeared to be the most cost-effective option amongst the 11 treatment options assessed, at any cost-effectiveness threshold between zero and £40,000/QALY, with a 0.78 probability (amongst the 11 options assessed) at the threshold of £20,000/QALY (Figure 3). When cognitive therapy for PTSD was excluded from analysis, narrative exposure (another individual form of TF-CBT) appeared to be the most cost-effective intervention at any cost-effectiveness threshold between zero and £40,000/QALY, with a 0.40 probability at the threshold of £20,000/QALY amongst the 10 remaining options (Figure 4).

Under scenario B [utility data from Gospodarevskaya (2013); beneficial treatment effect up to 3-month follow-up], cognitive therapy for PTSD remained the most likely cost-effective intervention followed by Cohen TF-CBT/CPT, group TF-CBT, narrative exposure and parent training. As with base-case analysis, the probabilities of cost-effectiveness for interventions ranked between second and seventh places were low, ranging between 0.30 and 0.48 in spite of the fact that increasingly fewer interventions were included in the analysis, indicating uncertainty around the results for high-to-middle rankings. Group TF-CBT appeared to be the most cost-effective option for cost-effectiveness thresholds up to £2,000/QALY; cognitive

therapy was shown to be the most cost-effective option at higher thresholds. The probability of cognitive therapy being the most cost-effective treatment at a threshold of £20,000/QALY was 0.67 amongst the 11 alternative options. When cognitive therapy was excluded from analysis, group TF-CBT appeared to be the most cost-effective option for thresholds up to £17,500/QALY, with Cohen TF-CBT/CPT becoming the most cost-effective option at higher thresholds, and a probability of 0.30 at the £20,000/QALY threshold amongst the 10 remaining options. The improvements in the relative cost-effectiveness of Cohen TF-CBT/CPT, group TF-CBT and parent training are justified by the relatively large effects of these interventions in the NMA of changes in PTSD symptoms between baseline and 1-4-month follow-up, which informed scenario B.

Under scenario C [utility data from Shearer and colleagues (2018); no beneficial effect beyond treatment endpoint], cognitive therapy remained the most likely cost-effective intervention followed by narrative exposure, play therapy, group TF-CBT and EMDR. Again the probabilities of cost-effectiveness for interventions ranked between second and seventh places were low, ranging between 0.21 and 0.43, confirming the uncertainty around the results for high-to-middle rankings. Supportive counselling appeared to be less cost-effective than no treatment. Cognitive therapy was shown to be the most cost-effective option at any cost-effectiveness threshold between zero and £40,000/QALY, with a 0.59 probability at the threshold of £20,000/QALY. When cognitive therapy was excluded from analysis, narrative exposure appeared to be the most cost-effective option at any cost-effectiveness threshold, with a 0.43 probability at the threshold of £20,000/QALY. This scenario utilised narrower utility gains after remission from PTSD, which favoured less costly interventions, such as group TF-CBT and EMDR, the relative cost-effectiveness of which improved.

Under scenario D [utility data from Shearer and colleagues (2018); beneficial effect up to 3-month follow-up], cognitive therapy was again shown to be the most cost-effective intervention, followed by group TF-CBT, Cohen TF-CBT/CPT, narrative exposure, and

parent training. Probabilities of cost-effectiveness for interventions ranked from first to seventh places ranged from 0.31 to 0.50, suggesting considerable uncertainty around the results for high-to-middle rankings. Supportive counselling was likely less cost-effective than no treatment. Group TF-CBT appeared to be the most cost-effective treatment for cost-effectiveness thresholds up to £15,500/QALY; cognitive therapy was shown to be the most cost-effective option at higher thresholds, with a probability of only 0.31 at the £20,000/QALY threshold. When cognitive therapy was excluded from analysis, group TF-CBT was the most cost-effective option at any threshold between zero and £40,000/QALY, with a 0.50 probability of being cost-effective at the £20,000/QALY threshold. Changes in results under this scenario were affected by a combination of the relatively large effects of some interventions at 1-4-month follow-up, according to the NMA results (such as Cohen TF-CBT/CPT, group TF-CBT, and parent training), and the narrower utility gains after remission from PTSD, which favoured less costly interventions (such as group TF-CBT and EMDR).

Full results of scenarios B, C and D are provided in Appendix S4.

In deterministic sensitivity analyses, results were overall robust to changes in the risk of relapse. Under scenarios A and B, there were only small changes in the ranking of interventions in middle places (top 4 interventions, including cognitive therapy, were unaffected). Under scenario C, there were more evident changes in ranking, in particular when the annual risk of relapse was increased to 0.20, however, the 2 likely most cost-effective interventions, which included cognitive therapy, remained the same. Under scenario D, there were moderate changes in ranking in middle-to-lower places, especially when the annual risk of relapse was increased to 0.20, but the top 4 interventions, including cognitive therapy, remained unchanged. Results of deterministic sensitivity analyses are provided in Appendix S5.

DISCUSSION

Overview of findings

Individual forms of TF-CBT, in particular cognitive therapy and narrative exposure, and, to a lesser degree, play therapy appear to be cost-effective in the treatment of children and young people with PTSD more than 3 months after trauma. Evidence on the cost-effectiveness of individual TF-CBT was consistent across different interventions within the class, however, we did not find robust evidence of differential cost-effectiveness amongst different forms of individual TF-CBT. Family therapy and supportive counselling are not expected to be cost-effective relative to other interventions and, under some scenarios, supportive counselling appears to be less cost-effective than no treatment. In-between, there are interventions (EMDR, group TF-CBT and parent training) with modest relative cost-effectiveness, which was affected by the alternative scenarios explored. Results were overall robust to assumptions tested through deterministic sensitivity analyses.

Strengths and limitations

Our analysis utilised effectiveness data derived from a systematic review and NMA of changes in PTSD symptoms (Mavranezouli et al., 2019). This methodology enabled us to consider information from both direct and indirect comparisons between interventions, and allowed simultaneous comparisons across all options while preserving randomisation (Caldwell, Ades, & Higgins, 2005). This approach for evidence synthesis is essential for populating model-based economic studies assessing more than two competing interventions. No inconsistency was detected between direct and indirect evidence. We used 10,000 iterations of the NMA models in the economic analysis, which are representative of the full posterior distributions, and thus the uncertainty in the input estimates was incorporated in the economic model.

The results of the NMAs of 1-4 month follow-up changes in PTSD symptoms showed considerable uncertainty due to the small number and size of the included studies. Thus, results based on these data (scenarios B and D) should be interpreted with caution.

Nevertheless, the NMA that informed the base-case economic analysis (changes in PTSD symptoms between baseline and treatment endpoint) was based on more robust data. Both NMAs were characterised by moderate-to-high heterogeneity. The strengths and limitations of the NMAs that informed the economic analyses should be considered when interpreting the cost-effectiveness results. Moreover, the quality and limitations of the RCTs considered in the NMAs have unavoidably impacted on the quality of the model input parameters. Some interventions were informed by limited evidence: effectiveness data on cognitive therapy and parent training were obtained from 25 and 49 individuals, respectively. Overall, the class of TF-CBT, in particular Cohen TF-CBT/CPT and group TF-CBT, had the largest evidence base.

The economic model structure did not incorporate discontinuation due to the limited discontinuation data available. However, for the NMAs that informed the economic analysis, intention-to-treat continuous data were extracted, where available, so that discontinuation has been implicitly considered in the economic model outcomes. Moreover, the probabilistic analysis took into account the completion rates of the interventions in the RCTs that informed the economic analysis, so that the number of sessions reflected, up to a degree, the attrition rates characterising each intervention.

The baseline risk of remission was estimated from a large longitudinal study that reported remission data for children and young people with PTSD (Rosellini et al., 2017), as the survey's target population was deemed to be directly relevant to our study population. The risk of relapse was not available in published literature, and was therefore based on expert opinion. However, a range of values was tested in deterministic sensitivity analyses.

The time horizon of the analysis was 3 years, which was considered adequate to capture longer-term effects and costs associated with a course of treatment for PTSD, without significant extrapolation over the natural course of PTSD.

Utility data were derived from a systematic literature review. The review included only two studies, each with different strengths and limitations, as discussed earlier. The economic analysis considered utility data from both studies in alternative scenarios, to explore the impact of use of different utility datasets on the results.

Intervention costs were estimated from information provided in the studies included in the NMAs supplemented by the guideline committee's expert opinion, in order to reflect routine UK practice. We assumed that all interventions were delivered by NHS Band 7 clinical psychologists in England, to reflect routine UK practice. The types of therapists delivering interventions in the RCTs that informed the economic analysis ranged from lay counsellors to clinical psychologists. Although the average level of expertise and seniority of therapists in the studies should be broadly equivalent with that assumed in our economic analysis, it is possible that in some RCTs therapists delivering the intervention had greater expertise than those expected to deliver the intervention in routine practice, meaning that the clinical and cost-effectiveness of interventions may have overall been overestimated in our analyses. This is a factor to consider when considering the transferability of RCT research to a practice setting. Nevertheless, we do not have indications of unequal spread of therapists' expertise across different types of interventions across the RCTs that informed our analyses, and therefore we are confident that the risk of potential systematic bias around this issue is small. Regarding NHS/PSS costs incurred by children and young people with PTSD and those remitting from PTSD, these were taken from a small RCT due to lack of other evidence.

Overall, our study is characterised by different strengths and limitations, which we have considered when constructing our model and interpreting the results of our analysis. We carried out probabilistic analyses, which took into account the uncertainty around model

parameters and, where possible, we conducted secondary and deterministic sensitivity analyses to address uncertainties and gaps in the evidence.

Comparison with existing economic evidence

Our findings are in agreement with previous economic evidence, which suggests that TF-CBT, either individual or group, is more cost-effective than waitlist (Shearer et al., 2018), treatment as usual (Aas et al., 2018; Mihalopoulos et al., 2015) or counselling (Gospodarevskaya & Segal, 2012). Our economic analysis estimated the cost-effectiveness of a wider range of psychological interventions available for youth with PTSD, such as different forms of TF-CBT, EMDR, parent training, family therapy, play therapy and supportive counselling and allowed, for the first time, simultaneous comparisons of cost-effectiveness across interventions, and their ranking from the most to the least cost-effective.

Generalisability of the results and implications of the study

Our analysis was conducted from the perspective of the NHS/PSS in England. Results may be generalisable to other settings with similar funding and structure of healthcare and personal social services and comparable care pathways for youth with PTSD. Conclusions on cost-effectiveness ultimately rely on the cost-effectiveness threshold adopted, and this depends on the policy makers' willingness-to-pay for treatment benefits, which may vary across countries and health systems.

Based on our findings, the NICE guideline on PTSD recommended individual TF-CBT for the treatment of children and young people with PTSD (National Institute for Health and Care Excellence, 2018) as the 4 individual forms of TF-CBT assessed in the guideline economic analysis appeared to be cost-effective as they occupied 4 out of the 5 top places in cost-effectiveness ranking in the base-case analysis. No recommendations were made for specific forms of individual TF-CBT, as we found no robust evidence that some individual forms of TF-CBT were more cost-effective than others. Although play therapy was shown to

be cost-effective, results were based on limited evidence (two RCTs). The committee had some difficulty in pinpointing the core active ingredient of play therapy and noted that the intervention resource use differed considerably between the two RCTs, suggesting a less well-defined intervention. Therefore no recommendation for play therapy was made. The committee considered the clinical and cost-effectiveness of EMDR and made a weaker ('consider') recommendation for children and young people aged 7-18 years who do not respond to or engage with TF-CBT. No recommendation was made for group TF-CBT, as overall it was found to be less cost-effective than individual TF-CBT, which was already recommended as a first-line option, so no further benefits were expected to be gained by a potential recommendation on group TF-CBT. Also, no recommendation was made on parent training, because it had modest cost-effectiveness relative to other interventions (it was less cost-effective than individual TF-CBT and, under the base-case analysis and some of the other scenarios, less cost-effective than EMDR), and this result was based on limited evidence (N=49).

CONCLUSION

Individual forms of TF-CBT and, to a lesser degree, play therapy appear to be cost-effective in the treatment of PTSD in youth. Family therapy and supportive counselling are probably not cost-effective relative to other interventions and, under some scenarios, supportive counselling appears to be less cost-effective than no treatment. In-between, there are interventions (EMDR, group TF-CBT and parent training) with modest relative cost-effectiveness. Results should be interpreted with caution due to the limited evidence base characterising some of the interventions. There is a need for well-conducted studies that examine the relative clinical and cost-effectiveness of a range of psychological treatments for children and young people with PTSD, including assessment of longer-term costs and effects, to reduce the uncertainty and limitations characterising current evidence.

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Key points

- PTSD in youth may lead to long-lasting psychological implications, educational difficulties and increased healthcare costs.
- A number of psychological interventions have been shown to be effective in the management of PTSD in youth.
- The cost-effectiveness of interventions for PTSD in youth has implications for policy and practice.
- Individual forms of TF-CBT and, to a lesser degree, play therapy appear to be cost-effective in the treatment of children and young people with PTSD. Family therapy and supportive counselling are likely less cost-effective relative to other interventions.
- There is a need for well-conducted studies that examine the long-term clinical and cost-effectiveness of a range of psychological treatments for children and young people with PTSD.

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Table 1: Intervention costs of psychological interventions for children and young people with PTSD (2017 prices)

Intervention	Resource use details	Intervention cost per person
Supportive counselling	12 x 75min individual sessions	£1,520
[TF-CBT] group CBT	10 x 60min group sessions, 1 therapist and 6 participants per group plus 1 x 60min individual orientation meeting	£270
[TF-CBT] Cohen TF-CBT/CPT	12 x 60min individual/family sessions	£1,216
[TF-CBT] cognitive therapy	10 x 90min individual sessions	£1,520
[TF-CBT] narrative exposure	6 x 60min individual sessions	£608
[TF-CBT] exposure/PE	14 x 60min individual sessions	£1,419
EMDR	8 x 45min individual sessions	£608
Family therapy	4 x 75min group sessions, 1 therapist & 6 families per group, plus 2 hours of individual contact	£287
Play therapy	20 x 30min individual sessions	£1,014
Parent training	12 x45 min individual sessions	£912
No treatment	No resource use	£0
All interventions assumed to be delivered by a Band 7 clinical psychologist CPT: cognitive processing therapy; EMDR: eye movement desensitisation reprocessing; PE: prolonged exposure; TF-CBT: trauma-focused cognitive behavioural therapy		

Table 2. Economic model input parameters

Input parameter	Deterministic value	Probability distribution (type, range)	Sources – comments
Odds ratios of remission versus no treatment at treatment endpoint			
		95% CrI	Mavranezouli et al., 2019; standardised mean differences converted to odds ratios according to Chinn (2000); distribution based on 300,000 samples from posterior distributions outputted from NMAs, thinned by 30 to obtain 10,000 values
Supportive counselling	2.97	0.84 to 10.64	
[TF-CBT] group CBT	5.21	1.87 to 14.60	
[TF-CBT] Cohen TF-CBT/CPT	8.43	2.74 to 26.05	
[TF-CBT] cognitive therapy	204.50	34.36 to 1271.56	
[TF-CBT] narrative exposure	15.14	3.99 to 59.20	
[TF-CBT] exposure/PE	11.42	2.65 to 50.55	
EMDR	6.09	1.52 to 24.80	
Family therapy	1.96	0.22 to 19.03	
Play therapy	11.52	1.51 to 90.65	
Parent training	5.83	0.49 to 66.95	
Odds ratios of remission versus no treatment at 3-month follow-up (secondary analysis only)			

		95% CrI	
Supportive counselling	3.83	0.89 to 12.99	Mavranezouli et al., 2019; Standardised Mean Differences converted to odds ratios according to Chinn (2000); distribution based on 300,000 samples from posterior distributions outputted from NMAs, thinned by 30 to obtain 10,000 values. 3-6 month probability of remission for cognitive therapy borrowed from Cohen TF-CBT/CPT; 3-6 month probability of remission for family therapy and play therapy assumed to equal that of no treatment
[TF-CBT] group CBT	15.51	2.90 to 91.56	
[TF-CBT] Cohen TF-CBT/CPT	23.82	2.19 to 285.43	
[TF-CBT] cognitive therapy	No data	No data	
[TF-CBT] narrative exposure	5.54	1.09 to 28.05	
[TF-CBT] exposure/PE	5.31	0.48 to 57.80	
EMDR	2.94	0.18 to 47.13	
Parent training	6.51	0.23 to 197.35	
Family therapy	No data	No data	
Play therapy	No data	No data	
Probability of remission – no treatment (also applied to all interventions between 3-6 months in base-case analysis & all interventions beyond 6 months in all analyses)			
0-3 months from PTSD onset	0.174	Beta: α=87.00; β=413.00	Rosellini et al., 2018; data averaged between children aged 0-12 years and young people aged 13-24 years. See Appendix S2 for details
0-12 months from PTSD onset	0.370	Beta: α=185.19; β=314.81	
0-24 months from PTSD onset	0.445	Beta: α=222.26; β=277.74	
0-36 months from PTSD onset	0.500	Beta: α=250.00; β=250.00	

Risk of relapse – all treatments			
3-month risk	0.026	Beta: α=2.60; β=97.40	Expert opinion
Utility values		Beta distribution	
<u>Base-case analysis</u>			
PTSD – 3-month	0.170	α=9.01; β=43.98	Gospodarevskaya, 2013; distribution estimated based on method of moments
No-PTSD – 3-month	0.218	α=1271.69; β=4575.15	
<u>Secondary analysis</u>			
PTSD – 3-month	0.185	α=808; β=3,567	Shearer et al., 2018
No-PTSD – 3-month	0.193	α=2,618; β=10,940	
Intervention costs – resource use			
<u>Number of sessions</u>			
Supportive counselling	12	0.60: 10-12, 0.22: 6-9, 0.18: 3-5	Different probabilities assigned to different numbers of sessions for individual therapies, based on intervention completion data and data on the actual and intended mean number of sessions reported in the RCTs that informed the economic analysis. The number of therapist sessions per person attending group therapies was not assigned a probability distribution because the number of group sessions
[TF-CBT] group CBT	10	No distribution	
[TF-CBT] Cohen TF-CBT/CPT	12	0.60: 10-12, 0.22: 6-9, 0.18: 3-5	
[TF-CBT] cognitive therapy	10	0.70: 8-10, 0.16: 6-7, 0.14: 3-5	
[TF-CBT] narrative exposure	6	0.80: 5-6, 0.10: 4, 0.10: 3	
[TF-CBT] exposure/PE	14	0.70: 11-14, 0.16: 7-10, 0.14: 3-6	

EMDR Family therapy Play therapy Parent training Unit cost of clinical psychologist Band 7	8 4 20 12 £101	0.60: 7-8, 0.22: 4-6, 0.18: 2-3 No distribution 0.60: 14-20, 0.22: 10-13, 0.18: 7-9 0.60: 10-12, 0.22: 6-9, 0.18: 3-5 Normal distribution SE = 0.05 of the mean	remains the same, whether a participant attends the full course of treatment or not. Estimated using data from the British Association for Behavioural & Cognitive Psychotherapies (2016); Curtis & Burns (2017); National College for Teaching and Leadership (2016) (see Appendix S3); distribution based on assumption
3-month NHS/PSS health state cost PTSD No-PTSD	 £549 £236	Gamma distribution α=19.53; β=28.12 α=10.37; β=22.74	Shearer and colleagues (2018) data, expressed in 2017 prices using the Hospital and Community Health Services Pay and Prices Index (Curtis & Burns, 2017)
Annual discount rate	0.035	No distribution	Applied to costs and outcomes (National Institute for Health and Care Excellence, 2014)
CBT: cognitive behavioural therapy; CPT: cognitive processing therapy; CrI: credible intervals; EMDR: eye movement desensitisation and reprocessing; NHS: national health service; PE: prolonged exposure; PSS: personal social services; PTSD: post-traumatic stress disorder; SE: standard error; TF: trauma-focused			

Table 3. Base-case results of economic modelling (Scenario A) [utility data from Gospodarevskaya (2013); no beneficial effect beyond treatment endpoint]

Intervention	Mean per person			NMB (£/ person)	Mean rank	Prob*
	QALY	Intervention cost (£)	Total cost (£)		(at a threshold of £20,000/QALY)	
[TF-CBT] cognitive therapy	2.467	1,202	4,347	44,993	1.57	0.78
[TF-CBT] narrative exposure	2.322	517	4,484	41,966	3.35	0.40
Play therapy	2.297	719	4,827	41,109	4.68	0.34
[TF-CBT] exposure/PE	2.297	1,089	5,200	40,742	5.35	0.27
[TF-CBT] Cohen TF-CBT/CPT	2.268	915	5,188	40,178	5.91	0.21
EMDR	2.241	460	4,897	39,920	5.88	0.30
Parent training	2.244	684	5,099	39,788	6.50	0.39
[TF-CBT] group CBT	2.224	270	4,798	39,687	5.83	0.72
Family therapy	2.168	287	5,133	38,222	8.20	0.43
Supportive counselling	2.183	1,141	5,902	37,753	9.57	0.49
No treatment	2.121	0	5,113	37,304	9.16	1.00

CPT: cognitive processing therapy; EMDR: eye movement desensitisation reprocessing; NMB: net monetary benefit; PE: prolonged exposure; Prob: probability of cost-effectiveness; TF-CBT: trauma-focused cognitive behavioural therapy

*estimated in a step-wise approach, according to which the most cost-effective intervention is omitted at each step, and the probability of cost-effectiveness of the next most cost-effective intervention amongst the remaining treatment options is re-calculated

Figure 1. Schematic diagram of the economic model

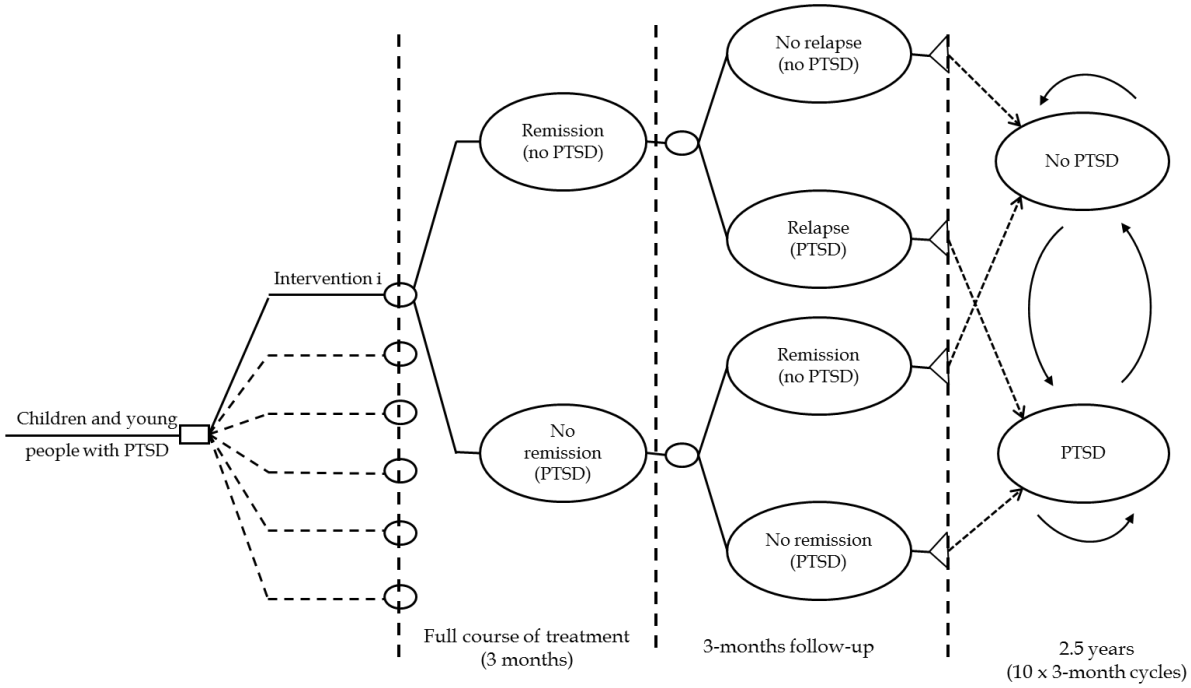


Figure 2. Cost-effectiveness plane: base-case analysis [utility data from Gospodarevskaya (2013); no beneficial effect beyond treatment endpoint]

Results for 1,000 children and young people with PTSD.

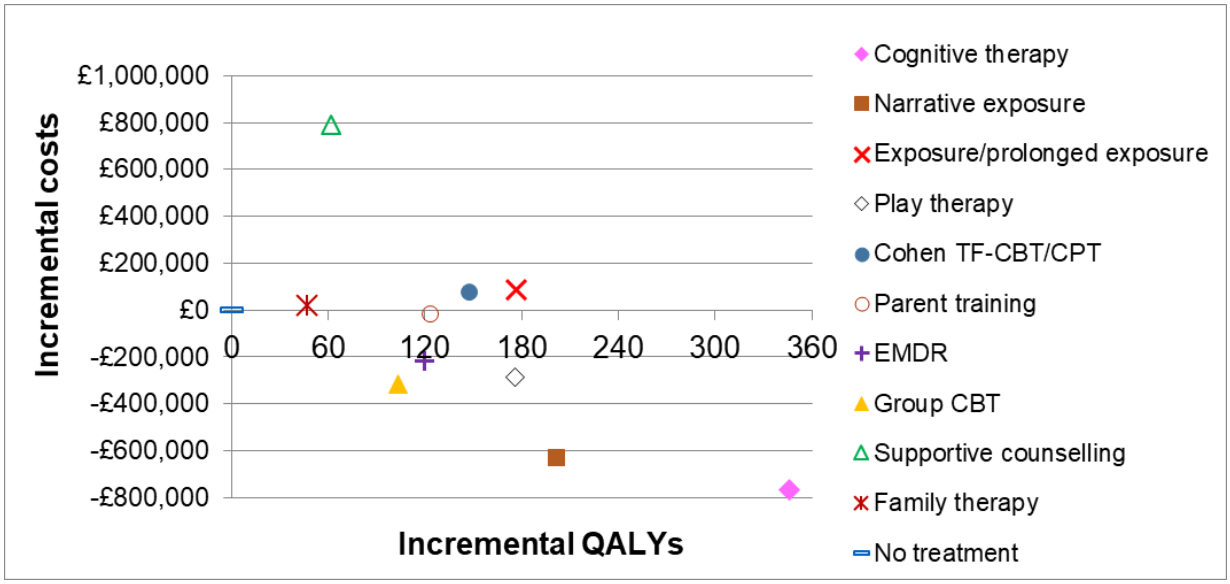
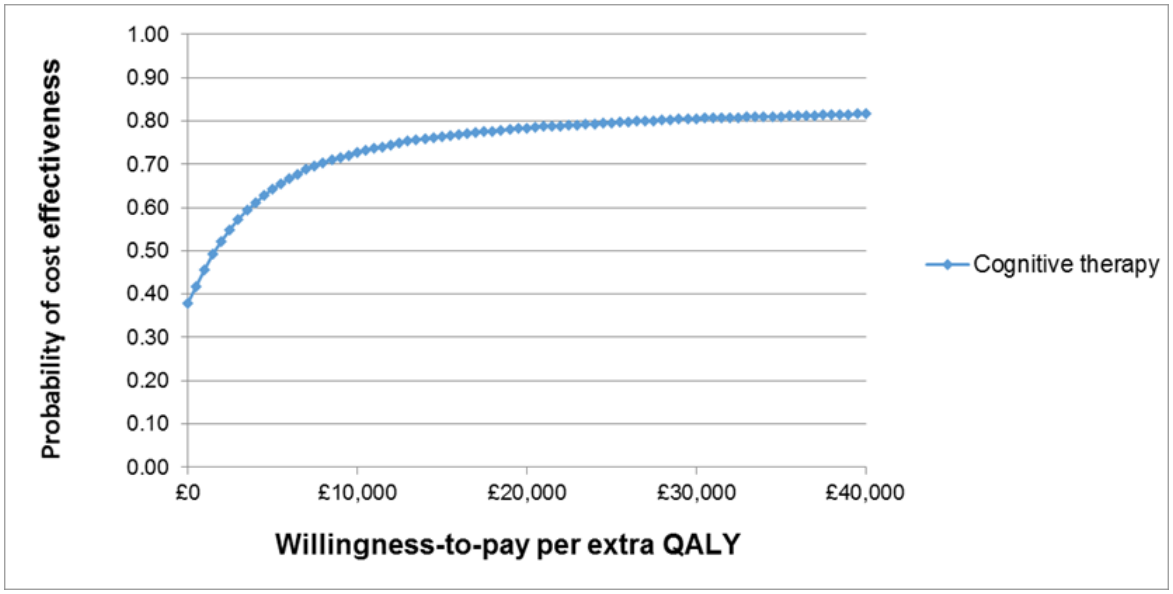
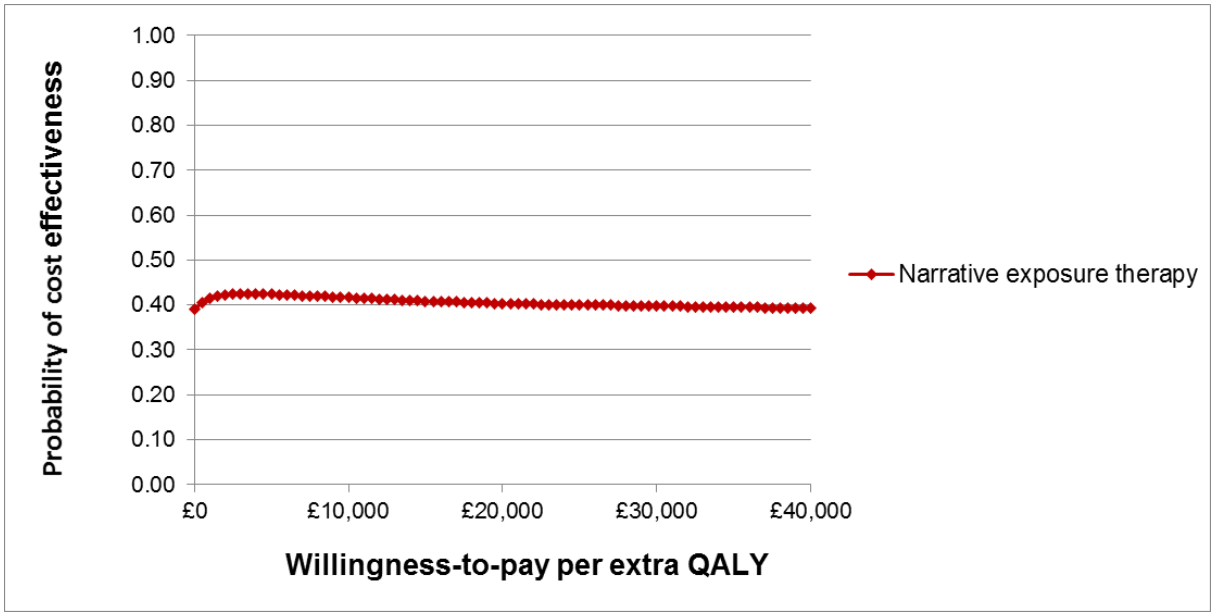


Figure 3. Cost-effectiveness acceptability frontier: base-case analysis [utility data from Gospodarevskaya (2013); no beneficial effect beyond treatment endpoint] – cognitive therapy for PTSD included in analysis



Comparison across 11 alternative treatment options: supportive counselling, group CBT [TF-CBT], Cohen TF-CBT/ CPT [TF-CBT], cognitive therapy for PTSD [TF-CBT], narrative exposure therapy [TF-CBT], exposure/PE [TF-CBT], eye movement desensitisation and reprocessing (EMDR), family therapy, play therapy, parent training, no treatment

Figure 4. Cost-effectiveness acceptability frontier: base-case analysis [utility data from Gospodarevskaya (2013); no beneficial effect beyond treatment endpoint] – cognitive therapy for PTSD excluded from analysis



Comparison across 10 alternative treatment options: supportive counselling, group CBT [TF-CBT], Cohen TF-CBT/ CPT [TF-CBT], narrative exposure therapy [TF-CBT], exposure/PE [TF-CBT], eye movement desensitisation and reprocessing (EMDR), family therapy, play therapy, parent training, no treatment