Cost-effectiveness of therapist-assisted internet-delivered psychological therapies for PTSD differing in trauma focus in England: an economic evaluation based on the STOP-PTSD trial

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Summary

Background Although there are effective psychological treatments for post-traumatic stress disorder (PTSD), they remain inaccessible for many people. Digitally enabled therapy is a way to overcome this problem; however, there is little evidence on which forms of these therapies are most cost effective in PTSD. We aimed to assess the cost-effectiveness of the STOP-PTSD trial, which evaluated two therapist-assisted, internet-delivered cognitive behavioural therapies: cognitive therapy for PTSD (iCT-PTSD) and a programme focusing on stress management (iStress-PTSD).

Methods In this health economic evaluation, we used data from the STOP-PTSD trial (n=217), a single-blind, randomised controlled trial, to compare iCT-PTSD and iStress-PTSD in terms of resource use and health outcomes. In the trial, participants (aged ≥18 years) who met DSM-5 criteria for PTSD were recruited from primary care therapy services in South East England. The interventions were delivered online with therapist support for the first 12 weeks, and three telephone calls over the next 3 months. Participants completed questionnaires on symptoms, wellbeing, quality of life, and resource use at baseline, 13 weeks, 26 weeks, and 39 weeks after randomisation. We used a cost-effectiveness analysis to assess cost per quality-adjusted life year (QALY) at 39 weeks post-randomisation, from the perspective of the English National Health Service (NHS) and personal social services and on the basis of intention-to-treat for complete cases. Treatment modules and the platform design were developed with extensive input from service users: service users also advised on the trial protocol and methods, including the health economic measures. This is a pre-planned analysis of the STOP-PTSD trial; the trial was registered prospectively on the ISRCTN Registry (ISRCTN16806208).

Findings NHS costs were similar across treatment groups, but clinical outcomes were superior for iCT-PTSD compared with iStress-PTSD. The incremental cost-effectiveness ratio for NHS costs and personal social services was estimated as £1921 per QALY. iCT-PTSD had an estimated 91·6% chance of being cost effective at the £20 000 per QALY threshold. From the societal perspective, iCT-PTSD was cost saving compared with iStress-PTSD.

Interpretation iCT-PTSD is a cost-effective form of therapist-assisted, internet-delivered psychological therapy relative to iStress-PTSD, and it could be considered for clinical implementation.

Funding Wellcome Trust and National Institute of Health Research Oxford Health Biomedical Research Centre.

Lancet Psychiatry 2024; 11: 339–47

Published Online March 27, 2024 https://doi.org/10.1016/S2215-0366(24)00055-5

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Introduction

Post-traumatic stress disorder (PTSD) is a severe mental condition that can occur following a traumatic event, and it affects between 1·3% and 3·6% of people each year in the UK.[1] Individuals with PTSD have distressing symptoms, including re-experiencing trauma, avoidance of reminders, negative cognitions about the self and the world, hyperarousal, and social and economic functional impairment. PTSD is associated with reduced quality of life,[2] substantial direct health-care costs, and wider societal impacts on employment and unpaid care requirements.[3] UK National Institute for Health and Care Excellence (NICE) guidance for treating PTSD currently recommends individual trauma-focused psychological therapies as first-line interventions.[1] In the UK National Health Service (NHS), these therapies are typically provided over 8–12 face-to-face sessions for single traumas, and 18–32 sessions for multiple traumas. The face-to-face, trauma-focused cognitive behavioural therapies (CBTs) recommended by NICE involve working on trauma memories and their meanings and unhelpful ways of coping with the trauma. These therapies have been shown to be both effective[1] and cost-effective[2,3] compared with no treatment or treatment as usual. However, a 2013 Cochrane review[4] found that non-trauma-focused, face-to-face CBT might be as effective in the short term as the NICE-recommended trauma-focused therapies. Moreover, model-based economic evaluation of face-to-face therapy

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Research in context

Evidence before this study

Relevant existing economic evaluations of post-traumatic stress disorder (PTSD) treatments were identified from a 2020 systematic review by von de Warth and colleagues. We identified an additional relevant study by searching PubMed from database inception to Sept 4, 2023, with the terms ((("PTSD") OR ("posttraumatic") OR ("post-traumatic")) AND (("CBT") OR ("therapy")) AND ("cost-effectiveness" OR "health economic")) with no language restrictions. Although face-to-face trauma-focused cognitive behaviour therapies (CBTs) for PTSD are recommended by the UK National Institute for Health and Care Excellence (NICE) as first-line treatments, evidence indicates that some face-to-face non-trauma-focused CBTs are also efficacious in the short term. A model-based economic evaluation of face-to-face therapy indicated that trauma-focused CBT is cost effective relative to non-trauma-focused CBT. Digitally enabled therapy has been proposed as a method to improve access to delivering CBT. A 2021 Cochrane review found that internet-delivered CBT programmes using trauma-focused CBT procedures lead to moderately better outcomes than waiting lists, but they are not superior to other treatments and outcomes are heterogeneous, and none of the eligible studies included an economic evaluation. A recent trial (STOP-PTSD) found that an internet-delivered, therapist-assisted cognitive therapy for PTSD (iCT-PTSD) was superior to an internet-delivered, therapist-assisted stress management therapy for PTSD (iStress-PTSD). The trauma-focused iCT-PTSD achieved comparable recovery rates to those found for face-to-face cognitive therapy in previous research. Economic evidence on internet-delivered CBTs is scarce. A recent trial (RAPID) compared a guided self-help, trauma-focused CBT programme for mild-to-moderate PTSD following single trauma with face-to-face therapy, but although the programme was cost saving, it was not cost effective at the £20 000 per quality-adjusted life year (QALY) threshold. A NICE assessment therefore recommended that the digitally enabled programmes in the STOP-PTSD and RAPID trials could be used in the English National Health Service (NHS) to generate further real-world evidence.

Added value of this study

The analysis in this study indicates that iCT-PTSD is a cost-effective form of therapy relative to iStress-PTSD, with an incremental cost-effectiveness ratio of £1921 per QALY. This is, to our knowledge, the first economic evaluation comparing a trauma-focused, internet-delivered, therapist-assisted CBT programme with comprehensive, internet-delivered, non-trauma-focused CBT. This study shows that there are important economic and clinical differences in the choice of internet-delivered therapy for PTSD. Our findings also show that the wider societal costs of PTSD should be an important consideration, as iCT-PTSD is more likely to be cost effective when costs outside the NHS and personal social services (ie, unpaid care, productivity loss, and privately funded health care) are also considered.

Implications of all the available evidence

iCT-PTSD is an effective and cost-effective form of internet-delivered, therapist-supported CBT compared with internet-delivered, therapist-supported non-trauma-focused CBT. It remains unclear whether iCT-PTSD would be a cost-effective alternative to face-to-face therapy or alternative digitally enabled trauma-focused CBT programmes. Use of iCT-PTSD and other internet-delivered CBT tools should be accompanied by research on patient outcomes and resource use in real-world settings. As digitally enabled therapies have become more relevant to the NHS, choosing evidence-based programmes is increasingly important.

indicates that trauma-focused CBT is cost effective relative to non-trauma-focused CBT.[5] In the author group's clinical practice, many patients do not receive a full course of trauma-focused treatment due to lack of resources or clinician confidence in delivering trauma-focused CBT.

Access to psychological treatment for PTSD is limited due to waiting lists for mental health services and individual circumstances, such as mobility difficulties, time constraints due to working hours and childcare, and personal stigma.[6] Failure to provide timely treatment can lead to a reduction in health-related quality of life, and can affect an individual's ability to work and function. Internet-delivered—or digitally enabled—psychological treatments have been proposed as an accessible and efficient alternative form of treatment for PTSD, with therapist-assisted or guided self-help approaches recommended over unguided self-help programmes.[7,8] A 2021 Cochrane review[8] found that internet-delivered CBT is superior to waiting lists for reducing PTSD symptoms. There is little evidence on which particular forms of digitally enabled therapies are most effective and appropriate for PTSD, which might contribute to ongoing reservations in patients, practitioners, and commissioners, despite ongoing increases in the adoption of internet-based treatments.[9,10] It remains to be tested whether trauma-focused-CBT is superior to non-trauma-focused-CBT when delivered as a digitally enabled therapy.

This study uses data from the STOP-PTSD trial[11] to evaluate the cost-effectiveness of therapist-assisted internet-delivered cognitive therapy for PTSD (iCT-PTSD).[11] This novel treatment implements all the procedures of cognitive therapy for PTSD, one of the NICE-recommended first-line treatments for PTSD, which has shown large effects on PTSD symptoms and quality of life.[12,13] Findings indicated that iCT-PTSD is acceptable to patients and showed recovery rates similar to those found in previous trials of face-to-face cognitive therapy for PTSD.[10] The aim of this study was to assess the cost-effectiveness of iCT-PTSD compared with a comprehensive

therapist-assisted internet-delivered cognitive behavioural treatment that focuses on coping with and managing stress (iStress-PTSD).

Methods

Study design and participants

In this health economic evaluation, we report on cost-effectiveness analysis of the STOP-PTSD trial by measuring resource use and health outcomes from baseline to 39 weeks after randomisation. A health economics analysis plan was developed before the start of analysis and is available in the appendix (pp 18–25). The study population used in the cost-effectiveness analysis consisted of STOP-PTSD trial participants who had completed the resource use and health outcomes questionnaires at all relevant assessments. Descriptive statistics of the population used (including individuals who did complete the questionnaires fully) and the complete case criteria are shown in the appendix (p 2). This approach is in line with best-practice recommendations for performing economic evaluation[14] and the study health economics analysis plan. The trial was registered prospectively on the ISRCTN Registry (ISRCTN16806208). Written informed consent forms were collected from all participants. The study, including the health economics component, had NHS Research Ethics approval (West Midlands–The Black Country Research Ethics Committee, 17/WM/0441; IRAS 224759) and a Trial Oversight Committee.

Interventions

The STOP-PTSD trial was a single-blind, randomised controlled trial, in which participants were recruited from primary care therapy services in three locations in South East England (Thames Valley, London, and Sussex), between Jan 15, 2018, and March 31, 2020. Participants were aged 18 years or older, met the DSM-5 diagnostic criteria for PTSD as assessed with the Structured Clinical Interview for DSM-5,[15] were able to read and write in English, and had access to the internet. If taking psychotropic medication, participants were required to have been on a stable dose for at least 1 month before randomisation and were asked to maintain this dose during treatment. Exclusion criteria were a history of psychosis, current substance dependence, current borderline personality disorder, or acute suicide risk. Participants (n=217) were randomly allocated (3:3:1) to iCT-PTSD (n=92), iStress-PTSD (n=93), or a 13-week waiting list with usual NHS care, consisting mainly of general practitioner support, a stable dose of medication, and treatment for pain and comorbid medical conditions when needed (n=32).[11] After 13 weeks, participants on the waiting list were randomly assigned (1:1) to a treatment group if they still met the inclusion criteria (n=27). The randomisation programme used minimisation with a random component by location, time since traumatic event, and baseline PTSD symptom severity. Further details on the trial design, the population assessed for eligibility, reasons for exclusions and dropout, and the flow of individuals are in the published trial protocol,[16] the paper reporting the clinical outcomes of the trial,[11] and the appendix (pp 2–3). Participants reported mild to severe current PTSD from one to four traumas, with a life-time history of on average five trauma types; 24% met self-reported criteria for complex PTSD,[17] as outlined in the ICD-11.

Treatment in iCT-PTSD and iStress-PTSD was through internet-delivered psychological therapy modules on the same platform, supported by secure messaging and weekly scheduled telephone calls (20–30 min) with a therapist over 12 weeks, followed by a 3-month booster period with monthly telephone calls. Modules were released by the therapist through an online interface at a rate of two to three per week during the weekly treatment phase, and as needed during the booster period. iCT-PTSD modules implement all the procedures of face-to-face cognitive therapy for PTSD,[12,13] including core modules for individual case formulation and psychoeducation, reclaiming life assignments, updating trauma memories, trigger discrimination, and working on individually relevant cognitive themes and unhelpful coping behaviours and cognitive strategies. The iStress programme[18] was adapted for the STOP-PTSD trial with the inclusion of psychoeducation about PTSD and techniques for coping with PTSD symptoms, and some additional modules.[16] iStress-PTSD focuses on learning coping strategies to reduce stress and manage PTSD symptoms, including exposure in vivo, cognitive restructuring, applied relaxation, and mindfulness exercises. iStress-PTSD is not trauma focused, but participants can choose to apply the tools and techniques they have learned to trauma-related memories and situations, with the support of the therapist. Details of the treatments and modules are in the appendix (pp 10–14).

See Online for appendix

Data collection

Participants completed questionnaires on measures of symptoms, quality of life, and resource use at baseline, 13 weeks, 26 weeks, and 39 weeks after randomisation. Symptoms were measured using the PTSD Checklist for DSM-5 (PCL-5),[19] which was the primary outcome measure of the STOP-PTSD trial, and quality of life was assessed through the EuroQol EQ-5D-5L questionnaire.[20]

The costs for each participant were estimated with the NHS and personal social services (PSS) perspective (referred to as the NHS perspective), which is based on therapist time spent delivering the intervention and publicly funded health and PSS resource use. The therapist time spent was measured as the total minutes spent on weekly and monthly calls with and writing messages to patients, recorded weekly by therapists for each patient. Health and PSS resource use was estimated from responses to the Client Service Receipt

	iCT-PTSD (n=75)	iStress-PTSD (n=76)
Site		
Thames Valley	56 (74·7%)	56 (73·7%)
London	10 (13·3%)	15 (19·7%)
Sussex	9 (12·0%)	5 (6·6%)
Months since trauma	44·8 (82·8)	39·0 (82·5)
Baseline PCL-5 score	43·9 (12·4)	47·7 (11·4)
Baseline EQ-5D* use	0·6 (0·2)	0·6 (0·2)
Baseline NHS costs, £	428·7 (1116·2)	248·2 (711·1)

Data shown are n (%) or mean (SD). iCT-PTSD=therapist-assisted, internet-delivered cognitive therapy for PTSD. iStress-PSTD= therapist-assisted, internet-delivered cognitive behavioural therapy programme focusing on stress management for PTSD. NHS=English National Health Service. PCL-5=PTSD Checklist for DSM-5. PTSD=post-traumatic stress disorder. *Standardised measure of health-related quality of life developed by EuroQol.

Table 1: **Descriptive statistics of participants with complete data at baseline**

	iCT-PTSD (n=75)	iStress-PTSD (n=76)	Difference (n=151)
PCL-5 score (13 weeks)	13·5 (12·6)	19·9 (15·6)	–5·1 (–9·3 to –1·0)
Clinically significant improvement (13 weeks)	81·3% (39·2)	56·6% (49·9)	22·7% (10·0 to 35·4)
EQ-5D* utility (13 weeks)	0·73 (0·25)	0·69 (0·25)	0·03 (–0·03 to 0·10)
EQ-5D* utility (26 weeks)	0·79 (0·23)	0·70 (0·28)	0·07 (0·01 to 0·14)
EQ-5D* utility (39 weeks)	0·77 (0·22)	0·71 (0·26)	0·04 (–0·02 to 0·10)
QALYs (baseline to 39 weeks)	0·55 (0·16)	0·51 (0·17)	0·03 (0·00 to 0·07)

Data are mean (SD) or adjusted mean difference (95% CI). Mean differences were calculated with adjustment for randomisation variables (site, months since trauma, and baseline PCL-5 score) in a regression model with Gaussian distribution. EQ-5D utility and QALYs were also adjusted for baseline EQ-5D utility. iCT-PTSD=therapist-assisted, internet-delivered cognitive therapy for PTSD. iStress-PSTD=therapist-assisted, internet-delivered cognitive behavioural therapy programme focusing on stress management for PTSD. PCL-5=PTSD Checklist for DSM-5. PTSD=post-traumatic stress disorder. QALY=quality-adjusted life year. *Standardised measure of health-related quality of life developed by EuroQol.

Table 2: **Outcomes descriptive statistics**

Inventory questionnaire,[21] with a recall period of 3 months. Following NICE guidance,[22] admissions to general hospitals unrelated to the traumatic event were excluded. Medication costs were also excluded as there was not sufficient detail on dosage collected in the trial. Costs were also estimated with a societal costing perspective, by adding privately paid health and PSS (measured using the Client Service Receipt Inventory) and unpaid care and productivity loss (measured by the widely used Productivity and Costs Questionnaire[23]) to the costs included in the NHS perspective.

Resource use was valued in 2020–21 terms using unit costs from the PSS Research Unit Costs of Health and Social Care, 2021.[24] Days of informal caregiving and reduced productivity were conservatively valued using the National Minimum Wage.[25] An overview of the unit costs and their sources is provided in the appendix (pp 5–6). All costs were estimated for the 13 weeks before baseline and the 13-week, 26-week, and 39-week assessments.

Data analysis

Following NICE guidance,[22] effectiveness was expressed in terms of health-related quality-adjusted life years (QALYs) using utility scores derived by mapping the responses to EuroQol's EQ-5D-5L questionnaire[20] to EQ-5D-3L health state utility scores using the cross-walks developed by van Hout and colleagues.[26] QALYs were calculated using the area-under-the-curve method for utility scores at baseline, 13 weeks, 26 weeks, and 39 weeks. Additionally, clinically significant improvement was used as a PTSD-specific outcome measure, based on responses to PCL-5.[19] A clinically significant improvement was defined a priori as a clinically significant change in PCL-5 score at 13 weeks in line with Jacobson and Truax,[27] if both the total PCL-5 score had reduced by at least 10 since baseline assessment as recommended for a clinically significant difference[28] and the total PCL-5 score was outside the range of the clinical population—ie, less than the population mean minus 2 SD of the trial population at initial randomisation.[27] Additional detail on the calculation of outcomes is in the appendix (p 9).

Incremental costs and incremental outcomes between the participants receiving iCT-PTSD or iStress-PTSD were estimated using generalised linear model analysis and controlling for randomisation variables (PCL-5 at baseline, log months since trauma, and a categorical variable for site). The baseline value of costs or outcomes was also included in the regression, following best practice.[29] The incremental costs and outcomes were estimated as the average treatment effect of iCT-PTSD across all participants. Statistical uncertainty was characterised by repeating this analysis on 10 000 bootstrapped samples with replacement (stratified by treatment assignment) and taking the mean of the bootstrapped results as incremental costs and outcomes, following NICE guidance.[22]

The estimated incremental costs and outcomes were used to calculate incremental cost-effectiveness ratios (ICERs), expressed as cost per QALY or cost per clinically significant improvement. Both the central and bootstrapped estimates of incremental costs and outcomes were plotted on a cost-effectiveness plane. For the analysis using QALYs as an outcome, cost-effectiveness acceptability curves were calculated showing the proportion of bootstrapped samples in which iCT-PTSD was cost effective relative to iStress-PTSD at willingness-to-pay thresholds ranging between £0 and £40 000 per

	iCT-PTSD		iStress-PTSD		Difference	
	Mean (SD)	Mean cost, £ (SD)	Mean (SD)	Mean cost, £ (SD)	Mean difference (95% CI)	Mean cost difference, £ (95% CI)
CSRI						
Admissions to hospital (mental health-related)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0 to 0·0)	0·0 (0·0 to 0·0)
Days in hospital (mental health-related)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0)	0·0 (0·0 to 0·0)	0·0 (0·0 to 0·0)
Visits to psychiatrist in hospital	0·2 (0·9)	13·2 (56·8)	0·1 (0·9)	8·1 (57·3)	0·1 (–0·2 to 0·4)	6·8 (–12·0 to 25·6)
Visits to another doctor in hospital	1·2 (3·1)	73·8 (189·5)	1·1 (2·5)	68·0 (151·9)	–0·2 (–0·9 to 0·5)	–14·4 (–58·0 to 29·1)
Visits to day hospital	0·5 (1·9)	408·0 (1601·6)	0·4 (1·3)	302·0 (1142·1)	0·1 (–0·4 to 0·6)	75·4 (–368·4 to 519·3)
Visits to a general practitioner	2·5 (3·0)	96·8 (118·6)	2·8 (3·8)	111·0 (147·4)	–0·3 (–1·3 to 0·7)	–11·1 (–50·5 to 28·3)
Visits to another doctor outside hospital	0·2 (0·8)	30·6 (98·0)	0·1 (0·4)	11·7 (51·7)	0·1 (–0·1 to 0·3)	13·9 (–6·8 to 34·7)
Contacts with a community psychiatric nurse	0·0 (0·2)	1·5 (12·7)	0·1 (0·3)	2·9 (15·3)	0·0 (–0·1 to 0·1)	–1·8 (–6·4 to 2·8)
Sessions with a counsellor or therapist excluding the trial	0·7 (2·4)	37·1 (126·9)	0·9 (2·8)	47·9 (150·3)	–0·2 (–1·0 to 0·7)	–9·0 (–54·6 to 36·7)
Social worker	0·0 (0·2)	1·2 (10·6)	0·1 (0·4)	3·0 (18·9)	0·0 (–0·1 to 0·1)	–0·7 (–4·5 to 3·2)
Self-help or support group	0·2 (1·0)	2·1 (9·7)	0·4 (2·6)	3·6 (24·2)	0·1 (–0·2 to 0·5)	1·2 (–2·3 to 4·6)
Total	NA	664·3 (1695·4)	NA	558·2 (1297·0)	NA	–275·1 (–1353·6 to 803·5)
Costs of intervention						
Therapist time (minutes)	446·1 (135·5)	484·5 (147·1)	365·0 (112·1)	396·4 (121·7)	86·4 (46·5 to 126·4)	93·9 (50·5 to 137·2)
Total NHS costs	NA	1148·8 (1718·2)	NA	954·6 (1297·8)	NA	61·2 (–381·0 to 428·7)

Differences in cost items are adjusted for randomisation variables and baseline values of each variable in a regression model with Gaussian distribution. Adjusted difference in total NHS costs controlled for the same variables in regressions with a gamma distribution and log link, repeated across 10 000 bootstraps. CSRI=Client Service Receipt Inventory. iCT-PTSD=therapist-assisted, internet-delivered cognitive therapy for PTSD. iStress-PSTD=therapist-assisted, internet-delivered cognitive behavioural therapy programme focusing on stress management for PTSD. NA=not applicable. NHS=English National Health Service. PTSD=post-traumatic stress disorder.

Table 3: **Descriptive statistics of NHS perspective costs at 39 weeks**

QALY. The willingness-to-pay thresholds recommended by NICE are £20 000 and £30 000 per QALY gained, indicating that this range represents good value of NHS resources.[22]

Statistical analysis was blind, based on intention-to-treat for complete cases, and performed using Stata 17.0. Treatment modules and the design of the platform were developed with extensive input from service users. The Trial Oversight Committee had service user representation and advised on the trial protocol and methods, including the health economic measures, and approved the statistical analysis plan and health economics analysis plan. Discounting of costs and outcomes was not applied due to the short time-horizon and no subgroup or distributional analysis was conducted in line with the trial.

Four sensitivity analyses were performed to address uncertainty in the estimated ICERs. For multiple imputation for missing data, a substantial number of participants (n=61) were excluded from the main analysis due to missing cost or outcome data at one or more time-points; multiple imputation was used to estimate missing observations, and the resulting dataset was used to repeat the primary analysis. Descriptive statistics on the individuals excluded due to missing data are in the appendix (pp 3–4). For the main analysis, these observations are assumed to be missing completely at random. The second sensitivity analysis repeated the primary analysis using costs with a societal perspective. Third, to evaluate the effect of including the post-waiting list assignments on cost-effectiveness

	iCT-PTSD (n=75), mean (95% CI)	iStress-PTSD (n=76), mean (95% CI)	Incremental mean (95% CI)	ICER
Cost-effectiveness results for QALYs over 39 weeks				
Costs to NHS and personal social services, £	1087 (843 to 1393)	1026 (757 to 1400)	61 (–283 to 386)	..
QALYs	0·55 (0·52 to 0·57)	0·51 (0·48 to 0·55)	0·03 (0·00 to 0·07)	£1921
Cost-effectiveness results for clinically significant improvement at 13 weeks				
Costs to NHS and personal social services, £	617 (511 to 754)	574 (439 to 755)	43 (–121 to 191)	..
Clinically significant improvement	80·6% (71·2 to 89·0)	58·0% (47·5 to 68·4)	22·6 (9·4 to 35·6)	£191

Mean and incremental values are central estimates of bootstrapped GLMs controlling for baseline outcome, time since trauma, PCL-5, and site. 95% CIs are constructed from the distribution of bootstrapped estimates. GLM=generalised linear model. ICER=incremental cost-effectiveness ratio. iCT-PTSD=therapist-assisted, internet-delivered cognitive therapy for PTSD. iStress-PSTD=therapist-assisted, internet-delivered cognitive behavioural therapy programme focusing on stress management for PTSD. PTSD=post-traumatic stress disorder. QALY=quality-adjusted life year.

Table 4: **Bootstrapped incremental costs, outcomes, and cost-effectiveness of iCT-PTSD and iStress-PTSD**

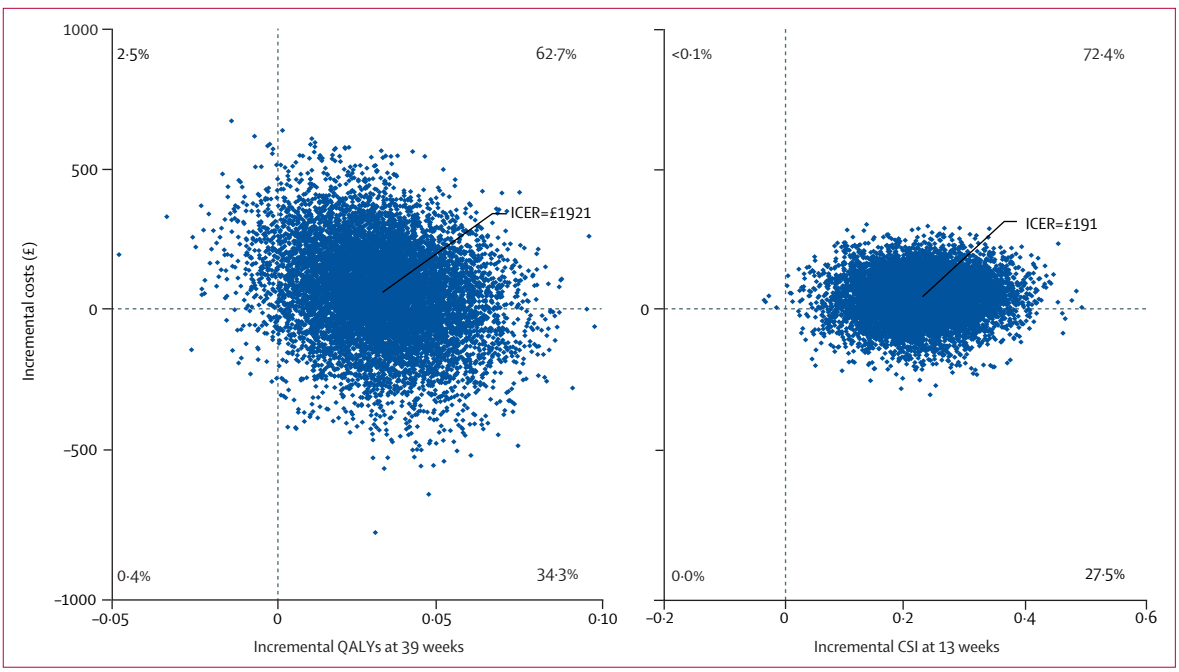

Figure 1: **Cost-effectiveness planes for iCT-PTSD versus iStress-PTSD**
CSI=clinically significant improvement. ICER=incremental cost-effectiveness ratio. QALY=quality-adjusted life year.

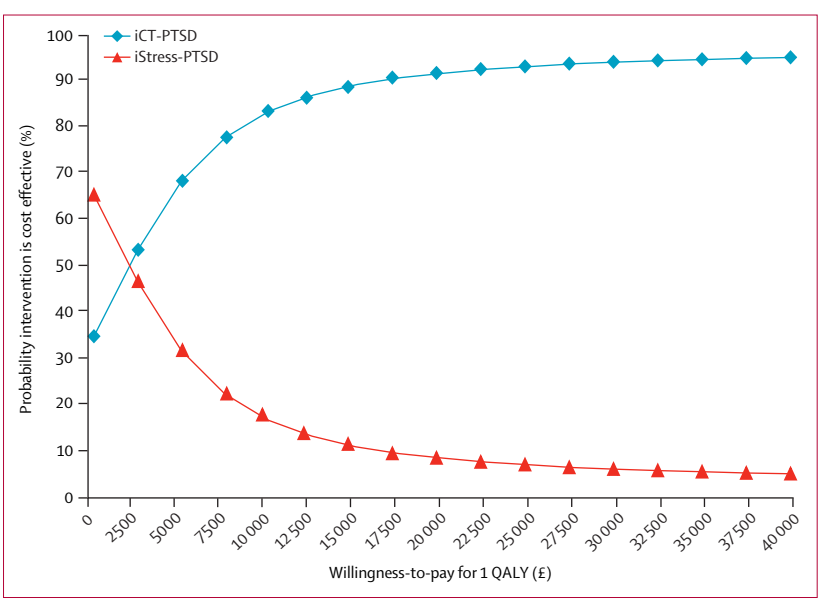

Figure 2: **Cost-effectiveness acceptability curve for QALYs at 39 weeks**
iCT-PTSD=therapist-assisted, internet-delivered cognitive therapy for PTSD. iStress-PSTD=therapist-assisted, internet-delivered cognitive behavioural therapy programme focusing on stress management for PTSD. PTSD=post-traumatic stress disorder. QALY=quality-adjusted life year.

estimates, the primary analysis was repeated on the basis of initial assignments. Finally, estimates of cost-effectiveness at alternative timepoints are provided for comparability. Further details on the sensitivity analyses are available in the appendix (pp 9–10).

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
The full trial population consisted of 217 participants, of whom 158 (73%) were female, 57 (26%) were male, and two (1%) had another gender. 170 (78%) were White (British), 20 (9%) were White (other), six were Asian (3%), ten (5%) were Black, eight (4%) had a mixed ethnic background, and three (1%) had another ethnic background. The mean age was 36·36 years (SD 12·11, range 18–71). Further descriptive statistics for the full trial population are in the appendix (p 3). 61 (28·1%) participants were excluded from the main analysis due to missing outcomes or costs data, and 151 (69·6%) participants had complete data and were included in the primary analysis (table 1). No significant differences in baseline and randomisation variables were observed by final assignment for excluded participants; descriptive statistics for excluded participants by treatment group are in the appendix (pp 3–4).

When compared with iStress-PTSD, iCT-PTSD led to an increase in QALYs of 0·03 (95% CI 0·00–0·07) over 39 weeks, due mainly to 0·07 (95% CI 0·01–0·14) higher EQ-5D utility at 26 weeks (table 2). The rates of clinically significant improvement were 22·7 (95% CI 10·0–35·4) percentage points higher for iCT-PTSD (table 2).

There were no significant differences in resource use costs except for the therapist costs, which were £93·87

(95% CI 50·5–137·2) higher in iCT-PTSD than in iStress-PTSD (table 3), driven by an additional 86·4 (95% CI 46·5–126·4) min of therapist time on average over 26 weeks. A complete list of resource use costs is provided in the appendix (p 7).

Compared with iStress, iCT-PTSD led to £61 (95% CI –283 to 386) higher costs and 0·03 (95% CI 0·00 to 0·07) additional QALYs over 39 weeks, resulting in an ICER of £1921/QALY (table 4). iCT-PTSD also led to £43 (95% CI –121 to 191) higher costs and 22·6 (95% CI 9·4 to 35·6) percentage points higher clinically significant improvement at 13 weeks (table 4).

The uncertainty in the ICERs was predominantly driven by uncertainty in incremental costs (figure 1). Considering this uncertainty, the probability of iCT-PTSD being cost effective was 91·6% at a £20 000 willingness-to-pay threshold and 94·0% at a £30 000 threshold (figure 2).

The results of the sensitivity analyses showed similar or higher cost-effectiveness of iCT-PTSD. The most notable differences with the results of the main analysis were that the probability of iCT-PTSD was 99% at a £20 000 willingness-to-pay threshold when taking the societal costing perspective, and uncertainty in the ICERs was higher when performing multiple imputation or removing participants who were initially assigned to the waiting list. The results of the sensitivity analyses are summarised in the appendix (p 8).

Discussion

The evidence provided in this study indicates that iCT-PTSD is cost effective compared with iStress-PTSD. The estimated ICER of £1921 per QALY is well below the £20 000 and £30 000/QALY willingness-to-pay thresholds used by NICE,[22] with a probability of iCT-PTSD being cost effective compared with iStress-PTSD of 91·6% and 94·0% at these thresholds, respectively. These probabilities were even higher when accounting for missing data, and iCT-PTSD surpassed iStress-PTSD at both 13 weeks and 39 weeks when taking the societal perspective in costs.

Assignment to iCT-PTSD resulted in an additional one in five patients recovering within the first 3 months of treatment, and the equivalent of approximately 12 additional days of healthy life. The improvement in QALYs for iCT-PTSD participants was significant over 39 weeks, but the observed difference in clinically significant improvement at 13 weeks between treatment groups did not immediately translate into improved quality of life. These findings are in line with the results of the STOP-PTSD trial, which reported an adjusted difference of –5·82 (95% CI –9·59 to –2·04; standardised effect size d=0·44 [0·15 to 0·72]) in PCL-5 scores.[11] When this relatively small-to-medium difference in outcomes was combined with a sufficiently small difference in costs, the treatment was deemed highly cost effective, because cost-effectiveness is driven by the joint distribution of incremental costs and incremental outcomes. Our findings are also in line with evidence that discriminative ability of the EQ-5D-5L for symptoms of PTSD is strong but responsiveness is weak.[30] Weak responsiveness of EQ-5D to PTSD symptoms might also in part be explained by the participants still learning to apply what they learned in treatment to their everyday lives, which then leads to larger effects on quality of life in the long term. An alternative measure of quality of life collected in this trial showed continued differences between trial groups in favour of iCT-PTSD up to 65 weeks.[11] In general, it is to be expected that symptom improvement (eg, reductions in intrusive memories and avoidance) might precede improvements in quality of life (such as improved satisfaction with work and social relationships) in PTSD. The temporal relationship of improvement in different outcomes warrants further research, especially when timing assessments and follow-ups in clinical research.

To our knowledge, this is the first economic evaluation comparing trauma-focused internet-delivered therapist-assisted cognitive therapy to comprehensive internet-delivered non-trauma-focused cognitive behaviour therapy. The incremental cost-effectiveness estimates in this study are similar to those implied by the modelling comparing in-person trauma-focused CBT with non-trauma-focused CBT.[5] The trial population used in this study was mainly recruited from the services providing primary care psychological therapy for PTSD in England (now NHS Talking Therapies for Anxiety or Depression), and results are therefore likely to be applicable to this population in practice.

This study adds to the evidence on the cost-effectiveness of internet-delivered CBT for PTSD, which is scarce so far.[8] A recent trial of a guided self-help CBT programme for mild-to-moderate PTSD to single trauma (the RAPID trial) was found to be non-inferior to face-to-face therapy in reducing PTSD symptoms at 16 weeks, but not at 52 weeks.[31] The cost-effectiveness analysis showed it was not more cost effective at the £20 000 per QALY and £30 000 per QALY thresholds compared with face-to-face therapy.[31]

There are limitations related to missing data for individual timepoints, leading to a smaller sample for the primary analysis, and some of the data collected on costs: data on the dosage of prescribed medication used for PTSD collected throughout the trial period were not sufficient to capture any effect of treatments on medication use across trial groups. Self-reported information on the use of health services was not consistently completed, leading to many participants being excluded due to missing observations. The sensitivity analyses that account for missing data using multiple imputation and a wider set of costs using a societal costing perspective both resulted in improved estimates of cost-effectiveness, suggesting that the central cost-effectiveness findings are more conservative as a result. However, the results of the multiple imputation sensitivity analysis should be interpreted with caution, as the assumption that data were missing at random might not hold.

This study provides evidence that iCT-PTSD is cost-effective relative to iStress-PTSD and could be considered for clinical implementation. However, the increasing adoption of digital interventions such as iCT-PTSD needs further evidence relative to existing face-to-face treatments and in real-world settings.

Contributors

AE and DMC wrote the grant application, with health economics input from AT. AE wrote the study protocol and ethics application, was the chief investigator of the randomised controlled trial (RCT), and supervised the RCT and iCT-PTSD supervision group to ensure treatment fidelity. EP and AT wrote the health economics analysis plan. EP analysed the health economics data and wrote the first draft of the manuscript. Analysis was overseen and checked by AT. AE, JW, EW-P, NG, RS, HM, AK, and DMC developed iCT-PTSD, GA developed iStress with his team, HM adapted iStress for PTSD and wrote additional modules, and AR provided supervision for iStress to ensure treatment fidelity. AE, JW, EW-P, NG, HM, and AK contributed to data collection, and RS to data extraction. All authors provided critical revisions and approved the final version of the paper, with the exception of Hannah Murray, who sadly died before the reviewers' comments were received, approved the final version of the paper.

Declaration of interests

Face-to-face CT-PTSD and iCT-PTSD were developed by AE and DMC's team. AE, NG, JW, EW-P, HM, and DMC have occasionally given paid workshops on CT-PTSD. iStress was developed by GA's team. All other authors declare no competing interests.

Data sharing

Trial materials can be obtained from AE. Given the highly personal nature of the study data, participants were asked for optional consent to sharing their anonymised data with other researchers. Many, but not all, participants consented, and their de-identified and anonymised data will be available from AE upon reasonable request, subject to submission and approval of a research proposal and review and contract with the University of Oxford (Oxford, UK), following the publication of all results from this study.

Acknowledgments

This study, along with the clinical trial by Ehlers and colleagues, was funded by the Wellcome Trust, grant 200976, and was supported by the National Institute of Health Research (NIHR) Oxford Health Biomedical Research Centre (BRC-1215–2000) and AE's NIHR Senior Investigator Award (NF-SI-0617–10052). AT acknowledges support from the NIHR Applied Research Collaboration Oxford and Thames Valley. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health. We gratefully acknowledge the invaluable advice of the Trial Oversight Committee (Kerry Hood, Richard Meiser-Stedman, Stephen Pilling, Roz Shafran, and Edel Daly). We thank the service users who provided suggestions and feedback on the design of the internet platform and the content of the therapy modules and materials for the trial. We thank the Primary Care Clinical Trials Unit at the University of Oxford for developing the randomisation programme and Ly-Mee Yu for statistical advice. We thank the participating clinical services for their collaboration. Our special thanks go to the research assistants and independent assessors who made the successful completion of the study possible (Rachelle Dawson, Maxie Scheske, Savannah Minihan, Rachel Maddox, Emily Gray, Alisha Smith, Chloe Ravenscroft, Laura Varnes, Annabel Burnley, Jennifer Thomson, Sophie Grant, Trinity de Simone, Gabriella Tyson, Kelly Wilson, and Guy Emery).

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