Guided, internet based, cognitive behavioural therapy for post-traumatic stress disorder: pragmatic, multicentre, randomised controlled non-inferiority trial (RAPID)

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ABSTRACT

OBJECTIVE
To determine if guided internet based cognitive behavioural therapy with a trauma focus (CBT-TF) is non-inferior to individual face-to-face CBT-TF for mild to moderate post-traumatic stress disorder (PTSD) to one traumatic event.

DESIGN
Pragmatic, multicentre, randomised controlled non-inferiority trial (RAPID).

SETTING
Primary and secondary mental health settings across the UK's NHS.

PARTICIPANTS
196 adults with a primary diagnosis of mild to moderate PTSD were randomised in a 1:1 ratio to one of two interventions, with 82% retention at 16 weeks and 71% retention at 52 weeks. 19 participants and 10 therapists were purposively sampled and interviewed for evaluation of the process.

INTERVENTIONS
Up to 12 face-to-face, manual based, individual CBT-TF sessions, each lasting 60-90 minutes; or guided internet based CBT-TF with an eight step online programme, with up to three hours of contact with a therapist and four brief telephone calls or email contacts between sessions.

MAIN OUTCOME MEASURES
Primary outcome was the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) at 16 weeks after randomisation (diagnosis of PTSD based on the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5). Secondary outcomes included severity of PTSD symptoms at 52 weeks, and functioning, symptoms of depression and anxiety, use of alcohol, and perceived social support at 16 and 52 weeks after randomisation.

RESULTS
Non-inferiority was found at the primary endpoint of 16 weeks on the CAPS-5 (mean difference 1.01, one sided 95% confidence interval −∞ to 3.90, non-inferiority P=0.012). Improvements in CAPS-5 score of more than 60% in the two groups were maintained at 52 weeks, but the non-inferiority results were inconclusive in favour of face-to-face CBT-TF at this time point (3.20, −∞ to 6.00, P=0.15). Guided internet based CBT-TF was significantly (P<0.001) cheaper than face-to-face CBT-TF and seemed to be acceptable and well tolerated by participants. The main themes of the qualitative analysis were facilitators and barriers to engagement with guided internet based CBT-TF, treatment outcomes, and considerations for its future implementation.

CONCLUSIONS
Guided internet based CBT-TF for mild to moderate PTSD to one traumatic event was non-inferior to individual face-to-face CBT-TF and should be considered a first line treatment for people with this condition.

TRIAL REGISTRATION
ISRCTN13697710.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Face-to-face trauma focused psychological treatments are recommended as first line for post-traumatic stress disorder (PTSD)

Guided self-help with internet based programmes based on cognitive behavioural therapy with a trauma focus has been recommended as an alternative, but whether guided self-help is non-inferior to current first line treatments has not been established

WHAT THIS STUDY ADDS

Guided internet based cognitive behavioural therapy with a trauma focus was found to be non-inferior to and cheaper than face-to-face cognitive behavioural therapy with a trauma focus at 16 weeks

Guided internet based cognitive behavioural therapy with a trauma focus should be made available as a low intensity treatment option for people with mild to moderate PTSD to one traumatic event

Introduction

Post-traumatic stress disorder (PTSD) is a common mental health condition that can develop after experiencing traumatic events that involve threatened or actual death, serious injury, or sexual violence. Characteristic symptoms include re-experiencing, avoidance, and a current sense of threat.[1][2] About 4% of the adult population of the UK have PTSD[3] and symptoms can last for many years if not treated.[4] PTSD is strongly associated with substantial physical and mental health comorbidity,[5][6] and major economic burden.[7] People with PTSD often report marked negative effects on their functioning in occupational, home management, social, and private leisure situations. Individual face-to-face trauma focused psychological treatments, especially

cognitive behavioural therapies with a trauma focus (CBT-TF) and eye movement desensitisation and reprocessing, are the best evidenced treatments for PTSD and recommended in guidelines across the world, including the UK's National Institute for Health and Care Excellence (NICE).[8-11]

Unfortunately, the limited number of suitably trained therapists to deliver trauma focused psychological treatments often precludes timely access to treatment, with NHS waits of a year or more in some areas of the UK. Treatment is typically delivered weekly, face to face over several months, making it difficult to access for some recipients (eg, because of stigma, work commitments, travel, and the need for childcare).[12-14] Also, some people with PTSD might be too afraid or lack motivation to leave their home and actively engage in starting treatment. Guided self-help combines the use of self-help materials with regular guidance from a trained professional, and requires less time with a therapist than recommended face-to-face trauma focused psychological treatments. Good evidence exists of the efficacy of guided self-help in other disorders, such as anxiety and depression.[15 16]

If effective for PTSD, guided self-help would offer a time efficient treatment option, with the potential to reduce waiting times and the cost of interventions. The need for less contact with a therapist, and the option of having contact with a therapist remotely, are also likely to make guided self-help more accessible than in-person treatment for some people and an attractive option when dealing with a pandemic and an increasing shift towards remote healthcare. These benefits, along with offering an effective intervention of lower intensity, would indicate progress in the care pathway for people with PTSD. By treating PTSD in a more timely and efficient manner, the burden of disease would be reduced, preventing avoidable morbidity and improving quality of life.

Through careful feasibility work,[17] four of the authors (JIB, NK, CL, and NPR) developed a web based programme called Spring (demonstration video: www.youtube.com/watch?v=rioynUw7LZ8), a highly promising guided internet based CBT-TF intervention for PTSD. A feasibility randomised controlled trial showed the efficacy of the programme in 42 adults with PTSD randomised to immediate guided internet based CBT-TF with the Spring programme or delayed treatment.[18] After treatment, the guided internet based CBT-TF group had significantly (P<0.001) lower PTSD symptoms assessed by a clinician than the control group with delayed treatment (effect size between groups, Cohen's d=1.86). The difference was maintained at the one month follow-up but was gone after both groups received treatment. Similar patterns of differences between the two groups were found for depression, anxiety, and functional impairment.

A recently published Cochrane review[19] of internet based CBT for PTSD in adults identified 13 relevant randomised controlled trials, 10 of which, including our earlier phase randomised controlled trial, included therapist guidance. Compared with a wait list, the authors concluded that internet based CBT-TF might be associated with a clinically important reduction in PTSD. Based on this research, guided internet based CBT-TF was included as a possible treatment for people with mild to moderate PTSD in the latest treatment guidelines from NICE[9] and the International Society for Traumatic Stress Studies (ISTSS)[8]. NICE and ISTSS recommended guided internet based CBT-TF less strongly than face-to-face trauma focused psychological treatments because of weaker evidence: NICE stated, "supported computerised trauma focused CBT should be considered as an option for adults with PTSD who prefer this to face-to-face trauma focused CBT or EMDR (eye movement desensitisation and reprocessing)." The cautious recommendations of NICE and ISTSS indicate the need for guided internet based CBT-TF that is non-inferior to face-to-face CBT-TF to provide greater choice, allow people with PTSD more control over treatment, establish a wider range of evidence based treatment options, and enhance access.

The few guided internet based CBT interventions for PTSD are varied in terms of content and delivery. The main differences between guided internet based CBT-TF with the Spring programme and other guided internet based CBT-TF interventions for PTSD include a greater amount of guidance and stricter adherence to evidence based CBT-TF techniques with the Spring programme. The Spring programme is more interactive than many other guided internet based CBT programmes for PTSD. The programme is audio narrated throughout, rather than the user having to read the text on screen, and includes eight steps based on: (1) psychoeducation, (2) grounding techniques, (3) management of anxiety, (4) behavioural activation, (5) imaginal exposure, (6) cognitive restructuring, (7) in vivo exposure, and (8) prevention of relapse. Branching screens allow the user some degree of control over the navigation through each step. The programme includes four characters with PTSD to different traumatic events, and video content follows their progress through the programme. A virtual toolkit provides shortcuts to key programme components and information input by users. The tools are based on core components of CBT-TF, such as building a fear ladder to overcome avoidance and writing a detailed trauma narrative to re-process trauma memories.

The Spring programme is different from other guided self-help or self-help programmes for PTSD because of the systematic way in which the programme was developed. Spring was co-produced with people with lived experience of PTSD following guidance from the Medical Research Council for the development of complex interventions. This methodology included: a modelling phase to develop an initial prototype based on existing evidence and qualitative work with key stakeholders; pilot work to refine the prototype based on qualitative feedback and quantitative outcome measures collected from purposively selected participants trialling the intervention; and a randomised controlled trial to

explore feasibility. This process was far more vigorous than those used in the development of similar interventions for PTSD and is likely to have improved the efficacy and acceptability of the approach. Largely influenced by the results of our earlier feasibility randomised controlled trial,[18] guided internet based CBT-TF is included as a possible treatment for people with mild to moderate PTSD in the latest treatment guidelines from NICE and ISTSS.

We report the results of our large scale trial to establish the clinical and cost effectiveness of guided internet based CBT-TF compared with face-to-face CBT-TF for people with mild to moderate PTSD. The results will allow decisions to be made about the suitability of the programme for use at scale in the NHS and beyond.

Methods

Trial design

We conducted a multicentre, pragmatic, randomised controlled non-inferiority trial with assessors blinded to treatment allocation. Individual randomisation was used. We used a non-inferiority design to determine if a new approach, with distinct advantages over existing strongly recommended treatments, was no worse than a current gold standard treatment for PTSD.[20] We did not expect guided internet based CBT-TF to be more effective than face-to-face CBT-TF and, therefore, a superiority design was not appropriate. The trial followed a published protocol,[21] was supported by a public advisory group, and was overseen by a trial steering committee and independent data monitoring committee. A health economic evaluation was included to assess cost effectiveness. A nested process evaluation was included to assess fidelity, adherence, and intervention mechanisms. The trial was conducted between 1 August 2017 and 31 January 2021. The trial adhered to the Consolidated Standards of Reporting Trials (CONSORT) guideline.[22]

Eligibility criteria

Wide eligibility criteria were used to ensure good external validity. Participants were aged ≥18 years and had a primary diagnosis of PTSD according to the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5), evaluated by the Clinician Administered PTSD Scale (CAPS-5).[23] Participants had mild to moderate PTSD symptoms based on a score of <50 on the CAPS-5 at the baseline assessment, had regular access to the internet to complete the steps and homework required by the guided internet based CBT-TF programme, and were willing and able to give informed consent to take part in the study. Exclusion criteria were inability to read and write fluently in English, previous completion of a course of trauma focused psychological treatments for PTSD, current PTSD symptoms to more than one traumatic event (individuals who experienced multiple traumatic events were included if their current PTSD symptoms were to one traumatic event), current engagement in psychological treatment, diagnosis of psychosis or substance dependence, active suicide risk, and change in psychotropic medication in the past four weeks.

Recruitment and consent

Participants were recruited from NHS Improving Access to Psychological Therapy (IAPT) services based in primary care in England (Coventry, Warwickshire, Greater Manchester, London, and South West Yorkshire) and NHS psychological treatment settings based in primary and secondary care in Scotland (Lothian) and South Wales (Cardiff, Gwent, Mid Glamorgan, and the Vale of Glamorgan). Potential participants were identified and approached by a clinician involved in their care, screened, and fully assessed by one of a team of researchers after providing informed consent. Individuals who met the eligibility criteria were randomised to receive guided internet based CBT-TF with the Spring programme or face-to-face CBT-TF.

Semi-structured telephone interviews were conducted with 19 participants and 10 therapists as part of the evaluation of the process, to collect perspectives of receiving and delivering the interventions, and to examine underlying mechanisms and factors influencing future implementation. Trial participants were sampled with a purposeful approach, to include maximum variation in terms of allocation of the intervention, research site, sex, age, ethnicity, educational level, nature of the trauma, and outcome. Therapists were sampled by sex and research site. Given the focus of our research, participants in the guided internet based CBT-TF group were over sampled.

Randomisation

We used preprogrammed software to generate the random allocation sequence with an online minimisation algorithm, designed by the database designer, with a ratio of 1:1. Minimisation was used to ensure balance between trial arms for sex, with an 80% random element and grouped by research centre. The data manager carried out the randomisation when eligibility was confirmed. The allocation was emailed to the trial manager who informed the local principal investigator or therapist. A randomisation protocol was written and signed off before recruitment began, in line with the policy of the Centre for Trials Research. Outcome assessors were blinded to treatment allocation as far as possible. Participants were asked not to disclose the intervention they received to assessors at the follow-up interviews.

Blinding

Blinding the therapists or participants was not possible, given the complex interventions under investigation. The outcome assessors were blind to treatment allocation, however, and the therapists and participants were asked not to discuss their allocation with the assessors. Participants were reminded of the importance of this process at each outcome assessment, and the outcome assessors reported any instances of potential unblinding.

Interventions

Face-to-face CBT-TF

CBT-TF is one of the primary treatments for PTSD adopted by IAPT in England and by psychological therapy services in Scotland and Wales. Cognitive therapy for PTSD (CT-PTSD),[24] one of the CBT-TF implemented by IAPT, was used as the CBT-TF in RAPID. Participants received up to 12 face-to-face individual sessions, of 60-90 minutes. The treatment sessions were supplemented with assignments which participants were required to complete between sessions.

CT-PTSD involves identifying the relevant appraisals, memory characteristics, triggers, and behavioural and cognitive strategies that maintain PTSD symptoms. These are dealt with by: modifying excessively negative appraisals of the trauma, its sequelae, or both; reducing re-experiencing by discussing the trauma memories through imaginal exposure or by narrative based memory updating with less threatening meanings and discrimination of triggers; stopping unhelpful behaviours and cognitive strategies, particularly those related to avoidance of triggers for intrusive symptoms; and, when possible, visiting the site of the trauma with the therapist to update the trauma memory.

Guided internet based CBT-TF

The guided internet based CBT-TF intervention used Spring, an eight step online guided self-help programme that uses the same principles as CBT-TF but aims to reduce contact time with the therapist by providing some of the therapy content and activities in an online format. The eight steps (table 1) cover psychoeducation, grounding techniques, management of anxiety, behavioural activation, imaginal exposure, cognitive restructuring, in vivo exposure, and prevention of relapse. The content of each step is audio narrated with keywords and images displayed on screen. The programme is interactive and user input dictates feedback to key activities within the programme. Branching screens allow the user some control over the navigation through each step, and

bookmarking enables re-entry at the point where the user left the programme.

The programme includes four characters with PTSD to different traumatic events, and video content follows their progress through each step of the programme. A toolkit area of the website or app allows easy access to key programme components and information input by users. The tools help participants engage with core CBT-TF techniques, such as building a fear ladder to overcome avoidance and writing a detailed trauma narrative to re-process trauma memories. At the start of treatment, the therapist meets with the participant for an hour to develop a relationship, learn about the participant's trauma, provide log in details, and describe and demonstrate the programme, which the participant then completes online in their own time. Four subsequent meetings of 30 minutes take place every two weeks, usually face to face. At each session, the therapist reviews progress by logging into a clinician dashboard and guides the participant through the programme. Specific activities become visible (with the participant's knowledge) to the therapist from the dashboard to help discussions during the guidance session. The aim of the guidance is to offer continued support, monitoring, motivation, and problem solving. The participant also receives four brief telephone calls or email contacts between sessions to discuss progress, identify any problems that have arisen, and agree new goals. The programme was designed to be accessible through a variety of devices, including PC, laptop, tablet, and smartphone (via a Spring app).

Therapists

The two trial interventions were delivered by experienced psychological therapists working in high intensity IAPT services or psychological services at the trial sites. All therapists had previous experience of delivering CBT-TF for PTSD. The study therapists received an extra one and a half days of face-to-face training in CT-PTSD, and a half day training in guided internet based CBT-TF. Training for each intervention was delivered by clinicians involved in the development of CT-PTSD and guided internet based CBT-TF. Clinicians treated at least one patient with each intervention during training, and were assessed as being competent by a trial clinical supervisor if they were judged to have delivered the interventions satisfactorily. Therapists followed treatment manuals for both interventions and received group clinical supervision specific to the trial once a month by video or telephone conference call with one of the authors (NK or NPR) throughout the trial. Two participants received their final therapy sessions by video conferencing rather than in person because of the covid-19 pandemic.

Training for the guided internet based CBT-TF intervention comprised an introduction to the programme, the rationale behind it, and a demonstration by the trainers. Therapists then worked through the delivery manual with the trainers, with a focus on how to guide people with PTSD through the programme. After the initial training, therapists and

Table 1 | Eight steps of the Spring self-help programme for post-traumatic stress disorder (PTSD)

Step	Description
Step 1: Learning about my PTSD	Psychoeducation about PTSD illustrated by four actors describing their experience of PTSD to different types of traumatic event
Step 2: Grounding myself	Explanation of grounding and its uses, along with descriptions and demonstrations of grounding exercises
Step 3: Managing my anxiety	Education about relaxation techniques with learning through videos of a controlled breathing technique, applied muscular relaxation, and relaxation through imagery
Step 4: Reclaiming my life	Behavioural reactivation to help individuals return to previously undertaken or new activities, or both
Step 5: Coming to terms with my trauma	Provides rationale for imaginal exposure, narratives of the four video characters. The therapist helps the participant to begin writing a narrative, which they complete remotely and read every day
Step 6: Changing my thoughts	Cognitive techniques to deal with PTSD symptoms
Step 7: Overcoming my avoidance	Graded real life exposure work
Step 8: Keeping myself well	This session reinforces what has been learnt during the programme, provides relapse prevention measures for prevention of relapse, and guidance on what to do if symptoms return

a colleague role played being a clinician and a person with PTSD while working through the programme. The therapists worked through the programme from the perspectives of a clinician and a patient to gain a fuller understanding of the programme and the guidance process. Monthly meetings were held to support the therapists, who could also contact the trainers in between sessions. When the therapists had completed the role play and felt confident with the programme, they used the programme to treat one or two people with PTSD under the supervision of a trainer. Therapists were only allocated trial participants when their trainer thought they were competent. The trainer then became their trial clinical supervisor.

Fidelity and adherence

To ensure that the interventions were delivered as intended and according to the manuals, each therapist aimed to audio record at least one session with every participant on a digital voice recorder. The audio recordings were rated with a general fidelity checklist and a fidelity checklist specific to the intervention by one of two independent experienced clinicians. To measure adherence, we recorded the number of sessions attended or missed for each participant, and the steps completed on the guided internet based CBT-TF programme.

Outcomes

All outcome measures were completed at baseline, and at 16 and 52 weeks after randomisation. The primary outcome was the severity of symptoms of PTSD over the previous week, as measured by CAPS-5[23] at 16 weeks after randomisation. CAPS-5 is a 30 item structured interview for assessing the diagnostic status and severity of symptoms of PTSD. Items correspond to the DSM-5 criteria for PTSD.[1] The CAPS-5 total severity score has high internal consistency (Cronbach's α=0.88) and inter-rater reliability (intraclass correlation coefficient =0.91), and good test-retest reliability (intraclass correlation coefficient=0.78). Good convergent validity was found for the total severity score on the CAPS-IV (Pearson correlation coefficient (r)=0.83) and the PTSD checklist for DSM-5 (r=0.66), and good discriminant validity with measures of anxiety, depression, somatisation, functional impairment, psychopathy, and alcohol abuse (r=0.02-0.54).[25]

We chose 16 weeks after randomisation as the measurement point for the primary outcome because the guided internet based CBT-TF intervention took about eight weeks to deliver and the face-to-face CBT-TF intervention took up to 12 weeks to deliver. We wanted to allow extra time for possible delays in the delivery of treatment (eg, participant and therapist holidays) and, therefore, 16 weeks after randomisation would ensure that all participants had completed treatment at the reassessment. A secondary outcome was the severity of PTSD symptoms at 52 weeks after randomisation, measured with the CAPS-5. Self-reported secondary outcomes were measured with validated measures, at 16 weeks (to determine the effect of the interventions) and at 52 weeks (to determine sustained effects) after randomisation. We also collected information on possible adverse events. The main possible adverse events were deterioration in mental health, assessed by the outcome measures, and suicidal ideation. An adverse event was defined as any untoward medical occurrence in a participant. A serious adverse event was defined as any adverse event that resulted in death, was life threatening, required admission to hospital or prolonged a stay in hospital, or caused persistent or major disability or incapacity.

The self-reported secondary outcomes were: traumatic stress symptoms, measured by the Impact of Event Scale-revised (IES-R)[26]; quality of life and functional impairment, measured by the Work and Social Adjustment Scale[27]; depression, measured by the Patient Health Questionnaire-9[28]; anxiety, measured by the Generalised Anxiety Disorder-7[29]; alcohol use, measured by the Alcohol Use Disorders Identification Test (AUDIT-O)[30]; perceived social support, measured with the Multidimensional Scale for Perceived Social Support[31]; level of use of healthcare resources for the health economic analysis, with an amended version of the Client Socio-Demographic and Service Receipt Inventory European version[32]; health related quality of life, with the EuroQol five dimensional, five level questionnaire (EQ-5D-5L)[33]; sleep, measured by the Insomnia Severity Index[34]; cognitions, measured with the Post-Traumatic Cognitions Inventory[35]; self-efficacy, measured with the General Self-Efficacy Scale[36]; and treatment satisfaction, measured with the Client Satisfaction Questionnaire[37] (at 16 weeks after randomisation only). The IES-R was also collected at each contact with a therapist to provide clinical feedback and to facilitate imputation for missing data, if required.

Sample size

Because we wanted to show the non-inferiority of guided internet based CBT-TF for PTSD compared with face-to-face CBT-TF, we used the non-inferiority margin rather than the effect size for the power calculation. The non-inferiority margin (determined a priori by consensus of clinicians involved in the trial design and the research management group) was five points on the 80 point CAPS-5 scale. The clinical experience of the team suggested that differences of less than five do not make a major difference to people with PTSD. This margin is also supported by the literature, suggesting that an appropriate non-inferiority margin is about 0.5 times the standard deviation of the baseline values of the outcome measures.[38]

A meta-analysis[39] indicated that the standardised mean difference between CBT-TF and wait list or usual care for the treatment of PTSD is −1.62. This value corresponds to 16.6 points on the CAPS-5. Hence if non-inferiority was shown to within five points of the gold standard, superiority over wait list or usual care would also be shown, in line with the International Conference on Harmonisation Harmonised Tripartite Guideline (Statistical Principles for Clinical Trials) E9 (ICH E9) guidance for non-inferiority studies.[40 41]

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Previous work indicated an intraclass correlation coefficient of 5.6% at the therapist level at 10 weeks. At 22 weeks, however, we found no observable clustering of CAPS-5 scores among therapists. Given that our primary outcome (CAPS-5) was measured at 16 weeks, we allowed for clustering, assuming an intraclass correlation coefficient of 0.01, and recalculated the sample size. We allowed for 20% attrition. With the average therapist cluster size predicted as four, the design effect was 1.03, requiring a 3% inflation of the sample size. This calculation resulted in a final target sample size of 192 (increased from 186), which provided 90% power (nQuery version 7.0[42]). The sample size for the qualitative elements of the study was guided by preliminary analysis and constant comparison (with themes from other interviews), during each data collection phase, until the research team was satisfied that data saturation had occurred and no new themes which were important to the research had emerged.

Statistical and other analysis methods

A statistical analysis plan was finalised before data collection was completed, and then followed. The primary analysis was an intention-to-treat analysis with multilevel analysis of covariance, predicting follow-up CAPS-5 score, controlling for baseline CAPS-5 score and important patient characteristics (sex, research site, baseline depression score (Patient Health Questionnaire-9) and time since traumatic event in months), and including therapist as a random effect. The results were summarised with point estimates and one sided 95% confidence intervals. Given the non-inferiority design, we checked whether the confidence interval for the difference between arms was entirely within the five point non-inferiority margin. For participants with missing CAPS-5 scores at follow-up, a CAPS-5 score was estimated from available IES-R scores by building a multilevel multiple imputation model with information from participants for both IES-R and CAPS-5 scores.

To avoid bias, the multiple imputation model was built separately for the guided internet based CBT-TF and face-to-face CBT-TF groups because of the different number of participant contacts. Sensitivity analyses were conducted as a complete case analysis and as a combined multiple imputation model pooling data from both the guided internet based CBT-TF and face-to-face CBT-TF groups. A further sensitivity analysis assessed adherence to the protocol by participants with complier adjusted causal effect analysis.[43] Continuous secondary outcomes were analysed with a multilevel analysis of covariance model as the primary outcome. We used the same multiple imputation approach for the secondary and primary outcomes. Secondary outcome results are reported as point estimates, one sided 95% confidence intervals, and non-inferiority P values. A non-inferiority margin of 0.5 times the pooled standard deviation of the baseline values was assumed for the secondary outcomes. All analyses were performed in the Stata programming language and environment,

apart from the multilevel multiple imputation, which was performed with the R programming language.[44 45]

Qualitative data were analysed by framework analysis.[46] The semi-structured interviews were audio recorded, transcribed verbatim, and cleaned, with pseudonyms assigned to interviewees, removing names, roles, and institutions to preserve anonymity. Transcripts were imported into QSR NVivo 12[47] qualitative data analysis software. The analysis and data collection were done at the same time, allowing for constant comparisons to explore themes and to ensure sufficient data saturation,[48] monitored through a double coding process. The codes and themes that were generated were discussed by the researchers to ensure clear understanding and interpretation. Final interpretations were made with input from the trial public advisory group.

A health economic evaluation was conducted from UK NHS, personal, and social services perspectives. Contacts with primary and secondary healthcare, and community social care, were self-reported in the trial at each time point. Use of resources related to the intervention was collected in the therapists' records and by interviews with the clinical staff involved in the trial. No discounting was applied because the time period covered was one year. To determine the cost effectiveness of guided internet based CBT-TF and face-to-face CBT-TF for PTSD, and the extent to which it can be regarded as representing value for money, two analyses were undertaken: we estimated the incremental cost of achieving a percentage improvement in PTSD symptoms, measured by CAPS-5; and the EQ-5D was used for a cost utility analysis, estimating the incremental costs per quality adjusted life year gained, and a net benefit analysis based on accepted NICE thresholds for value for money.[49] A health economics analysis plan was finalised before the end of data collection. Analyses were conducted in Microsoft Excel and Stata.[45]

Patient and public involvement

A public advisory group, comprising people with lived experience of PTSD, was formed, and met regularly to inform study design, conduct, data analysis, and dissemination strategy and activity. The group was chaired by one of the authors (SC), a co-applicant with lived experience of PTSD, and a participant in a previous study of guided internet based CBT-TF with the Spring programme. The public advisory group reviewed and approved all participant facing material. The trial steering committee included two members of the public.

Results

Recruitment and retention

The number of participants referred to the trial was 726; 196 were recruited and randomised. Ten participants withdrew from guided internet based CBT-TF and four from face-to-face CBT-TF. Four participants withdrew from follow-up assessments by 16 weeks, and one other participant by 52 weeks. The completion rates
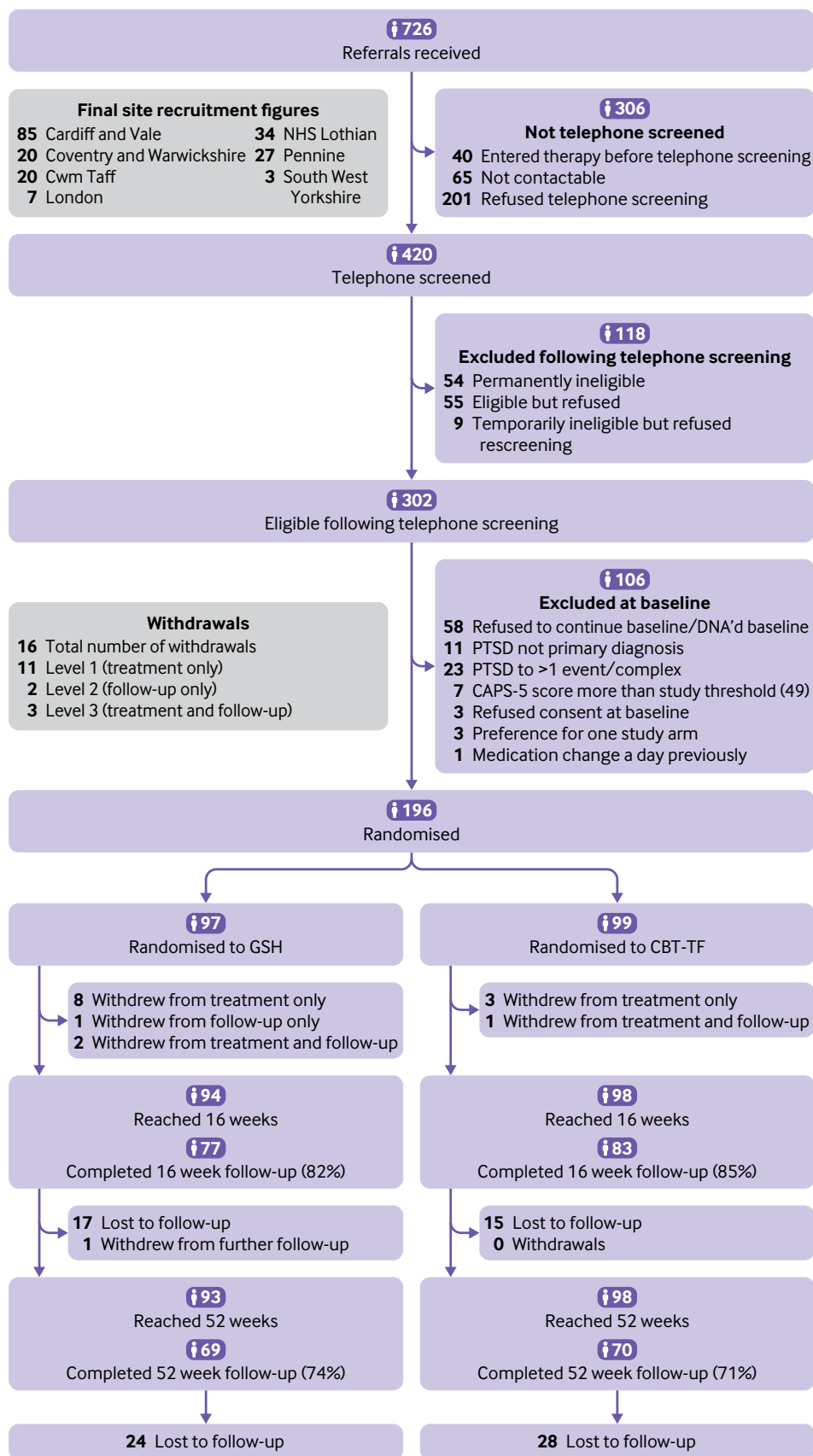
Fig 1 | Consolidated Standards of Reporting Trials (CONSORT) flow diagram of population selection for the RAPID trial. Participants were randomised to receive guided self-help (GSH) internet based cognitive behavioural therapy with a trauma focus (CBT-TF) or face-to-face CBT-TF. PTSD=post-traumatic stress disorder; CAPS-5=Clinician Administered PTSD Scale for DSM-5 (diagnosis of PTSD based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5)
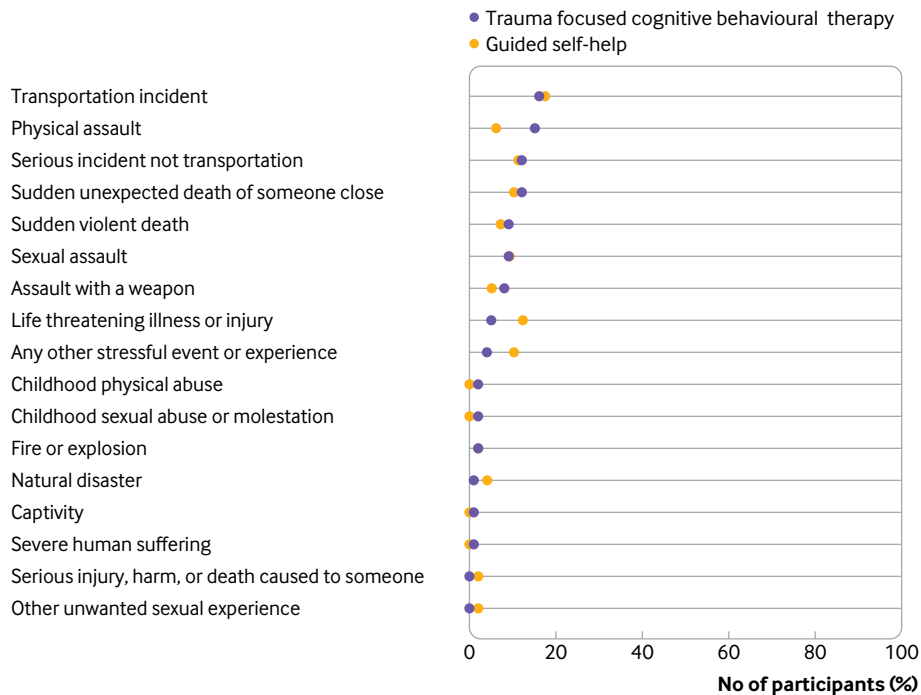
Fig 2 | Precipitating traumatic events in post-traumatic stress disorder

for assessments for those consenting to follow-up were 82% and 85% at the 16 week primary endpoint and 74% and 71% at 52 weeks in the guided internet based CBT-TF and face-to-face CBT-TF groups, respectively (fig 1).

Background information

One hundred and twenty five (63.8%) participants were women and 71 (36.2%) were men. Mean age was 36.5 (standard deviation 13.4) years with 180 (91.8%) participants identifying their ethnicity as white. Sixty four (32.7%) participants reported undergraduate degree or higher level education. The face-to-face CBT-TF group had higher levels of education, but the groups were well matched for baseline demographics overall (supplementary table 1). Most participants reported a history of anxiety disorder (129, 65.8%) and depressive disorder (112, 57.1%) diagnosed by a health professional, but low rates for other mental health conditions, and we found no differences between the groups. Most participants reported having a diagnosis of a physical condition; migraine headache (65, 33.2%) was the most commonly reported condition. Slightly more people in the guided internet based CBT-TF group reported physical comorbidities than in the face-to-face CBT-TF group.

Participants reported experiencing 1078 different traumatic events (that is, a mean of 5.5 traumatic events per person). A range of traumatic events had precipitated PTSD in participants (fig 2), with the commonest being transportation incident (33, 16.8%), serious incident not involving transportation (23, 11.7%), sudden unexpected death of someone close (22, 11.2%), physical assault (21, 10.7%), sexual assault (18, 9.2%), and sudden violent death (16,

8.2%). More people in the face-to-face CBT-TF group reported physical assault than in the guided internet based CBT-TF group, and more people in the guided internet based CBT-TF group reported exposure to life threatening illness or injury.

Outcome data

Table 2 provides data on the outcome measures at baseline, and at 16 and 52 weeks after randomisation. Figure 3 and supplementary figure 1 show non-inferiority for the primary outcome of CAPS-5 at 16 weeks and all secondary outcomes at this time point, except for general self-efficacy and client satisfaction that were inconclusive but in favour of face-to-face CBT-TF. Of those interviewed at 16 weeks, 12 (14.5%) participants in the face-to-face CBT-TF group and 14 (18.2%) in the guided internet based CBT-TF group continued to satisfy the DSM-5 criteria for PTSD (P=0.52). At 52 weeks, improvements in adjusted mean CAPS-5 score were maintained in both groups with some further improvement in the face-to-face CBT-TF group (fig 4).

Note that the non-inferiority margin for Clinician Administered PTSD Scale for DSM-5 (CAPS-5) was set at five points and for all other outcomes as 0.5 standard deviation.

Mean differences were less than the predetermined non-inferiority margin for CAPS-5 for the different analyses at 52 weeks (fig 5) but the non-inferiority analyses were inconclusive in favour of face-to-face CBT-TF for four of the five analyses because the confidence intervals were above the non-inferiority margin. The sensitivity analysis showed non-inferiority (IES-R scores at therapy sessions were used for imputation of missing data). Of those interviewed at 52

Table 2 | Summary statistics for primary and secondary outcome measures

Study outcomes	CBT-TF (No, mean (SD))			GSH (No, mean (SD))			Regression analysis					
							16 weeks			52 weeks		
	Baseline	16 weeks	52 weeks	Baseline	16 weeks	52 weeks	Effect size	One sided 95% CI	Non-inferiority P value	Effect size	One sided 5% CI	Non-inferiority P value
Clinician Administered PTSD Scale for DSM-5 (CAPS-5)	99, 35.6 (6.7)	83, 13.0 (11.1)	70, 10.9 (11.1)	97, 34.6 (6.8)	77, 13.1 (11.7)	69, 12.9 (11.6)	0.15	(−∞ to 0.59)	0.01	0.48	(−∞ to 0.89)	0.15
Impact of event scale-revised (IES-R)	99, 55.7 (12.2)	78, 20.3 (19.1)	57, 13.2 (14.8)	97, 53.5 (14.5)	68, 19.9 (18.0)	54, 21.7 (22.1)	0.10	(−∞ to 0.48)	0.04	0.88	(−∞ to 1.27)	0.06
Work and Social Adjustment Scale (WSAS)	99, 20.9 (9.8)	75, 10.4 (10.8)	55, 6.5 (8.1)	97, 21.1 (10.2)	68, 8.9 (9.8)	53, 8.0 (10.5)	−0.14	(−∞ to 0.13)	<0.001	0.24	(−∞ to 0.53)	0.07
Patient Health Questionnaire (PHQ-9)	99, 15.1 (5.7)	75, 7.1 (6.5)	55, 4.8 (5.0)	97, 15.1 (6.7)	69, 7.1 (6.8)	52, 6.5 (7.0)	0.006	(−∞ to 0.25)	<0.001	0.32	(−∞ to 0.58)	0.12
General Anxiety Disorder (GAD-7)	99, 13.4 (4.6)	75, 5.3 (5.3)	55, 3.8 (4.1)	97, 13.9 (4.9)	67, 5.6 (5.4)	52, 5.3 (5.6)	0.10	(−∞ to 0.41)	0.02	0.47	(−∞ to 0.78)	0.44
Alcohol Use Disorders Test (AUDIT-O)	99, 5.8 (5.2)	75, 4.9 (5.0)	55, 4.9 (4.4)	97, 5.7 (5.5)	68, 5.7 (5.7)	52, 5.9 (6.5)	0.15	(−∞ to 0.32)	<0.001	0.13	(−∞ to 0.35)	0.003
Multidimensional Scale for Perceived Social Support (MSPSS)	99, 5.2 (1.0)	75, 5.8 (1.0)	55, 5.8 (0.9)	97, 5.6 (0.9)	67, 6.0 (0.8)	52, 6.1 (0.8)	−0.06	(−∞ to 0.20)	<0.001	−0.17	(−∞ to 0.10)	<0.001
EQ-5D-5L (quality of life)	94, 56.7 (18.3)	75, 71.3 (17.3)	55, 76.6 (16.0)	96, 59.4 (21.5)	67, 70.1 (20.8)	52, 73.3 (20.0)	0.09	(−∞ to 0.33)	0.002	0.22	(−∞ to 0.50)	0.05
EQ-5D-5L (utilities)	99, 0.6 (0.2)	75, 0.8 (0.2)	55, 0.8 (0.2)	97, 0.5 (0.3)	67, 0.7 (0.3)	52, 0.7 (0.3)	0.12	(−∞ to 0.37)	0.006	0.28	(−∞ to 0.57)	0.10
Insomnia Severity Index (ISI)	99, 17.4 (5.4)	75, 9.1 (7.6)	55, 7.1 (7.1)	97, 16.5 (7.5)	67, 8.6 (7.7)	52, 7.7 (7.8)	0.06	(−∞ to 0.38)	0.01	0.28	(−∞ to 0.60)	0.12
Post-Traumatic Cognitions Inventory (PTCI)	99, 79.2 (20.5)	77, 51.0 (26.6)	56, 43.3 (23.1)	97, 80.6 (23.7)	68, 46.3 (23.7)	54, 48.3 (25.7)	−0.20	(−∞ to 0.08)	<0.001	0.29	(−∞ to 0.62)	0.14
General Self-Efficacy Scale (GSES)	99, 24.8 (6.3)	75, 30.1 (6.8)	55, 31.3 (6.8)	97, 24.8 (6.8)	67, 29.4 (7.0)	52, 30.5 (6.6)	0.26	(−∞ to 0.51)	0.05	0.21	(−∞ to 0.49)	0.05
Client Satisfaction Questionnaire (CSQ-8)	NA	75, 29.8 (3.3)	NA	NA	70, 26.9 (6.3)	NA	0.60	(−∞ to 0.87)	0.27	—	—	—

GSH=guided self-help; CBT-TF=cognitive behavioural therapy with a trauma focus; PTSD=post-traumatic stress disorder; DSM-5=*Diagnostic and Statistical Manual of Mental Disorders*, fifth edition; EQ-5D-5L=EuroQol five dimensional, five level questionnaire; NA=not applicable.
Analysis adjusted for sex, research site, baseline depression score (Patient Health Questionnaire-9), and time since traumatic event (months).
P values are from multilevel analysis of covariance model after multiple imputation (50 imputations).
Effect sizes are Cohen's d calculated by dividing the regression estimate of the difference in means by the pooled standard deviation at baseline. Effect sizes are standardised so that values <0 are in favour of guided self-help cognitive behavioural therapy and those >0 are in favour of face-to-face cognitive behavioural therapy with a trauma focus.

weeks, 6 (8.5%) participants in the face-to-face CBT-TF group and 10 (14.5%) in the guided internet based CBT-TF group continued to satisfy the DSM-5 criteria for PTSD (P=0.27). Multidimensional Scale for Perceived Social Support, AUDIT-O, EQ-5D-5L (quality of life), and General Self-Efficacy Scale secondary outcome variables showed non-inferiority at 52 weeks. Non-inferiority was not shown for the other secondary outcomes at 52 weeks, but the results, which were inconclusive, were in favour of face-to-face CBT-TF (table 2 and supplementary fig 2).

Adverse events
The risk assessment framework was triggered 105 times; once because of a report of self-harming and the rest for reported suicidal ideation. The risk assessment was triggered 70 times during telephone screening, 28 times during the baseline assessment, once during a conversation between a researcher and a referrer before screening, and once during a qualitative interview. During follow-up assessments, risk assessment was triggered twice at 16 weeks and three times at 52 weeks. After following the risk assessment framework, none of the referrals was thought to be actively suicidal.

We recorded six serious adverse events; none was related to involvement in the RAPID trial. One participant informed their therapist of a suicide plan at their first treatment session. One participant reported relapse into alcohol dependence and receiving successful treatment between their 16 and 52 week follow-up assessments. Four participants were admitted to hospital because of physical health difficulties.

Dose: duration of treatment
Therapists saw a median of 5 (interquartile range 4-11, range 2-26) participants across the two treatment groups. Participants allocated to face-to-face CBT-TF received an average of 9 (interquartile range 6-12) sessions and 767.0 (standard deviation 278.2) minutes of contact with their therapist. Participants in the guided internet based CBT-TF group received an average of 5 (interquartile range 3-5) sessions and 208.4 (standard deviation 69.3) minutes of contact with their therapist. Five (5.2%) participants in the guided internet based CBT-TF group and three (3%) in the face-to-face CBT-TF group were offered but did not attend therapy sessions. Seventy seven (79.4%) participants in the guided internet based CBT-TF group completed three or more therapy sessions, and 55 (55.6%) in the face-to-face CBT-TF group completed eight or more sessions or were judged to need less than eight sessions (our a priori agreed definitions of full adherence).

Fidelity
Audio recordings of 74 therapy sessions involving different participants were assessed. All but one
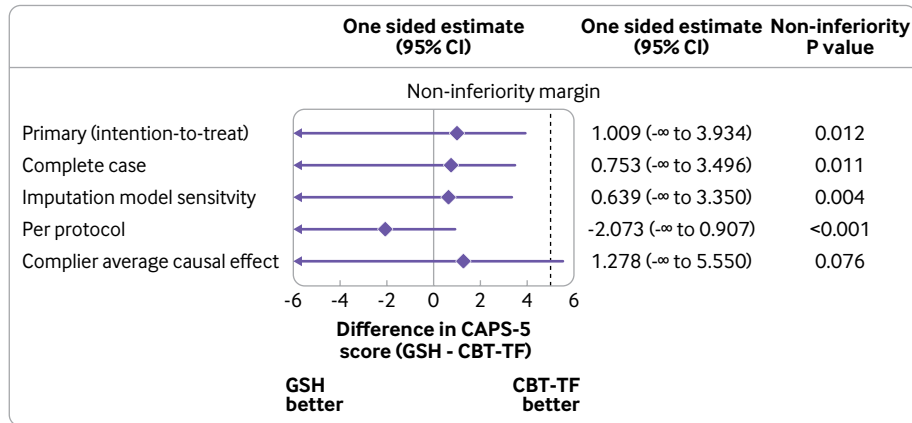
Fig 3 | Primary outcome: non-inferiority analyses for Clinician Administered Post-Traumatic Stress Disorder Scale for DSM-5 (CAPS-5) at 16 weeks (diagnosis of PTSD based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5) in the two groups: guided self-help (GSH) group (internet based cognitive behavioural therapy with a trauma focus (CBT-TF)) and face-to-face CBT-TF group

session was rated as at least satisfactory. For guided internet based CBT-TF, one session (3%) was rated as mediocre, 12 (39%) as satisfactory, 13 (42%) as good, and 5 (16%) as very good. For face-to-face CBT-TF, 10 (23%) sessions were rated as satisfactory, 20 (42%) as good, 10 (23%) as very good, and three (7%) as excellent.

Acceptability of intervention, context, mechanisms, and implementation

The absence of major adverse effects reported for guided internet based CBT-TF supports its acceptability, although 10 (10.3%) participants dropped out of guided internet based CBT-TF compared with four (4%) in the face-to-face CBT-TF group. Why people dropped out was unclear although a desire for face-to-face CBT-TF rather than guided internet based CBT-TF at randomisation seemed to be a reason for some participants. Contextual factors, acceptability, and barriers and facilitators of the intervention were explored qualitatively. The full qualitative results, including evaluation of the trial processes, will be presented in a separate paper.

We conducted interviews after treatment in eight participants allocated to receive guided internet based CBT-TF, two participants allocated to receive face-to-face CBT-TF, and seven therapists. Supplementary table 2 summarises the findings of the interviews. Interviewees highlighted barriers and challenges and facilitators and opportunities for engagement with guided internet based CBT-TF. A range of views were expressed, with guided internet based CBT-TF generally considered to offer flexibility for people with PTSD and therapists. Good engagement with guided internet based CBT-TF was described, particularly where individuals expressed being motivated to get better or where guided internet based CBT-TF was the preferred treatment. Some described the internet programme as positive and calming, and a progressive, structured therapy method that helped them feel their emotions were more controllable. Some therapists thought that guided internet based CBT-TF was a good option for people who prefer not to engage in traditional face-to-face therapy over several weeks and noted the value to therapists of having an alternative. Some participants who received guided internet based CBT-TF said they would have preferred face-to-face CBT-TF, and some therapists said that their preconceptions that individuals would prefer face-to-face therapy had been challenged, suggesting views had altered through experience.

The therapeutic relationships and contact between participant and therapist were considered important. Several trial participants described a positive therapeutic connection, with therapists motivating them towards engagement and recovery. Some therapists remarked on a therapeutic relationship in guided internet based CBT-TF, facilitated by the initial hour long face-to-face session, which allowed the participant and therapist to connect. Not all views expressed by interviewees were positive. Some participants described a limited connection with, and support from, their therapist. Some therapists raised concerns about exposure work conducted through the guided internet based CBT-TF approach, specifically about an individual conducting behavioural work alone, and some felt that flexibility was more difficult
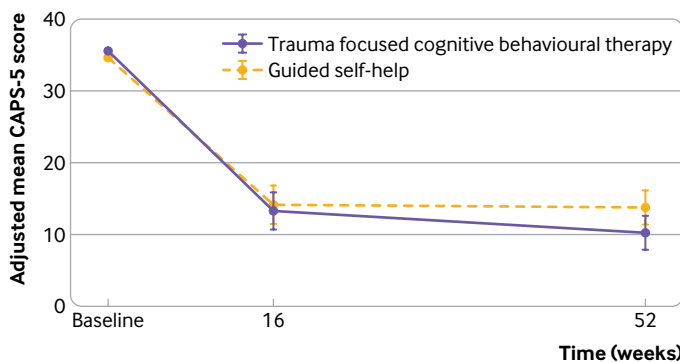

Fig 4 | Adjusted mean Clinician Administered Post-Traumatic Stress Disorder Scale for DSM-5 (CAPS-5) scores over time in the two groups (diagnosis of PTSD based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5)
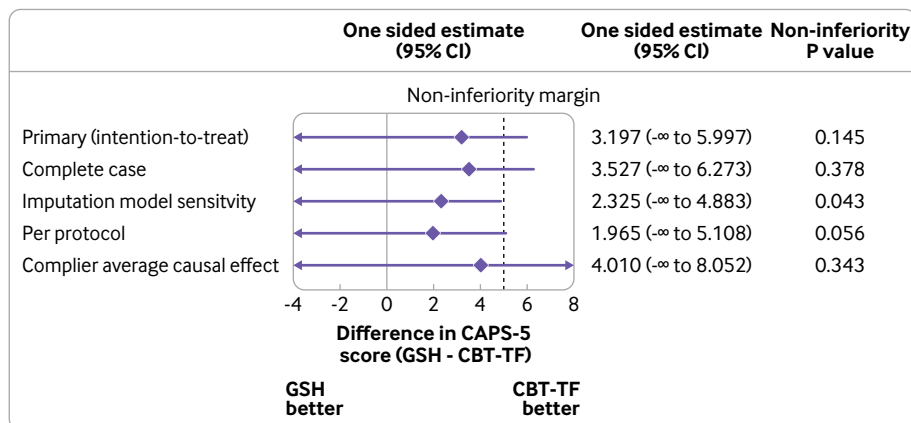
Fig 5 | Non-inferiority analyses for Clinician Administered Post-Traumatic Stress Disorder Scale for DSM-5 (CAPS-5) at 52 weeks (diagnosis of PTSD based on criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition, DSM-5) in the two groups: guided self-help (GSH) group (internet based cognitive behavioural therapy with a trauma focus (CBT-TF)) and face-to-face CBT-TF group

when delivering guided internet based CBT-TF. Therapists also talked about spending more time on some of the components of the Spring programme, and on occasion omitting some activities that they thought were not required (eg, exercises concerning guilt in the absence of guilt).

Several opposing views were expressed about the length of the guided internet based CBT-TF treatment and the time allocated to some intervention components. Some participants felt the treatment was too short for their difficulties, and therapists indicated that people with more complex presentations might require more therapy. Those wishing for an accessible treatment, that could fit around other commitments, felt the length of treatment was perfect.

Health economic analysis

The full health economic results will be presented in a separate paper. The mean cost per participant for delivering guided internet based CBT-TF, including therapy sessions, telephone calls, note taking, and training was £277 (€327; US$346) (95% confidence interval £253 to £301). The mean cost of delivering face-to-face CBT-TF was considerably more (£729, £671 to £788) (P<0.001). Table 3 and table 4 show the results of the primary health economic analysis at 52 weeks. Total costs to the NHS of the intervention and other health and social care over 52 weeks were significantly (P=0.02) less for guided internet based

CBT-TF than for face-to-face CBT-TF (incremental cost −£573, −£1080 to −£65), with no significant difference in accruing quality adjusted life years (incremental quality adjusted life years −0.04, −0.10 to 0.01). Negative values of net monetary benefit indicated that guided internet based CBT-TF was not cost effective at willingness to pay thresholds of £20 000 per quality adjusted life year and £30 000 per quality adjusted life year (supplementary fig 3). Sensitivity analyses on 16 week data, with a societal perspective and a variety of subgroup scenarios produced similar results.

Discussion

Principal findings

The RAPID trial showed that guided internet based CBT-TF with the Spring programme was non-inferior to face-to-face CBT-TF in reducing PTSD symptoms at the primary endpoint, 16 weeks after randomisation. This finding was also apparent for all secondary outcomes at 16 weeks, except for client satisfaction, which was inconclusive but in favour of face-to-face CBT-TF. Clinically substantial improvements were maintained at 52 weeks after randomisation, when most results were inconclusive but in favour of face-to-face CBT-TF. Guided internet based CBT-TF was not shown to be more cost effective than face-to-face CBT-TF but was significantly (P<0.001) cheaper to deliver and seemed to be well tolerated.

Table 3 | Primary health economic analysis: costs and quality adjusted life years

Group	No of participants	Adjusted mean cost* (£; mean (95% CI))	Adjusted QALYs† (mean (95% CI))	Incremental costs (95% CI)	Incremental QALYs (95% CI)	Incremental NMB (£) at £20 000/QALY (95% CI)	Incremental NMB (£) at £30 000/QALY (95% CI)
Primary analysis							
CBT-TF	99	1897.91 (1565.24 to 2230.58)	0.72 (0.69 to 0.76)	—	—	—	—
GSH	97	1325.36 (941.97 to 1708.74)	0.68 (0.64 to 0.72)	−572.55 (−1080.14 to −64.96)	−0.04 (−0.10 to 0.01)	−104.56 (−1286.39 to 1077.26)	−460.41 (−2143.27 to 1222.45)

£1=€1.17; $1.25. CBT-TF=cognitive behavioural therapy with a trauma focus (face-to-face group); GSH= guided self-help (internet based CBT-TF group); QALY=quality adjusted life year; NMB=net monetary benefit.
*Mean cost adjusted for site, baseline costs, age, and time to event.
†Mean quality adjusted life years adjusted for site, baseline utility, age, and time to event.

Table 4 | Primary health economic analysis: costs and change in scores

Group	No of participants	Adjusted mean costs* (£; mean (95% CI))	Adjusted mean change in score (mean (95% CI))	Incremental costs (95% CI)	Incremental outcome (95% CI)	Indicative ICER (cost (£) per point change)
Change in CAPS-5†						
CBT-TF	99	1897.91 (1565.24 to 2230.58)	−24.59 (−26.79 to −22.39)	—	—	—
GSH	97	1325.36 (941.97 to 1708.74)	−21.37 (−23.80 to −18.94)	−572.55 (−1080.14 to −64.96)	3.22 (−0.20 to 6.65)	177 saved per 1 point increase in CAPS-5
Change in IES-R‡						
CBT-TF	99	1897.91 (1565.24 to 2230.58)	−40.12 (−44.57 to −35.66)	—	—	—
GSH	97	1325.36 (941.97 to 1708.74)	−29.62 (−35.13 to −24.10)	−572.55 (−1080.14 to −64.96)	10.50 (3.01 to 17.99)	55 saved per 1 point increase in IES-R
Change in WSAS§						
CBT-TF	99	1897.91 (1565.24 to 2230.58)	−13.19 (−15.67 to −10.71)	—	—	—
GSH	97	1325.36 (941.97 to 1708.74)	−10.95 (−13.82 to −8.08)	−572.55 (−1080.14 to −64.96)	2.24 (−1.61 to 6.09)	255 saved per 1 point increase in WSAS

£1=€1.17; $1.25. ICER=incremental cost effectiveness ratio; CBT-TF=cognitive behavioural therapy with a trauma focus (face-to-face group); GSH= guided self-help (internet based CBT-TF group); CAPS-5=Clinician Administered PTSD Scale for DSM-5; DSM-5=*Diagnostic and Statistical Manual of Mental Disorders*, fifth edition; IES-R=Impact of Event Scale-revised; WSAS=Work and Social Adjustment Scale.
*Mean cost adjusted for site, baseline costs, age, and time to event.
†Mean change in CAPS-5 adjusted for site, baseline CAPS-5, age, and time to event.
‡Mean change in IES-R adjusted for site, baseline CAPS-5, age, and time to event.
§Mean change in WSAS adjusted for site, baseline CAPS-5, age, and time to event.

Results in the context of other research

The results consolidate previous work that has shown the efficacy of guided internet based CBT-TF for the treatment of PTSD.[17-19] Meta-analyses of face-to-face CBT-TF for PTSD found lower mean levels of improvement than our results for face-to-face CBT-TF and guided internet based CBT-TF,[50] although participants could have had more severe PTSD, given the focus on mild to moderate PTSD to one event in our trial. However, the mean participant score of 35.1 (standard deviation 6.7) on the CAPS-5 at baseline indicates severe PTSD[51] and the mean number of traumatic events reported per participant was 5.5, including 42 reports of exposure to childhood abuse. The mean number of reported traumatic events was similar to that found in general population representative large scale epidemiological research.[52] Although not explicitly investigated, the mechanism of action of the guided internet based CBT-TF used in this trial was probably similar to other CBT-TF treatments, with processing of the trauma through imaginal and in vivo exposure, coupled with effective challenges to patterns of thinking, improving the symptoms of PTSD.[24 53]

Previous studies of guided internet based CBT-TF for PTSD have shown smaller effect sizes compared with wait list than guided internet based CBT-TF with the Spring programme[18 19]. This finding might be because more guidance was included in the Spring programme than in most other web assisted interventions for PTSD, the programme was co-produced with people with lived experience of PTSD, it adhered to a CBT-TF approach, and was compliant with NICE's minimum recommended standards for guided internet based CBT-TF for PTSD.[9] Caution is needed when interpreting these findings, however, because head-to-head comparisons have not been carried out and hence the superiority of guided internet based CBT-TF with the Spring programme cannot be confirmed. Guided internet based CBT-TF interventions for PTSD are highly variable and attributing differences in effect to specific characteristics of the available approaches is currently not possible. To the best of our knowledge, this is the largest study of guided internet based CBT-TF for PTSD so far and the only study of guided internet based CBT-TF compared with a manual based gold standard treatment. Previous studies have usually compared guided internet based CBT-TF for PTSD with wait list controls, and major concerns have been raised about the various approaches used, overall quality of the methodology used, absence of follow-up, and higher dropout rates than found in our trial.[19 54]

The largely inconclusive findings for non-inferiority at 52 weeks seem to be derived from ongoing improvements in the face-to-face CBT-TF group that were not found in the guided internet based CBT-TF group. Determining why this is happening is difficult, and further analysis is required. A higher dose of treatment through face-to-face CBT-TF could have facilitated ongoing improvement. Other possibilities include chance, and the slightly lower levels of education and greater physical comorbidity in the guided internet based CBT-TF group, factors that have been found to influence the outcome of treatment in previous research.[16 55 56] We did not expect guided internet based CBT-TF to outperform face-to-face CBT-TF, hence the non-inferiority design of the study, and the added benefits in time, cost, and convenience, and having another evidence based treatment option could be argued as outweighing what seem to be minor differences at 52 weeks.

The qualitative analysis of in-depth interviews showed that guided internet based CBT-TF was acceptable, which was further supported by a relatively low dropout rate of 10.3% from treatment, although the dropout rate was greater than for face-to-face CBT-TF (4%). The rates of dropout were lower than rates generally seen in psychological treatment trials for PTSD,[57] suggesting good acceptability overall, but issues with equipoise (the belief that both interventions would be of equivalent benefit at the point of randomisation) were encountered in the study.

Some participants and therapists clearly felt face-to-face CBT-TF would result in better outcomes, and this antipathy towards guided self-help has been found in previous research.[58] [59]

The health economic analysis confirmed that guided internet based CBT-TF is a cheaper alternative to face-to-face CBT-TF, in terms of treatment costs and total NHS costs at the 16 and 52 week assessment points. This finding is consistent with clinically effective guided self-help interventions for other conditions.[15] [16] The lack of evidence that guided internet based CBT-TF is more cost effective than face-to-face treatment with standard methodology is perhaps not surprising given that the standard NICE adopted methodology for cost effectiveness was designed to determine this in the context of trials determining the clinical superiority of one intervention over another rather than non-inferiority.[20] With a £20 000 willingness to pay threshold, the added cost of face-to-face CBT-TF could be considered worthwhile for the extra health benefit, which is equal to 14 days in full health annually compared with guided internet based CBT-TF. Analyses of cost effectiveness should be considered together with other considerations, however, including those discussed above, and budget impact and feasibility.[60]

Strengths and limitations
Our study was a well designed, pragmatic, effectiveness randomised controlled trial that adhered to current methodological recommendations.[22] The fact that the originators of the guided internet based CBT-TF tested in this trial played key roles in the trial was identified as a risk. This risk was mitigated, however, at least in part, by robust methodology and involvement of one of the originators of CT-PTSD, independent trial managers, statisticians, and qualitative and health economic researchers. A major strength of the trial was the thorough training and supervision of the therapists and the use of quantitative and qualitative approaches.

Identifying an ideal control condition is always difficult; we believed that a gold standard face-to-face CBT-TF comparator would make it easier to interpret the results than one of usual care, and would facilitate robust evaluation of guided internet based CBT-TF. Unfortunately, usual care is not standard for PTSD in the UK, and variations in treatment would have made the results difficult to interpret. All therapists in our trial received formal CT-PTSD training and treated a patient under supervision in the control condition before seeing trial participants, and therefore the results for the control condition would likely have been better than if usual care was the comparator. The eligibility criteria mean that the results are not generalisable to people with PTSD to more than one traumatic event but are applicable to people with PTSD to one event who have experienced multiple traumatic events. We also cannot say whether guided internet based CBT-TF is more or less helpful for people with PTSD to some precipitating events rather than others. Other factors to consider when interpreting the results are the larger dropout rate from treatment in the guided internet based CBT-TF group and the possibility that the results are because 208 minutes of therapist time is as effective as 767 minutes of therapist time, with the internet programme not being a major contributing factor.

Clinical implications
Guided internet based CBT-TF for PTSD is part of a growing list of guided internet based interventions that can be as clinically effective as face-to-face treatments for various common mental disorders, but with reduced associated costs.[15] [16] The results of the RAPID trial should stimulate a step change in the approach of services to the provision of evidence based treatment to people with mild to moderate PTSD. Adherence to NICE's recommended standards, the extent of improvement in a real world setting, and the non-inferiority to a manual based current gold standard treatment for PTSD strongly support the clinical effectiveness of guided internet based CBT-TF. These factors mean that guided internet based CBT-TF could be recommended by guidelines in the future as a first line treatment for mild to moderate PTSD. Guided internet based CBT-TF can now be recommended as an evidence based, low intensity treatment option for people with PTSD, saving time and money, and allowing more people to receive effective treatment.

Research implications
How best to effectively disseminate and implement guided internet based CBT-TF at scale, to maximise its effect, is a key research question that has been explored with NHS commissioners and managers.[61] Identifying the specific skills and competencies required by a guiding clinician to promote effective relationships and engagement with patients, and the optimal level of training and supervision required for the provision of guided internet based CBT-TF would help determine if this form of treatment can be effectively delivered by less qualified therapists. The optimal amount of guidance is unclear. The quantitative and qualitative results suggest that some people could probably benefit from more therapy, and the amount of therapy could be influenced by particular characteristics (eg, severity and complexity of PTSD, type of traumatic exposure, demographic factors). Hence further research into increased flexibility in delivery and more personalised adaptations seem desirable.[62] Further work is required in terms of digital support, by using innovative advances in information technology. For example, the development of interactive programmes that allow ecological momentary sampling, where people are prompted to do things and provide information on how they are feeling and what they are doing, could increase effectiveness and reduce the amount of guidance needed from the therapist.

Conclusions
The RAPID trial showed that guided internet based CBT-TF was clinically effective, cheaper, well tolerated, and a non-inferior treatment to face-to-face CBT-TF for

people with mild to moderate PTSD to one traumatic event. The results should provide more choice and facilitate improvements to current care pathways for people with PTSD, that result in improved health and wellbeing.

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The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: A webinar has been held to disseminate the results of the study to research participants and related patient and public communities. An account of the event and summary of the findings will be published on the National Centre for Mental Health website to coincide with publication of this manuscript. Participants will be advised when this is available. A full National Institute for Health Research (funder) report, including a lay summary, will be published and disseminated once the review process is complete.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Web appendix: Supplementary materials