

Number of figures: 3

*(Editorial advice will be taken on the Figure
to include- 3 are given to aid peer review)*

Number of tables: 3

Internet-based guided self-help for post-traumatic stress disorder (PTSD): randomised controlled trial

**Catrin E. Lewis¹, Daniel Farewell¹, Vicky Groves¹, Neil J. Kitchiner², Neil P.
Roberts², Tracey Vick², Jonathan I. Bisson¹**

¹Cardiff University

²Cardiff and Vale University Health Board

Work conducted at the Institute of Psychological Medicine and Clinical Neurosciences, Cardiff
University School of Medicine, Hadyn Ellis Building, Maindy Road, Cardiff, CF24 4HQ

Correspondence to: Dr. Catrin Lewis, Hadyn Ellis Building, Maindy Road, Cathays, Cardiff, CF24 4HQ.

+44 7878211716 – LewisCE7@Cardiff.ac.uk

Short title: Guided self-help for PTSD: RCT

Keywords: Trauma; Treatment; CBT; Computer; Internet Technology

Disclosures and acknowledgements: This study was undertaken as part of a *Knowledge Transfer Partnership* between Cardiff University and Healthcare Learning Smile-on. If the programme is marketed, royalties will be payable to Cardiff University and Cardiff and Vale University Health Board, with a proportion of these being shared with CL, NK, NR, TV and JB. DF and VG have no conflicts of interest to disclose.

Abstract

Background: There are numerous barriers that limit access to evidence-based treatment for post-traumatic stress disorder (PTSD). Internet-based guided self-help is a treatment option that may help widen access to effective intervention, but the approach has not been sufficiently explored for the treatment of PTSD.

Methods: 42 adults with DSM-5 PTSD of mild to moderate severity were randomly allocated to internet-based self-help with up to 3 hours of therapist assistance, or to a delayed treatment control group. The internet-based programme included 8 modules that focused on psycho-education; grounding; relaxation; behavioural activation; real-life and imaginal exposure; cognitive therapy and relapse prevention. The primary outcome measure was reduction in clinician-rated traumatic stress symptoms using the clinician administered PTSD scale for DSM-V (CAPS-5). Secondary outcomes were self-reported PTSD symptoms; depression; anxiety; alcohol use; perceived social support; and functional impairment.

Results: Post-treatment, the internet-based guided self-help group had significantly lower clinician assessed PTSD symptoms than the delayed treatment control group (between-group effect size Cohen's $d=1.86$). The difference was maintained at one-month follow-up and dissipated once both groups had received treatment. Similar patterns of difference between the two groups were found for depression, anxiety and functional impairment. The average contact with treating clinicians was 2½ hours.

Conclusions: Internet-based trauma-focused guided self-help for PTSD is a promising treatment option that requires far less therapist time than current first line face-to-face psychological therapy.

Introduction

Post-Traumatic Stress Disorder (PTSD) is a common psychological disorder with a lifetime prevalence of approximately 8% (Kessler 2000). A substantial body of literature supports trauma-focused psychological therapies as effective treatments for PTSD (Bisson, Roberts et al. 2013, Jonas, Cusack et al. 2013), but numerous barriers limit access to these evidence-based interventions (Koenen, Goodwin et al. 2003, Hoge, Castro et al. 2004). Trauma-focused psychological therapies require significant therapist input, and are time-consuming and costly to deliver (NICE 2005). This, combined with additional barriers to treatment including the perceived stigma associated with psychological therapy (Cuijpers, van Straten et al. 2008) and inadequate service provision in rural areas (Griffiths and Christensen 2007), has resulted in long waiting times (Hitt, Kitchiner et al. 2004) and low rates of treatment uptake (Norris, Kaniasty et al. 1990, Hoge, Castro et al. 2004). In response, there has been a growing interest in using the internet as a platform for the delivery of psychological therapy (Amstadter, Broman-Fulks et al. 2009). Using the internet to deliver evidence-based treatment has the capacity to reduce the cost of effectively delivering evidence-based therapy (Hedman, Andersson et al. 2011) and has the potential to overcome many other barriers that currently limit the availability and uptake of treatment (Griffiths, Lindenmeyer et al. 2006).

Since the emergence of the first internet-based self-help treatments, a number of systematic reviews have supported their efficacy for depression, anxiety, and other disorders (Olthuis, Watt et al. 2015, Richards, Richardson et al. 2015). Internet-based interventions are delivered as stand-alone self-help therapies or with minimal professional guidance, with evidence supporting superiority of the latter (Richards and Richardson 2012). Self-help therapies delivered with support from a therapist are known as guided self-help interventions and they combine use of online psychological therapy with active input from a trained professional, but to a much lesser degree than therapist administered interventions. The content of existing therapies is not usually altered, deviating from

traditional psychological in terms of method of delivery (Cuijpers, Donker et al. 2010). A randomised controlled trial (RCT) of book-based self-help for PTSD (Ehlers, Clark et al. 2003) found the intervention to be no more effective than repeated assessments, however, the self-help materials may not have been optimal and no therapist support or follow-up appointments were provided.

The first formally evaluated internet-based self-help intervention for PTSD was developed in the Netherlands and was known as 'Interapy' (Lange, Schrieken et al. 2000). 'Interapy' showed promise for the treatment of sub-threshold PTSD symptoms, but was not evaluated within a population with a formalised diagnosis of PTSD (Amstadter, Broman-Fulks et al. 2009). Within a clinical population, the first published RCT evaluated internet-based CBT in comparison to internet-based supportive counselling (Litz, Engel et al. 2007). Both groups showed significant symptom improvement, but there were no differences between the two groups post-treatment. A second study compared guided internet-based CBT with or without exposure (Spence, Titov et al. 2014). Both groups improved significantly, but again, there were no differences between the two groups. These studies support the potential of delivering psychological therapy for PTSD online, but the results contradict established findings from the wider literature on psychological therapy for PTSD, which indicates superiority of trauma-focused/exposure-based therapies in comparison to those without a trauma-focus (Bisson, Roberts et al. 2013, Jonas, Cusack et al. 2013).

Two more recent studies evaluated internet-based guided self-help in comparison to wait-list groups. The first found a large within-group effect size in the treatment group from pre to post treatment, but a smaller between-groups effect size was found, due to symptom improvement in the control group (Spence 2011). The second RCT compared internet-based guided self-help to delayed treatment minimal attention and a larger between-group effect-size was found (Ivarsson, Blom et al. 2014).

Meta-analyses of the available evidence have concluded that internet-based treatments for PTSD are potentially effective (Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016). However, there has been relatively limited development of these approaches for PTSD when compared to other mental disorders, and further exploration is needed. The current study aimed to evaluate a novel trauma-focused internet-based guided self-help programme for PTSD, which had been carefully developed and pilot tested systematically over a number of years with the aim of producing an intervention that was optimally effective and acceptable to users (Lewis, Roberts et al. 2013). The online programme was designed for delivery with up to three hours of therapist guidance provided face-to-face or remotely, an approach which sets it apart from previous internet-based interventions for PTSD. In contrast to many previous studies of self-help for PTSD, the trial was conducted with a treatment seeking population that met diagnostic criteria for PTSD. This was the first RCT of the intervention and the aim was to establish efficacy of guided internet-based self-help for PTSD in comparison to a delayed treatment control group.

Methods

Design

The study was an exploratory single blind randomised parallel group controlled trial, which followed CONSORT guidelines for non-pharmacological trials (Boutron, Moher et al. 2008). Ethical approval was granted by the South East Wales Research Ethics Committee. Although a standard power calculation is not required for a Phase II exploratory trial, it was considered appropriate to use a power calculation based on a previous study of TFCBT for PTSD (Shalev, Ankri et al. 2012) to inform the sample size and ensure it was likely to be adequate. The calculation suggested that for an 80% chance of detecting a mean 15 point difference on the Clinician Administered PTSD Scale between guided self-help for PTSD and waiting list at the 5% significance level, assuming a standard deviation of 15.2, 17 subjects in each group would be needed. Allowing for a conservative estimate of a 20-

25% drop out, an extra 4 subjects were to be recruited to each arm representing a total proposed sample size of 42.

Initial screening for the study was completed by telephone. An inclusion checklist was used to assess eligibility and PTSD was screened for using the Trauma Screening Questionnaire (TSQ) with a cut off score of 6 taken to indicate possible PTSD (Brewin, Rose et al. 2002). Eligible participants were asked to monitor their traumatic stress symptoms for two weeks before attending a face-to-face meeting with a trained assessor. Written informed consent was taken and eligibility was confirmed by full assessment including the CAPS-5 (Weathers 2013). Participants were not given any financial incentive to take part in the study.

Participants were randomly assigned, through a system of sealed, opaque envelopes containing an allocation code generated by an independent statistician, to an immediate or delayed treatment group. Participants in the treatment group were followed up 10 weeks (post-treatment), 14 weeks (1 month post-treatment) and 22 weeks (3 months post-treatment) after randomisation. Participants in the delayed treatment group were followed up at 10 and 14 weeks after randomisation, before crossing over to receive treatment and being followed up 22 weeks after randomisation (post-treatment).

Participants

Participants were adults aged 18 or over, who continued to meet diagnostic criteria for DSM-5 PTSD of mild to moderate severity (CAPS-5 score of 55 or less) after a two-week period of symptom monitoring. Participants were recruited between March 2013 and June 2014. Recruitment was initiated at a specialist secondary care Traumatic Stress Service, which resulted in slow recruitment on the basis that PTSD was often too severe to meet the inclusion criteria. Participants were recruited more rapidly when the recruitment strategy was adapted to include mental health services at a primary care level. Exclusion criteria were psychosis, previous trauma-focused psychological therapy, DSM-5 severe major depressive episode, substance dependence, inability to read and write

fluently in English, inability to access the internet, change in psychotropic medication within one-month, concurrent psychological therapy, and suicidal intent. Earlier pilot testing of the intervention indicated that the programme was best suited to participants with PTSD symptoms to a single trauma experienced in adulthood, due to difficulties disentangling symptoms arising from multiple traumas without more intensive therapist assistance (Lewis, Roberts et al. 2013). The pilot work also indicated that the treatment was not well suited to individuals with severe PTSD. Individuals who had symptoms linked to multiple traumas or a CAPS-5 score of over 55 were, therefore, excluded. Trauma histories were established with use of the Life Events Checklist (LEC) (Weathers 2013).

Primary and secondary care clinicians in mental health services provided by Cardiff & Vale University Health Board referred participants in accordance with a brief screening protocol and a checklist of inclusion criteria. The study was also advertised through local media and by means of posters and leaflets in high-footfall National Health Service (NHS) waiting areas. Ninety-three individuals expressed an interest in joining the trial and were screened by telephone. Forty-nine met the initial screening criteria and were invited to attend a face-to-face interview. Four participants dropped out before baseline assessment. Of the 45 participants who were assessed at baseline, three were excluded (one due to having a CAPS score over 55 and the other two for not meeting diagnostic criteria for PTSD). Forty-two participants were randomised to either immediate treatment (n = 21) or to the delayed treatment control group (n = 21). Of these participants 40 (95%) had been referred to the study by treating clinicians and two (5%) were recruited by means of adverts in the media. Eight participants withdrew from the study, six from the immediate treatment group and two from the delayed treatment control group. Details of participant flow are presented in Figure 1.

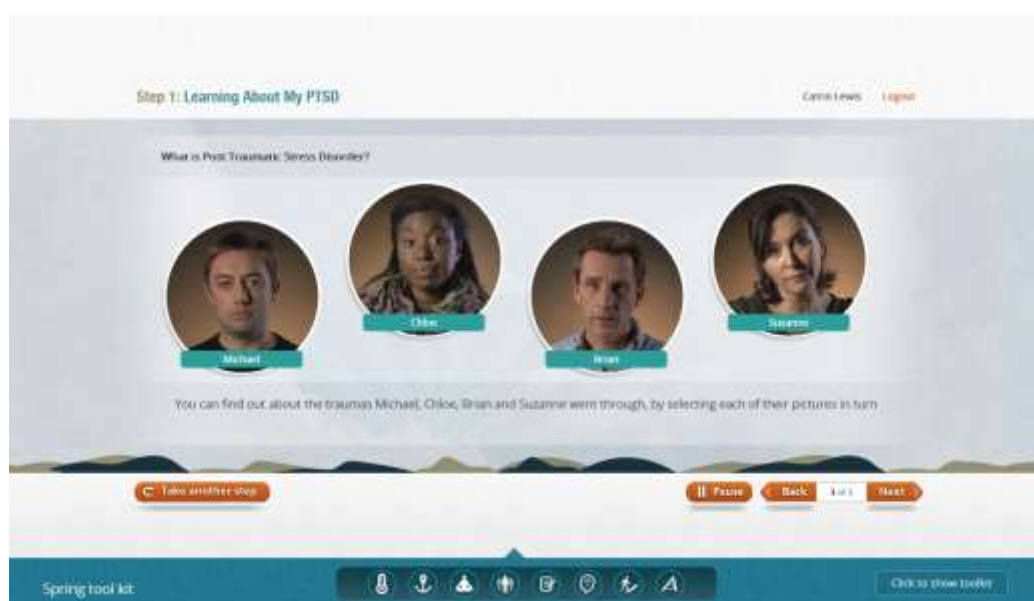
Figure 1: Participant flow (*approximately here*)

Intervention

The guided self-help intervention was developed systematically following Medical Research Council (MRC) guidance for the phase 1 development of a complex intervention (Medical Research Council 2000). The work followed an iterative process incorporating qualitative work to model the intervention, followed by two pilot studies to refine it on the basis of quantitative and qualitative outcomes (Lewis, Roberts et al. 2013). Collaboration with a software development company, as part of a *Knowledge Transfer Partnership*, produced an interactive online version of the programme, which included eight online steps designed for delivery over 8 weeks. The 8 steps are outlined in table 1.

Table 1: Programme content (*approximately here*)

Each of the 8 steps activated a ‘tool’, which became live in the ‘toolkit’ area of the website. The screenshot below, taken from Step 1, shows the actors whose PTSD case histories are followed throughout the intervention. The toolkit can be seen at the bottom of the webpage.



Therapists

The programme was initiated with an hour-long face-to-face session with a therapist-guide and fortnightly 30-minute appointments thereafter, which were delivered face-to-face or by telephone, according to participant preference. The therapist-guide also contacted the participant by telephone or email during the weeks between appointments to check-in briefly and prompt the participant to complete the sections of the programme that had been agreed in the previous session. The aim of the therapist guidance was to offer continued support, monitoring, motivation and problem solving. Participant programme accounts were linked to the therapists' accounts, enabling progress to be monitored remotely and completed tasks to be shared. Three male and two female therapists (a psychiatrist, a clinical psychologist and three cognitive behavioural therapists), who were experienced in the delivery of trauma-focused CBT guided the programme. They were trained to deliver the internet-based therapy, followed an intervention manual, and attended regular supervision meetings to maximise adherence to the manual. Therapists had no role in the assessment of participants at any time-point. The delayed treatment group did not have any contact with a therapist until they crossed over to receive the internet-based guided self-help treatment. Therapists were asked to record any adverse events arising during the trial.

Primary Outcome Measure

The primary outcome measure was the CAPS-5 (Weathers 2013). The CAPS is considered to be the 'gold standard' for PTSD assessment (Weathers 2001). It is a 30-item structured interview that corresponds to the DSM-5 criteria for PTSD (American Psychiatric Association 2013). A trained post-doctoral researcher who was blind to group allocation carried out all assessments. The researcher was not involved in the delivery of therapy and participants were asked not to reveal their group allocation.

Secondary Outcome Measures

PTSD Checklist for DSM-5 (PCL-5) (Weathers, Litz et al. 2013) - a 20-item self-report measure that assesses the 20 symptoms of DSM-5 PTSD.

Beck Depression Inventory (BDI) (Beck, Ward et al. 1961) - a 21 item self-report inventory designed to measure current mood.

Beck Anxiety Inventory (BAI) (Beck and Steer 1993) - a 21 item self-report inventory indicating the presence or absence of common symptoms of anxiety over the previous week.

Alcohol Use Disorders Identification Test (AUDIT) (Bush, Kivlahan et al. 1998) - a simple screening tool to pick up signs of harmful drinking and identify possible dependence.

Social Support Questionnaire (SSQ) (Sarason, Levine et al. 1983) - a self-administered scale measuring perceived social support.

Sheehan Disability Scale (SDS) (Leon, Olfson et al. 1997) – a self-report measure used to assess functional impairment in three domains: work/school; social life; and family life.

Statistical Methods

At each observation time, means and SDs specific to each treatment group were calculated. We therefore required CAPS scores (for example) for every individual, at every observation time. Since not all individuals provided scores at all possible assessments, we imputed these missing data.

Reflecting our uncertainty about the values that would have been recorded on these occasions, we used multiple imputation (with 100 imputations), and considered two possible imputation strategies. The first assumed a missing at random mechanism, wherein subjects with the same longitudinal measurements have the same expected future trajectory (as predicted by a simple

random effects model) irrespective of whether they drop out or not. The second used a last observation carried forward approach, wherein subjects are expected to continue at the same level as their final observed measurement. We deemed the missing at random imputations too optimistic, and the last observation carried forward approach too pessimistic, so ultimately sampled values uniformly between these two extremes. To make inference about our mean and SD estimates, bootstrap resampling (that is, sampling with replacement from study participants) was employed, with 100 replicate datasets generated. Throughout, varying engagement in the trial and with the treatment was handled using intention-to-treat principles. Effect modification was explored using standard regression adjustment, but using a simplified model for longitudinal data in which the contrast of interest compared measurements taken before, and after, the planned initiation of treatment. These were exploratory analyses based on theoretical indications of internet-based treatment effect. As in the missing at random imputations, random effects were used to account for correlation within a particular participant's measurements, and within a particular therapist's patients. All statistical analyses were conducted in R (R Core Team 2016).

Results

Baseline Characteristics

The mean age of participants was 39.29 (SD = 12.7, range = 20-65) and 59.5 % were female. The average time since trauma was 37.33 months (SD = 46.95, range = 3-228 months). Traumatic events included transportation accidents (n=9); witnessing a sudden, violent, or accidental death (n=9); traumatic childbirth or stillbirth (n=8); sexual assault or rape (n=5); physical attack (n=4); life threatening illness or injury (n=3); serious accident (n=1); learning of the violent death of a loved one (n=1); seeing a mutilated body (n=1); and being held hostage/detained (n=1). Baseline demographic characteristics are presented in table 2.

Table 2: Demographic characteristics pre-treatment (*approximately here*)

Adherence and Attrition

Of the 42 participants, 8 (19%) dropped-out prematurely: 6 from the immediate treatment group and 2 from the delayed treatment group. Of those who dropped out, 5/8 (63%) failed to attend their first appointment with a therapist and did not therefore log in to the programme. One additional participant did not log into the programme, despite having attended an initial appointment with a therapist. The remaining two dropouts completed 2 and 5 modules respectively. 15/42 (35.7%) completed all 8 of the modules, 30/42 (72%) completed more than half. A perceived lack of time to dedicate to the programme was the reason for drop-out in two cases; finding the programme difficult was the reason in another two cases; one individual felt that their symptoms had improved sufficiently and did not wish to complete the intervention; the reason for the remaining three dropouts is unknown. Male gender was significantly associated with completing a greater number of modules (Odds Ratio (OR) = 2.01, $p = 0.02$, 95% CI [1.12, 3.61]), as was University education (OR = 3.76, $p = 0.01$, 95% CI [1.46, 9.73]), with those who had a University education completing more modules. The number of modules completed was not significantly associated with age, time since trauma, baseline traumatic stress symptoms or baseline social support. Dropout was not significantly associated with age, gender, education, baseline CAPS 5 score, or baseline social support.

Primary Outcome

Immediately after treatment (10 weeks after randomisation), participants allocated to internet-based guided self-help ($n=21$) had significantly lower levels of clinician-assessed traumatic stress symptoms in comparison to the delayed treatment control group. The analysis revealed a group

mean difference post-treatment of 18.60 points (95% CI [-24.65, -13.41]), and similar differences were seen at week 14, with a group mean difference of 17.16 (95% CI [-23.78,-10.68]). At week 22 (post-treatment for the delayed-treatment group) group differences became non-significant (mean difference = 0.97, 95% CI [-7.84, 8.44]). Observed CAPS scores for the two groups are presented in figure 2. Means and SDs at each time point are given in table 3. There was no significant effect modification by age, gender, baseline CAPS score, number of modules completed or number of therapist minutes. However, those with more recent trauma experienced a slightly improved effect. Every month elapsed since trauma corresponded to an effect reduction of 0.07 points (95% CI [-0.02, 0.22]). Higher education was associated with greatest treatment effect, with those with a university higher degree experiencing a benefit 16.69 points (95% CI [-28.99, -4.38) greater than those with secondary education, and intermediate benefits for intermediate educational levels.

Figure 3 illustrates the findings of the multiple imputation method used compared to results using missing at random and last observation carried forward imputation methods. The overall effect size using the multiple imputation method was Cohen's $d = 1.86$ (compared to $d = 2.60$ using the missing at random imputation and $d = 1.42$ using last observation carried forward imputation). The standardised mean difference (SMD) was -1.82 (95% CI -2.55 to -1.09).

Figure 2: Observed CAPS scores at each assessment point for the guided self-help and delayed treatment group (*approximately here*)

Secondary Outcomes

A similar pattern of outcomes emerged in relation to the secondary measures (table 3). Post-treatment, there was a statistically significant difference between the two groups in terms of depression (between-group mean difference of 10.83 (95% CI [-16.66, -5.14]), anxiety (between-group mean difference of 13.40 (95% CI [-19.91, -6.35]) and functional impairment (between-group mean difference of 9.36 (95% CI [-13.56, -3.93])). These differences remained 14 weeks post-

randomisation but were no longer evident once both groups had received treatment. There were no statistically significant differences between the two groups on measures of alcohol misuse post-treatment (between-group mean difference of 2.13 (95% CI [-6.02, 1.63]) or at any other time-point, but scores were very low at baseline assessment. There were no statistically significant differences in perceived social support post treatment (between-group mean difference of -0.18 (95% CI [-5.37, 5.33]) or at other time-points.

Table 3: ITT analysis estimated means and standard deviations (*approximately here*)

Therapist Assistance

The mean amount of therapist input per participant was 147.53 (SD = 57.01) minutes. This included a mean of 3.09 (SD = 1.84) face-to-face meetings, 2.09 (SD = 1.85) telephone calls, and 1.00 (SD = 1.62) emails.

Adverse Events

No adverse events were reported.

Discussion

The study findings suggest that internet-based guided self-help can be effective for the treatment of PTSD. Participants in the guided self-help group reported significant reductions in traumatic stress symptoms in comparison to the delayed treatment control group post-treatment and at 1-month follow up. Once the delayed treatment group had received treatment, their mean CAPS-5 scores reduced to the same degree as those of the immediate treatment group. The same pattern of results emerged in relation to symptoms of anxiety, depression and functional impairment. These results were obtained with a mean of less than 2½ hours of therapist input, around a fifth of that for the

first-line face-to-face therapies currently recommended by NICE (NICE 2005). The findings support the use of internet-based guided self-help as a potentially clinically and cost effective treatment option for PTSD of mild to moderate severity.

Strengths and weaknesses of the study

Rigorous efforts were made to minimise the potential for bias by ensuring allocation concealment and using an assessor and a statistician who were blind to the group allocation of participants. The intervention itself had been developed systematically following MRC guidelines, with the aim of maximising efficacy and acceptability, which sets it apart from interventions evaluated by many other trials of internet-based CBT. Wide eligibility criteria were used to maximise generalisability and participants were included regardless of the time elapsed since the trauma, or co-morbidity with disorders other than current psychosis, major depressive episode or substance dependence.

Participants were primarily treatment seeking individuals who were under the care of local primary and secondary mental health services and, therefore, likely to be representative of this population.

Nonetheless, some limitations remained. Firstly, the sample size for the study was small. Secondly, the therapists who provided guidance were experienced at delivering trauma-focused CBT, which limits our ability to predict the outcomes that could be achieved by less experienced or non-specialist therapists. Participants were only followed up for three months after the end of treatment.

Whilst treatment gains were maintained for this duration, we cannot draw conclusions related to the longer-term effects of the intervention, which is a common issue within the field of internet-based self-help (Palmqvist, Carlbring et al. 2007, Kuester, Niemyer et al. 2016). Also, the generalisability of results to PTSD sufferers more widely, may be limited by the fact that participants were highly educated and mostly employed, indicating that they were higher functioning.

Another limitation, shared by the majority of RCTs, was the need to account for some missing data. It is impossible to know what the true values of the missing data would have been. To address this, we used a multiple imputation method and also undertook analyses using last observation carried

forward and missing at random methods of imputation as sensitivity analyses, assuming that the former would provide results that were too pessimistic and the latter results that were too optimistic. The multiple imputation method produced results in between these two likely extremes and is considered likely to be as accurate as possible an estimate of what the true results would have been. Finally, the team that developed the intervention conducted the RCT and replication by other groups is desirable.

Comparison to other studies

Effect sizes were comparable to those reported for therapist administered trauma-focused psychological treatments for PTSD (Jonas, Cusack et al. 2013). This should, however, be interpreted with caution since the current study only included participants with mild to moderate symptoms after a single traumatic event, making comparison with studies including a wider range of PTSD sufferers difficult. In agreement with the findings of recent meta-analyses of internet-based self-help for PTSD, the intervention was found to be effective in comparison to waitlist (Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016), with the magnitude of effect lying at the higher end of the effect sizes reported by these reviews. The effect size was larger than that reported previously for internet-based CBT for clinical populations of PTSD sufferers (Spence 2011, Ivarsson, Blom et al. 2014), which may be influenced by the fact that the intervention was systematically developed through an iterative process of modelling and pilot testing intended to create an optimally effective programme (Lewis, Roberts et al. 2013). The programme had a greater trauma-focus and emphasis on imaginal exposure work via writing and reading a narrative, than other internet-based CBT programmes for PTSD. Although meta-analyses have not found trauma-focus to be a significant moderator of treatment effect for internet-based PTSD therapies, it is likely that subgroup analyses were not sufficiently powered to detect a difference (Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016). Trauma-focus is associated with improved outcome in face-to-face therapies for PTSD (Bisson, Roberts et al. 2013) and there is little reason to think that internet-based therapies

would be any different. In addition, the programme was professionally developed and interactive, with minimal reliance on reading on-screen text. Despite meta-analyses of the small number of existing studies failing to demonstrate moderating effects of any particular programme component, it is likely that many of these factors have supported the efficacy of the programme and that future meta-analyses will include a sufficient number of studies to identify factors that influence treatment response.

Dropout rates from the study were comparable to previous trials of internet-based guided self-help for PTSD (Spence 2011, Ivarsson, Blom et al. 2014) and other mental disorders (Spek, Cuijpers et al. 2007). They were also of a similar magnitude to dropout from therapist-administered therapy (Bisson, Roberts et al. 2013). 75% of those who dropped out of the trial did so before logging-in to the programme, demonstrating a reluctance to engage in guided self-help, as opposed to an issue related to the tolerability of the treatment itself. This is consistent with previous research that has reported disappointing rates of uptake of internet-based interventions (Proudfoot, Goldberg et al. 2003) and a tendency for wariness of internet-based treatments due to low expectancies for symptom improvement (Mitchell and Gordon 2007).

Clinical implications

There is inevitably a delay between the onset of mental disorder and the initiation of appropriate evidence-based treatment (Wang, Angermeyer et al. 2007). Although some PTSD sufferers are motivated and able to access timely intervention, the interval between symptoms arising and receipt of appropriate treatment varies substantially, and the disorder often goes untreated for many years (Wang, Berglund et al. 2005). If left untreated, PTSD is associated with functional and emotional impairment (Amaya-Jackson, Davidson et al. 1999), reduced quality of life (Olatunji, Cisler et al.

2007), a predisposition for the development of other psychiatric and physical illnesses (Brady, Killeen et al. 2000, Pacella, Hruska et al. 2013), increased suicidal ideation (Krysinska and Lester 2010), higher healthcare utilisation (Domin Chan, Cheadle et al. 2009), and higher rates of alcohol abuse and dependence (Breslau, Davis et al. 2003). Understanding and overcoming traditional barriers to treatment and providing alternatives that serve to maximise the number of PTSD sufferers able to quickly access and engage in evidence-based therapy is, therefore, an important public health concern. Demanding around 80% less therapist time than existing trauma-focused psychological therapies, internet-based guided self-help for PTSD has the potential to maximise the use of healthcare resources and widen access to effective treatment. It has the potential to increase therapeutic capacity and reduce waiting lists, thereby enabling timely intervention and resolution of traumatic stress symptoms, which has numerous likely benefits including reduced distress and minimised interference with normal role functioning. Internet-based interventions also provide scope to overcome many traditional barriers to treatment including difficulties committing to weekly appointments due to work, childcare commitments or transport issues.

Research Implications

Little is known about the mechanisms of change associated with internet-based CBT (Andersson, Carlbring et al. 2009, Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016). Further work is needed to determine the moderators and mediators of treatment-effect. This is especially pertinent to the field of PTSD, which has previously failed to find an advantage of trauma-focused/exposure internet-based psychological therapy in direct comparisons with non-trauma focused interventions (Litz, Engel et al. 2007, Spence, Titov et al. 2014, Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016). The effect sizes obtained in this study were greater than those found in other RCTs of internet-based CBT for PTSD. This warrants further scrutiny and investigation. A possible explanation is that previously tested programmes have failed to deliver a sufficient 'dose' of imaginal exposure. This programme included a key role for exposure and encouraged initiation early in the 8-week

programme (Lewis, Roberts et al. 2013). Pilot work indicated that PTSD sufferers were able to tolerate a larger 'dose' of exposure than included in the original prototype and later iterations of the programme had a greater trauma-focus with improved results and no reported adverse effects (32). As noted earlier, this contradicts the findings of a meta-analysis that found no significant differences between effect sizes when comparing interventions with exposure, to those without, however, very few studies have included programmes without exposure (Kuester, Niemeyer et al. 2016, Sijbrandij, Kunovski et al. 2016).

Large multi-centre effectiveness trials with nested process-evaluation are needed to confidently recommend internet-based guided self-help as an evidence-based treatment option for PTSD. Further trials are also required to ascertain the optimal balance between minimising therapist input and maximising outcome. For example, it may be possible to augment programmes with inbuilt self-reinforcement strategies to reduce or eliminate the need for therapist-assistance. There is also a need to explore predictors of outcome and dropout, such as participant age, trauma type, levels of computer literacy, educational attainment and symptom severity. This will provide a greater understanding of PTSD sufferer characteristics likely to be associated with positive responses to internet-based CBT and allow a more personalised approach to treatment (Hamburg and Collins 2010).

Funding: This work was funded through a *Knowledge Transfer Partnership* (KTP008512).

References

Amaya-Jackson, L., J. R. Davidson, D. C. Hughes, M. Swartz, V. Reynolds, L. K. George and D. G. Blazer (1999). "Functional impairment and utilization of services associated with posttraumatic stress in the community." Journal of Traumatic Stress **12**(4): 709-724.

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition). Washington.

Amstadter, A. B., J. Broman-Fulks, H. Zinzow, K. J. Ruggiero and J. Cercone (2009). "Internet-based interventions for traumatic stress-related mental health problems: a review and suggestion for future research." *Clinical psychology review* **29**(5): 410-420.

Andersson, G., P. Carlbring, T. Berger, J. Almlöv and P. Cuijpers (2009). "What makes internet therapy work?" *Cognitive Behaviour Therapy* **38**(S1): 55-60.

Beck, A. T. and R. A. Steer (1993). *Beck Anxiety Inventory Manual*. San Antonio, The Psychological Corporation.

Beck, A. T., C. H. Ward, M. Mendelson, J. Mock and J. Erbaugh (1961). "An Inventory for Measuring Depression." *Arch Gen Psychiatry* **4**(6): 561-571.

Bisson, J., N. Roberts, M. Andrew, R. Cooper and C. Lewis (2013). "Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults (Review)." *Cochrane Database of Systematic Reviews* **12**(CD003388).

Bisson, J. I., N. P. Roberts, M. Andrew, R. Cooper and C. Lewis (2013). "Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults." *The Cochrane Library*.

Boutron, I., D. Moher, D. G. Altman, K. F. Schulz and P. Ravaud (2008). "Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration." *Annals of Internal Medicine* **148**: 295-309.

Brady, K. T., T. K. Killeen, T. Brewerton and S. Lucerini (2000). "Comorbidity of psychiatric disorders and posttraumatic stress disorder." *Journal of Clinical Psychiatry*.

Breslau, N., G. C. Davis and L. R. Schultz (2003). "Posttraumatic stress disorder and the incidence of nicotine, alcohol, and other drug disorders in persons who have experienced trauma." *Archives of General Psychiatry* **60**(3): 289-294.

Brewin, C. R., S. Rose, B. Andrews, J. Green, P. Tata, C. McEVEDY, S. Turner and E. B. Foa (2002). "Brief screening instrument for post-traumatic stress disorder." The British Journal of Psychiatry **181**(2): 158-162.

Bush, K., D. R. Kivlahan, M. B. McDonell, S. D. Fihn and K. A. Bradley (1998). "The AUDIT alcohol consumption questions (AUDIT-C): An effective brief screening test for problem drinking for the ambulatory care quality improvement project." Archives of Internal Medicine **158**(16): 1789-1795.

Cuijpers, P., T. Donker, A. van Straten, J. Li and G. Andersson (2010). "Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies." Psychological medicine **40**(12): 1943-1957.

Cuijpers, P., A. van Straten and G. Andersson (2008). "Internet-administered cognitive behavior therapy for health problems: a systematic review." Journal of Behavioral Medicine **31**(2): 169-177.

Domin Chan, P., A. D. Cheadle, G. Reiber, J. Unützer and E. F. Chaney (2009). "Health care utilization and its costs for depressed veterans with and without comorbid PTSD symptoms." Psychiatric Services **60**(12): 1612-1617.

Ehlers, A., D. M. Clark, A. Hackmann, F. McManus, M. Fennell, C. Herbert and R. Mayou (2003). "A Randomized Controlled Trial of Cognitive Therapy, a Self-help Booklet, and Repeated Assessments as Early Interventions for Posttraumatic Stress Disorder." Arch Gen Psychiatry **60**(10): 1024-1032.

Griffiths, F., A. Lindenmeyer, J. Powell, P. Lowe and M. Thorogood (2006). "Why are health care interventions delivered over the internet? A systematic review of the published literature." Journal of Medical Internet Research **8**(2).

Griffiths, K. M. and H. Christensen (2007). "Internet-based mental health programs: A powerful tool in the rural medical kit." Australian Journal of Rural Health **15**(2): 81-87.

Hamburg, M. A. and F. S. Collins (2010). "The path to personalized medicine." New England Journal of Medicine **363**(4): 301-304.

Hedman, E., E. Andersson, B. Ljótsson, G. Andersson, C. Rück and N. Lindefors (2011). "Cost-effectiveness of Internet-based cognitive behavior therapy vs. cognitive behavioral group therapy for

social anxiety disorder: results from a randomized controlled trial." Behaviour Research and Therapy **49**(11): 729-736.

Hitt, D., N. J. Kitchiner and J. I. Bisson (2004). "Developments in treating post traumatic stress disorder using a cognitive behavioural therapy model." Mental Health Practice **8**(1): 30-35.

Hoge, C. W., C. A. Castro, S. C. Messer, D. McGurk, D. I. Cotting and R. L. Koffman (2004). "Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care." New England Journal of Medicine **351**(1): 13-22.

Ivarsson, D., M. Blom, H. Hesser, P. Carlbring, P. Enderby, R. Nordberg and G. Andersson (2014). "Guided internet-delivered cognitive behavior therapy for post-traumatic stress disorder: A randomized controlled trial." Internet Interventions **1**(1): 33-40.

Jonas, D., K. Cusack, C. Forneris, T. Wilkins, J. Sonis, J. Middleton, C. Feltner, D. Meredith, J. Cavanaugh and K. Brownley (2013). Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD). Comparative Effectiveness Review No. 92.

Kessler, R. C. (2000). "Posttraumatic stress disorder: the burden to the individual and to society." Journal of Clinical Psychiatry. **61**(5): 4-14.

Koenen, K., R. Goodwin, E. Struening, F. Hellman and M. Guardino (2003). "Posttraumatic stress disorder and treatment seeking in a national screening sample." Journal of Traumatic Stress **16**: 5-16.

Krysinska, K. and D. Lester (2010). "Post-traumatic stress disorder and suicide risk: a systematic review." Archives of Suicide Research **14**(1): 1-23.

Kuester, A., H. Niemeyer and C. Knaevelsrud (2016). "Internet-based interventions for posttraumatic stress: A meta-analysis of randomized controlled trials." Clinical psychology review **43**: 1-16.

Lange, A., B. Schriecken, J.-P. van de Ven, B. Bredeweg, P. M. Emmelkamp, J. van der Kolk, L. Lydsdottir, M. Massaro and A. Reuvers (2000). "'Interapy': The effects of a short protocolled treatment of posttraumatic stress and pathological grief through the Internet." Behavioural and Cognitive Psychotherapy **28**(02): 175-192.

Leon, A., M. Olfson, L. Portera, L. Farber and D. Sheehan (1997). "Assessing psychiatric impairment in primary care with the Sheehan Disability Scale." International Journal of Psychiatry in Medicine **27**(2): 93-105.

Lewis, C., N. Roberts, T. Vick and J. I. Bisson (2013). "Development of a guided self help (GSH) programme for the treatment of mild to moderate post traumatic stress disorder (PTSD)." Depression and Anxiety **30**(11): 1121-1128.

Litz, B. T., C. C. Engel, R. A. Bryant, A. Papa, B. T. Litz, C. C. Engel, R. A. Bryant and A. Papa (2007). "A randomized, controlled proof-of-concept trial of an Internet-based, therapist-assisted self-management treatment for posttraumatic stress disorder." American Journal of Psychiatry **164**(11): 1676-1683.

Medical Research Council (2000). A framework for the development and evaluation of randomised controlled trials for complex interventions to improve health. London.

Mitchell, N. and P. K. Gordon (2007). "Attitudes towards computerized CBT for depression amongst a student population." Behavioural and Cognitive Psychotherapy **35**(04): 421-430.

NICE (2005). Post-traumatic stress disorder (PTSD): the management of PTSD in adults and children in primary and secondary care. National cost-impact report. London.

Norris, F. H., K. Z. Kaniasty and D. A. Scheer (1990). "Use of mental health services among victims of crime: frequency, correlates, and subsequent recovery." Journal of Consulting and Clinical Psychology **58**(5): 538.

Olatunji, B. O., J. M. Cisler and D. F. Tolin (2007). "Quality of life in the anxiety disorders: a meta-analytic review." Clinical Psychology Review **27**(5): 572-581.

Olthuis, J. V., M. C. Watt, K. Bailey, J. A. Hayden and S. H. Stewart (2015). "Therapist-supported internet cognitive-behavioural therapy for anxiety disorders in adults." BJPsych Advances **21**(5): 290-290.

Pacella, M. L., B. Hruska and D. L. Delahanty (2013). "The physical health consequences of PTSD and PTSD symptoms: a meta-analytic review." Journal of Anxiety Disorders **27**(1): 33-46.

Palmqvist, B., P. Carlbring and G. Andersson (2007). "Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost?" Expert Review of Pharmacoeconomics & Outcomes Research **7**(3): 291-297.

Proudfoot, J., D. Goldberg, A. Mann, B. Everitt, I. Marks and J. A. Gray (2003). "Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depression in general practice." Psychological Medicine **33**(2): 217-227.

Richards, D. and T. Richardson (2012). "Computer-based psychological treatments for depression: a systematic review and meta-analysis." Clinical psychology review **32**(4): 329-342.

Richards, D., T. Richardson, L. Timulak and J. McElvaney (2015). "The efficacy of internet-delivered treatment for generalized anxiety disorder: A systematic review and meta-analysis." Internet Interventions **2**(3): 272-282.

Sarason, I. G., H. M. Levine, R. B. Basham and B. R. Sarason (1983). "Assessing social support: The Social Support Questionnaire." Journal of Personality and Social Psychology **44**(1): 127-139.

Shalev, A. Y., Y. Ankri, Y. Israeli-Shalev, T. Peleg, R. Adessky and S. Freedman (2012). "Prevention of posttraumatic stress disorder by early treatment: results from the Jerusalem Trauma Outreach And Prevention study." Archives of general psychiatry **69**(2): 166-176.

Sijbrandij, M., I. Kunovski and P. Cuijpers (2016). "Effectiveness of internet-delivered cognitive behavioural therapy for posttraumatic stress disorder: a systematic review and meta-analysis." Depression and Anxiety **33**(9): 783-791.

Spek, V., P. Cuijpers, I. Nyklíček, H. Riper, J. Keyzer and V. Pop (2007). "Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis." Psychological Medicine **37**(03): 319-328.

Spence, J., N. Titov, L. Johnston, M. P. Jones, B. F. Dear and K. Solley (2014). "Internet-based trauma-focused cognitive behavioural therapy for PTSD with and without exposure components: A randomised controlled trial." Journal of Affective Disorders **162**: 73-80.

Spence, J., Titov, N., Dear, B. F., Johnston, L., Solley, K., Lorian, C. & Schwenke, G. (2011). "Randomized controlled trial of Internet-delivered cognitive behavioral therapy for posttraumatic stress disorder." Depression and Anxiety **28**(7): 541-550.

Wang, P. S., M. Angermeyer, G. Borges, R. Bruffaerts, W. T. Chiu, G. De Girolamo, J. Fayyad, O. Gureje, J. M. Haro and Y. Huang (2007). "Delay and failure in treatment seeking after first onset of mental disorders in the World Health Organization's World Mental Health Survey Initiative." World Psychiatry **6**(3): 177.

Wang, P. S., P. Berglund, M. Olfson, H. A. Pincus, K. B. Wells and R. C. Kessler (2005). "Failure and delay in initial treatment contact after first onset of mental disorders in the National Comorbidity Survey Replication." Archives of General Psychiatry **62**(6): 603-613.

Weathers, F., B. Litz, T. Keane, P. Palmieri, B. Marx and P. Schnurr. (2013). "The PTSD Checklist for DSM-5 (PCL-5). ."

Weathers, F. W., Blake, D.D., Schnurr, P.P., Kaloupek, D.G., Marx, B.P., & Keane, T.M. (2013). "The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)." Interview available from the National Center for PTSD at www.ptsd.va.gov.

Weathers, F. W., Blake, D.D., Schnurr, P.P., Kaloupek, D.G., Marx, B.P., & Keane, T.M. . (2013). " The Life Events Checklist for DSM-5 (LEC-5)."

Weathers, F. W., Keane, T. M., & Davidson, J. R. (2001). "Clinician-Administered PTSD Scale: A review of the first ten years of research." Depression and Anxiety **13**: 132-156.

Figure Legends

Figure 1: Participant flow (*editorial advice will be taken on the one Figure to include – three are included to aid peer review*)

Figure 2: Observed CAPS scores at each assessment point for the guided self-help and delayed treatment group (grey lines indicate interpolation across a missing measurement) (*editorial advice will be taken on the one Figure to include – three are included to aid peer review*)

Figure 3: Findings of the multiple imputation method used compared to results using missing at random and last observation carried forward imputation methods (*editorial advice will be taken on the one Figure to include – three are included to aid peer review*)

Tables and Figures

Step	Content
Step 1: Learning About My PTSD	Psycho-educational material related to PTSD, illustrated by video-clips of four characters describing their experiences
Step 2: Grounding Myself	Explanation of grounding and its uses along with descriptions and demonstrations of grounding exercises
Step 3: Managing My Anxiety	Education around relaxation with learning through videos of a controlled breathing technique, deep muscular relaxation, and relaxation through imagery
Step 4: Reclaiming My Life	Behavioural re-activation to help individuals return to previously undertaken/new activities
Step 5: Coming to Terms with My Trauma	Provides rationale for imaginal exposure, narratives of the four video characters are provided. The therapist helps the participant to begin writing a narrative, which they complete remotely and read every day for at least 30 minutes
Step 6: Changing My Thoughts	Cognitive techniques to address associated negative appraisals
Step 7: Overcoming My Avoidance	Graded in-vivo exposure work to trauma related avoided/feared situations
Step 8: Keeping Myself Well	Reinforces what has been learnt during the programme, provides relapse prevention measures and guidance on what to do if symptoms return

Table 1: Programme content

Variable	Treatment Group (n = 21)		Delayed Treatment Control Group (n = 21)	
	N	%	N	%
Gender				
Male	8	38	9	42.9
Female	13	62	12	57.1
Age				
Mean	38.86	11.91 (SD)	37.71	13.8 (SD)
Range	20-65		21-64	
Marital Status				
Single/never married	8	38.1%	8	38.1%
Married/co-habiting	12	52.4%	11	52.4%
Widowed/separated/divorced	1	4.8%	2	9.5%
Highest Level of Education				
Secondary	2	9.5%	4	19%
Tertiary	9	42.9%	4	19%
University degree	8	38.1%	10	47.6%
University higher degree	2	9.5%	3	14.3%
Employment				
Employed	15	71.4%	16	76.1%
Student	2	9.5%	1	4.8%
Retired	1	4.8%	0	0%
Unemployed	3	14.3%	4	19.0%
Time in months since trauma				
Mean	32.68	52.07 (SD)	42.53	41.44 (SD)
Range	3-228		4-120	

Table 2: Demographic characteristics of the two groups pre-treatment

	Pre-treatment	10 weeks	14 weeks	22 weeks
Clinician Administered PTSD Scale (CAPS)				
Guided self-help	35.99 (6.29)	17.93 (12.25)	16.47 (13.22)	15.77 (13.01)
Delayed treatment	37.12 (6.95)	36.53 (7.1)	33.63 (8.42)	14.8 (13.71)
PTSD Checklist (PCL)				
Guided self-help	50.78 (12.54)	25.44 (15.84)	22.26 (16.90)	21.30 (16.79)
Delayed treatment	49.87 (12.58)	51.23 (9.97)	44.74 (14.29)	21.81 (17.61)
Beck Anxiety Inventory (BAI)				
Guided self-help	30.97 (13.60)	17.10 (11.06)	15.49 (11.63)	14.16 (11.75)
Delayed treatment	30.58 (15.72)	30.05 (14.43)	28.08 (15.10)	13.95 (12.94)
Beck Depression Inventory (BDI)				
Guided self-help	24.72 (10.36)	15.97 (10.42)	14.66 (10.94)	15.24 (9.88)
Delayed treatment	26.04 (8.47)	26.80 (9.08)	23.61 (10.88)	15.85 (9.69)
Sheehan Disability Scale (SDS)				
Guided self-help	17.93 (7.14)	9.29 (8.09)	9.55 (10.18)	9.35 (9.76)
Delayed treatment	18.56 (5.73)	18.65 (6.95)	16.24 (8.39)	9.87 (8.70)
Alcohol Use Disorders Identification Test (AUDIT)				
Guided self-help	3.89 (4.18)	3.74 (3.64)	3.93 (4.40)	4.00 (4.16)

Delayed treatment	5.41 (5.47)	5.88 (6.51)	5.39 (5.67)	5.19 (5.92)
Social Support Questionnaire (SSQ)				
Guided self-help	13.73 (9.01)	15.25 (7.97)	14.32 (7.55)	16.28 (9.23)
Delayed treatment	18.62 (10.88)	15.43 (9.74)	16.23 (8.89)	21.52 (11.73)

Table 3: ITT analysis estimated means and standard deviations (*mean (SD)*)

Figures

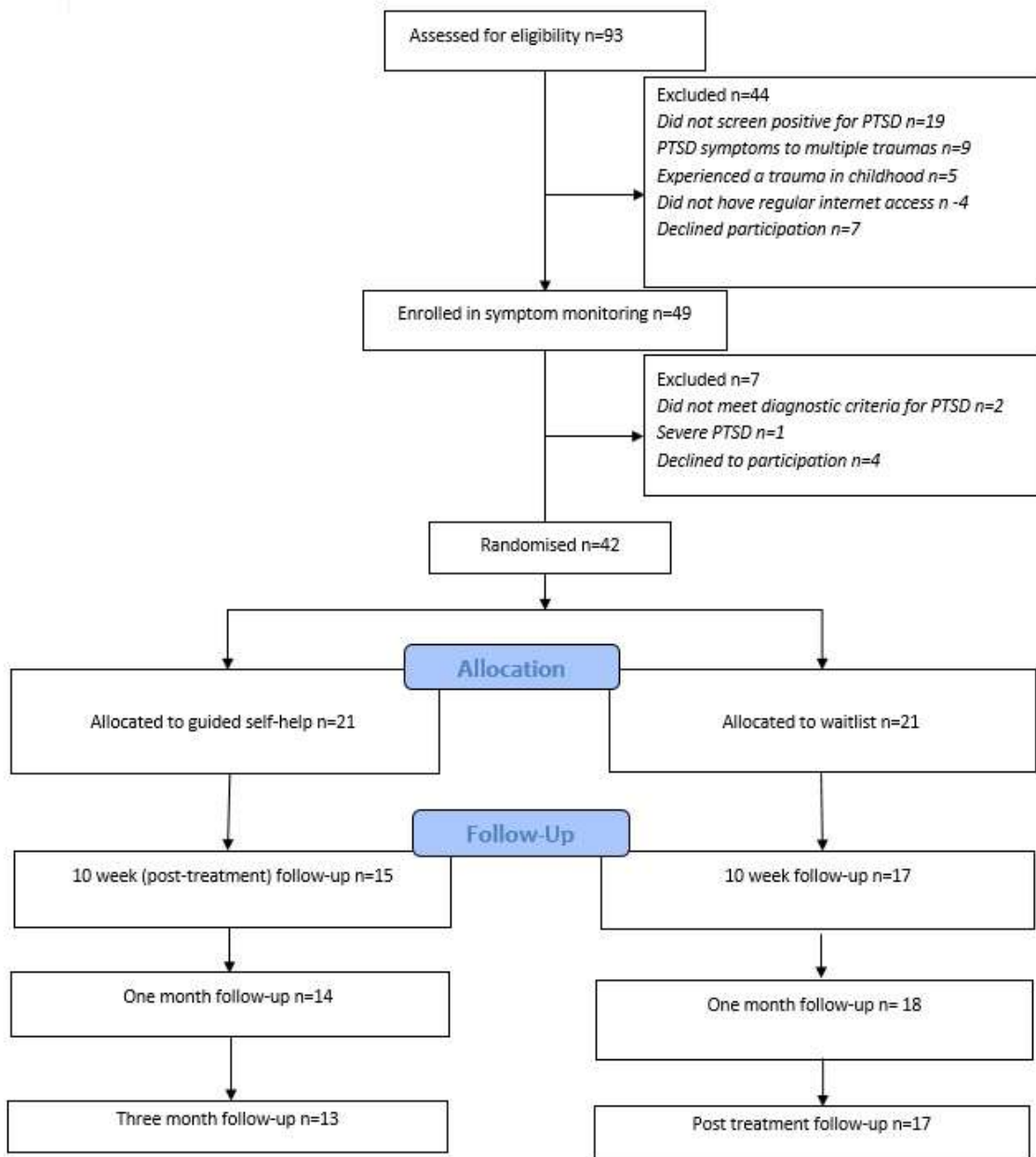


Figure 1: Participant flow (editorial advice will be taken on the one Figure to include – three are included to aid peer review)

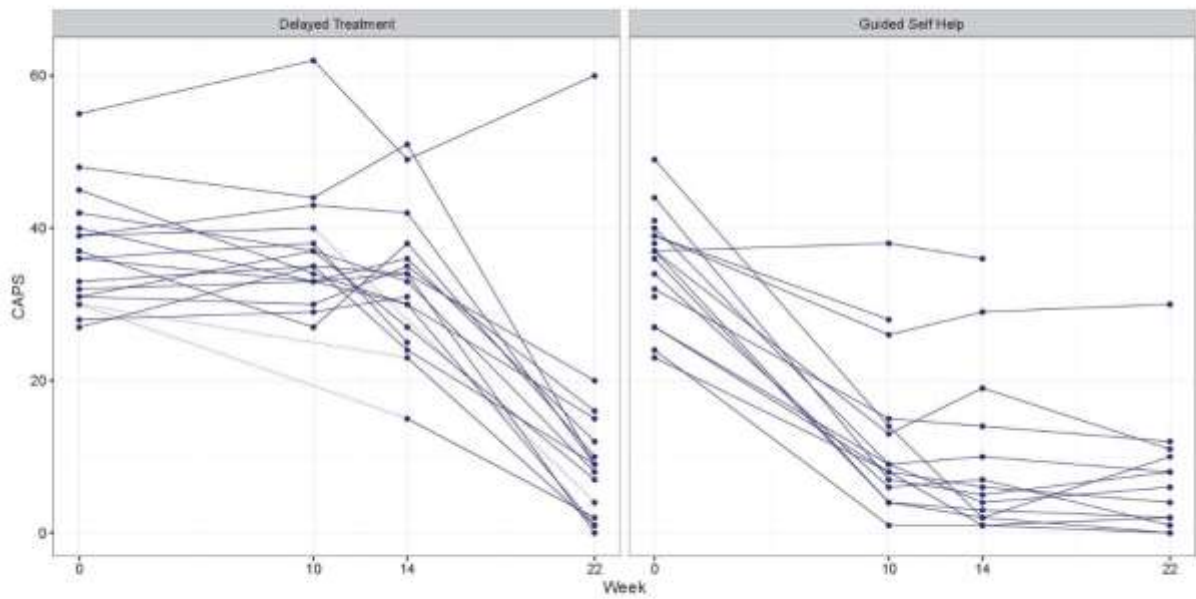


Figure 2: Observed CAPS scores at each assessment point for the guided self-help and delayed treatment group (grey lines indicate interpolation across a missing measurement) (editorial advice will be taken on the one Figure to include – three are included to aid peer review)

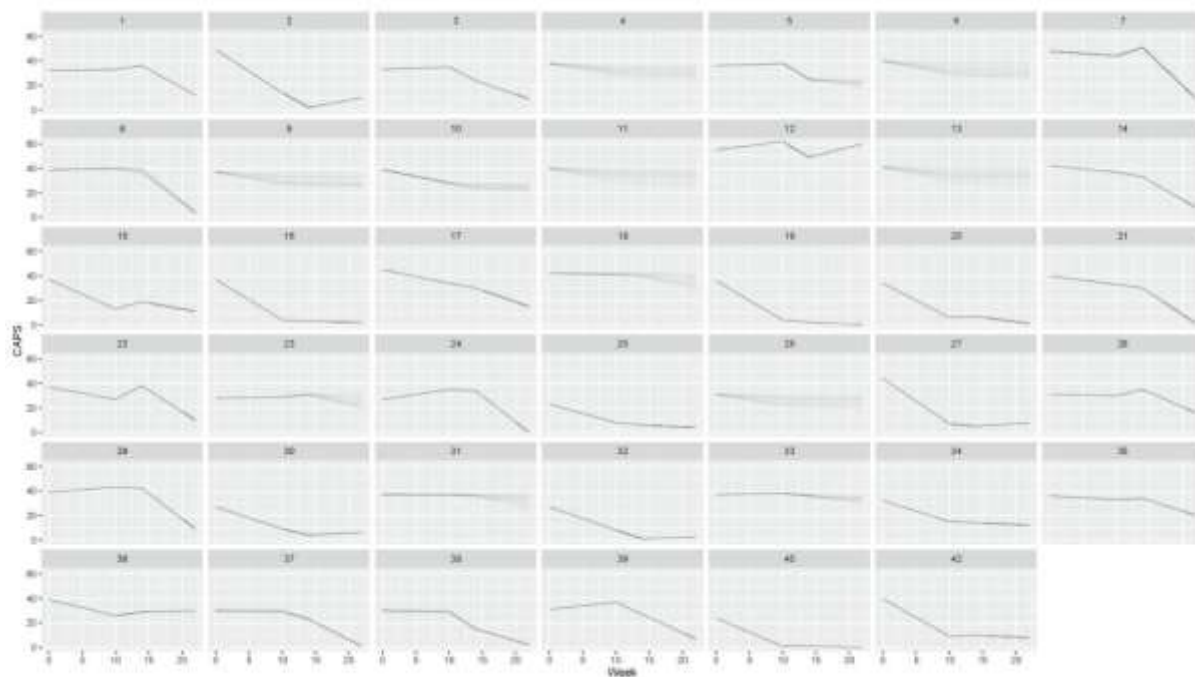


Figure 3: Findings of the multiple imputation method used compared to results using missing at random and last observation carried forward imputation methods (editorial advice will be taken on the one Figure to include – three are included to aid peer review)