Interventions for adults with a history of complex traumatic events: the INCiTE mixed-methods systematic review

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Scientific summary

The INCiTE study

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Scientific summary

Background

There is growing evidence that, in addition to post-traumatic stress disorder symptoms, exposure to prolonged and repetitive trauma of an interpersonal nature, such as childhood sexual abuse, is associated with mental health symptoms related to problems of emotional regulation, negative self-concept and interpersonal dysfunction. To better capture the symptom profile of people exposed to prolonged and multiple forms of trauma, a separate diagnosis of complex post-traumatic stress disorder has been proposed as part of the new *International Classification of Diseases*, Eleventh Edition.

Evidence-based treatments exist for single-event post-traumatic stress disorder and these include trauma-focused psychological interventions, which are recommended as first-line therapies, and also pharmacological therapies. However, it is not known if these therapeutic approaches are effective for people with a history of complex trauma or if they are safe and acceptable among this population. People with complex mixes of comorbidities may be excluded from clinical trials and they are further disadvantaged because their health needs are not well met by health services, such as Improving Access to Psychological Therapy services.

Complex trauma is increasingly prominent and relevant to the NHS, but existing mental health services are not well equipped to appropriately manage patients with complex traumatic histories. There is a need to identify candidate psychological and pharmacological treatments for this group with a view to informing practice and prioritising future research.

Objectives

The primary research question set by the Health Technology Assessment programme was the following: how effective are interventions that treat mental health problems associated with a history of complex traumatic events? The funding brief further elaborated on this research question by stating that the global objective was to undertake a broad evidence synthesis that builds on and extends previous reviews, reflective of the patient group seen in clinical practice, and to include pharmacological as well as non-pharmacological interventions. A key objective was to identify leading candidate interventions that the Health Technology Assessment programme could fund as part of a future round of primary research.

To achieve these objectives, we specifically aimed to:

- descriptively synthesise evidence from randomised and non-randomised controlled trials of psychological and/or pharmacological interventions for mental health in people with a history of complex traumatic events
- quantitatively assess, with meta-analysis if feasible, the clinical effectiveness of interventions delivered to adults, aged $\geq$ 18 years, with trauma and stressor disorders after exposure to complex traumatic events
- provide evaluations of the comparative clinical effectiveness of psychological interventions and pharmacological interventions using a network meta-analysis

- identify, appraise and synthesise qualitative and quantitative data that address service user and provider perspectives about the acceptability and feasibility of using psychological and/or pharmacological interventions to treat mental health problems after complex traumatic events
- identify leading candidate interventions that could be feasibly tested and used in the NHS and make recommendations to the Health Technology Assessment programme about future research priorities.

Methods

A mixed-methods systematic review was conducted that included eligible studies to address questions about the effectiveness and acceptability of psychological and/or pharmacological interventions for mental health problems in adults, aged ≥ 18 years, with a history of complex trauma. The methods for screening and data extraction and analysis followed guidance from the Cochrane Collaboration and the Centre for Reviews and Dissemination.

The quantitative and qualitative findings were presented at a stakeholder research prioritisation day attended by the research team, as well as by practitioners with an interest and experience in complex trauma, by voluntary and third-sector providers of services to people affected by complex trauma, and by experts through experience. Research priorities were co-produced during workshops and ranked following an online voting exercise, which was facilitated by the Beyond The Room (http://beyondtheroom.net/).

Data sources

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO*host* (1937 onwards; search date: 20 April 2017).
- Cochrane Central Register of Controlled Trials (CENTRAL) via The Cochrane Library (from inception; search date: 21 April 2017).
- EMBASE via Ovid (1974 to 2017 week 16; search date: 19 April 2017).
- International Pharmaceutical Abstracts via ProQuest (1970 onwards; search date: 30 August 2017).
- MEDLINE Epub Ahead of Print and In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE via Ovid (1946 to present; search date: 18 April 2017).
- Published International Literature On Traumatic Stress (PILOTS) via ProQuest (1987 onwards; search date: 2 May 2017).
- PsycINFO via Ovid (1806 to April week 2 2017; search date: 18 April 2017).
- Science Citation Index via Web of Science (1900 onwards; search date: 20 April 2017).

Two separate searches were run to capture eligible studies relevant to questions of effectiveness and acceptability of interventions.

Study selection

We identified the population of interest as adults, aged ≥ 18 years, exposed to deliberate and premeditated events, to a series of events that were extreme and prolonged or to events of a repetitive nature from which escape was difficult or impossible. Studies were included if they assessed treatment effectiveness and acceptability in this population. This approach approximated the definition of complex trauma used to describe complex post-traumatic stress disorder, although we did not use the newly defined *International Classification of Diseases*, Eleventh Edition, diagnostic category of complex post-traumatic stress disorder to search for eligible studies. Eligible studies for the effectiveness review needed to be randomised or non-randomised controlled trials and needed to measure post-traumatic stress disorder and/or mental health outcomes. Eligible studies for the qualitative acceptability review

needed to have used qualitative methods, such as in-depth interviews or focus groups. Studies that evaluated any first- or second-line psychological therapy that aimed to improve symptoms (including comorbidities) of trauma- and stressor-related disorders, delivered to either individuals or groups, were included. Complementary and alternative therapeutic interventions were excluded. All drug treatments subjected to experimental testing in the context of the treatment of mental health problems in people with a history of complex trauma were considered for inclusion.

Data extraction

Data were singly extracted by the review team using a prespecified data extraction Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA) spreadsheet that included domains for study and participant characteristics, outcomes and attrition. The risk of bias for randomised controlled trials was assessed using the Cochrane risk-of-bias tool. The risk of bias for non-randomised controlled intervention studies was assessed using a bespoke version of a quality appraisal checklist used by the National Institute for Health and Care Excellence in public health guidance, and based on the Graphical Appraisal Tool for Epidemiological studies.

Quality assessments of the qualitative data were undertaken using the Critical Appraisal Skills Programme checklist and the validity and relevance of the data to the questions were assessed using the GRADE-CERQual checklist.

Data synthesis

For the quantitative review of effectiveness, we undertook a series of meta-analyses that pooled results across all populations for each intervention category. Mean differences and 95% confidence intervals were computed for outcomes measured using the same scale. Standardised mean differences with 95% confidence intervals were computed for outcomes measured using different scales. We also evaluated the effectiveness of interventions with a meta-analysis across population subgroups. In addition to the meta-analyses, we explored if the treatment effects of interventions were moderated by population subgroup, intervention components and delivery methods (e.g. individual or group). We further explored whether or not certain components of composite interventions were more effective than each other using a component network meta-analysis.

For the qualitative review of acceptability of interventions, we undertook a narrative synthesis of qualitative data extracted from the included studies, mapping data to themes and subthemes related to acceptability and feasibility.

Results

In the effectiveness review, 104 studies were included. Of these, 95 were randomised controlled trials and nine were non-randomised controlled trials. The population subgroups that were included were veterans, childhood sexual abuse, war affected, refugees and domestic violence.

Effectiveness of psychological interventions across all populations

The pooled results across all populations with complex trauma showed that existing evidence-based psychological interventions were effective at reducing post-traumatic stress disorder symptoms when compared with the control post treatment (standardised mean difference –0.90, 95% confidence

interval −1.14 to −0.66; number of trials = 39), and there was some evidence that this finding held when treatment effects were measured up to 6 months post treatment. Trauma-focused cognitive–behavioural therapy and more broadly single-component and trauma-focused interventions were more effective than the control post treatment and at follow-up. Multicomponent and trauma-focused interventions for post-traumatic stress disorder symptoms post treatment were also effective, but the treatment effects were smaller than for single-component and trauma-focused interventions.

For the symptom cluster associated with complex post-traumatic stress disorder, we found no evidence that either trauma- or non-trauma-focused psychological interventions were superior in improving emotional dysregulation or interpersonal problems. Multicomponent and single-component trauma-focused interventions showed benefits for negative self-concept. Phase-based interventions that included stabilisation work before exposure therapy had positive effects on emotional dysregulation and interpersonal problems, although the results for these outcomes were of borderline significance.

Collectively, psychological interventions were superior to the control, but not the active control, post treatment and at follow-up for managing associated symptoms of depression in all populations with complex trauma (standardised mean difference −0.94, 95% confidence interval −1.20 to −0.68; number of trials = 22). The most consistent and the largest effects for depression across all time points were observed in trials that tested single-component and trauma-focused interventions. Similarly, pooled results showed that psychological interventions of any type were effective for reducing anxiety in all populations with complex trauma (standardised mean difference −0.81, 95% confidence interval −1.18 to −0.46; number of trials = 13). Trauma-focused approaches, when delivered as either a single-component or a multicomponent intervention, were superior to the control for anxiety symptoms when effects were pooled across all populations.

There were insufficient data to assess the effectiveness of psychological interventions for other secondary outcomes.

Effectiveness of psychological interventions across population subgroups

Among veterans, psychological interventions were effective for reducing post-traumatic stress disorder symptoms, but the size of the treatment effect was much smaller than in analyses that pooled results across all populations (standardised mean difference −0.48, 95% confidence interval −0.72 to 0.24; number of trials = 14). Trauma-focused cognitive–behavioural therapy and eye movement desensitisation and reprocessing therapy were the most efficacious treatments in this subgroup for post-traumatic stress disorder, but superior effects were observed when multicomponent and trauma-focused interventions were compared with the control. These two therapies were also effective for reducing depression and anxiety in veterans.

For people exposed to childhood sexual abuse, psychological interventions were effective for reducing post-traumatic stress disorder symptoms (standardised mean difference −0.90, 95% confidence interval −1.43 to −0.37; number of trials = 9). The largest effects for reducing depression in this subgroup were observed in the meta-analysis that compared multicomponent trauma-focused interventions with the control. There was no clear indication about which treatments were effective for reducing anxiety in people with a history of childhood sexual abuse.

Among war-affected populations, psychological interventions as a whole were effective at reducing symptoms of post-traumatic stress disorder (standardised mean difference −0.46, 95% confidence interval −0.68 to −0.25; number of trials = 8). Individual trauma-focused cognitive–behavioural therapy was the most effective intervention in this subgroup for post-traumatic stress disorder symptoms and for depression; there was insufficient evidence to draw firm conclusions about the effectiveness of interventions for anxiety symptoms among war-affected populations.

Large and positive effects in favour of psychological interventions for post-traumatic stress disorder symptoms were observed in refugee populations (standardised mean difference −1.84, 95% confidence interval −2.18 to −1.49; number of trials = 6). Trauma-focused cognitive–behavioural therapy and eye movement desensitisation and reprocessing therapy were the most effective interventions for both post-traumatic stress disorder and depression in this subgroup; meta-analyses that assessed the effectiveness of interventions for anxiety among refugees were not possible.

Only two trials were included in the meta-analyses of psychological interventions for people exposed to domestic violence. Trauma-focused cognitive–behavioural therapy was effective for reducing post-traumatic stress disorder and depression in this subgroup.

The meta-regression showed that psychological interventions were most effective for post-traumatic stress disorder symptoms in populations exposed to domestic violence and were least effective among veterans. The component network meta-analysis showed that cognitive restructuring, imaginal exposure and relaxation were effective components of trauma-focused cognitive–behavioural therapy. Mindfulness and phase-based interventions were also effective components of composite interventions for post-traumatic stress disorder symptoms.

Effectiveness of pharmacological interventions

All but one of the six trials that compared pharmacological interventions with placebo were conducted in veterans. Overall, only antipsychotic medicine was effective in reducing post-traumatic stress disorder symptoms in veterans (standardised mean difference −0.45, 95% confidence interval −0.85 to −0.05; number of trials = 5). No pharmacological intervention was effective for reducing symptoms of depression or psychosis in veterans. There was evidence from just two studies that prazosin had positive benefits for sleep quality among veterans.

Quality of evidence

The risk of bias across randomised controlled trials was difficult to ascertain for five of six domains of the Cochrane risk-of-bias tool, owing to inadequate reporting. Only a small proportion (20–30%) of randomised controlled trials were rated as being at low risk of bias for sequence generation, allocation concealment and blinding of outcome assessments, which were the primary indicators of study quality. Similarly, study quality was variable among the non-randomised controlled trials. There was a high risk of bias for outcome assessment, with only three of nine studies taking steps to blind investigators; domains related to allocation bias were poorly reported, leading to judgements that the internal validity of non-randomised trials was low or difficult to assess.

Acceptability of interventions

Eight qualitative studies were included in the acceptability synthesis. The acceptability of interventions was associated with how congruent they were with participants' therapeutic needs and social contexts, as well as the means by which they were able to provide participants with opportunities to engage in personal and interpersonal improvement and confer demonstrable improvements. The feasibility of interventions hinged on more instrumental features, such as scheduling and timing of treatment sessions.

Conclusions

Trauma-focused cognitive–behavioural therapy and other trauma-focused interventions, including eye movement desensitisation and reprocessing therapy, delivered as single-component or multicomponent approaches, are superior to the control for post-traumatic stress disorder symptoms and associated

mental disorder comorbidities. Positive effects were mainly found post treatment, with few studies showing benefit over the long term. The quality of the randomised controlled trial evidence was generally low or sufficiently unclear to be able to make fundamental recommendations about the effectiveness of interventions. We identified only a small subset of evidence from non-randomised controlled studies in which study quality was variable and internal validity was low. The sizes of the positive treatment effects were not evenly distributed across populations exposed to complex trauma, with the smallest effects observed among veterans and war-affected populations and the largest effects observed in those affected by domestic violence. Phase-based interventions, along with non-trauma-focused intervention components including mindfulness and relaxation, are potentially among the most effective approaches for post-traumatic stress disorder symptoms in people with a history of complex trauma, such as childhood sexual abuse. In addition, there is inconclusive evidence that existing trauma-focused interventions are effective in treating the symptom cluster associated with disturbances of self-organisation typically seen in complex post-traumatic stress disorder. There was little evidence of effectiveness of pharmacological interventions for post-traumatic stress disorder or for associated mental comorbidities.

Recommendations for research

Following the research prioritisation day and based on the synthesis of the effectiveness and acceptability reviews, we have identified the following priorities for future research:

- definitive and fully powered evaluations of effectiveness of interventions in complex trauma with long-term follow-up (i.e. at least 12 months), especially in veterans, people exposed to childhood sexual abuse and populations affected by humanitarian crises
- qualitative and quantitative process evaluations to assess the relationship between intervention and programme theory and anticipated outputs and trial results
- qualitative evaluations of the acceptability and feasibility of interventions among people exposed to complex interventions to inform barriers to and facilitators of treatment uptake, especially in refugees and asylum seekers
- evaluations of the lived experience of people with a history of complex trauma across population subgroups
- safety and adverse event profiles of trauma- and non-trauma-focused interventions for people with complex trauma
- a core outcome set for trials in complex trauma that includes outcomes related to disturbances of self-organisation and mental comorbidities
- the validity of the new *International Classification of Diseases*, Eleventh Edition, diagnostic category for complex post-traumatic stress disorder to identify and recruit eligible participants to experimental studies.

Study registration

This study is registered as PROSPERO CRD42017055523.

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HTA programme

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This report

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